SHARPENING OUR TOOL-KITS FOR VISUAL REHABILITATION

AN INVESTIGATION INTO THE DIAGNOSIS AND TREATMENT OF PATIENTS WITH HOMONYMOUS VISUAL FIELD DEFECT OR UNILATERAL NEGLECT

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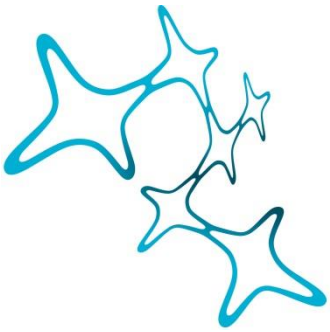

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Summary

The goal of the current dissertation is to provide a contribution to visual rehabilitation. In particular, we focus on the diagnosis and treatment of homonymous visual field defects (HVFDs) and unilateral neglect. In each of the three manuscripts, we address one issue that impedes the translation of neuroscientific outputs into the clinic.

Several treatment approaches aim to restitute visual functions within the HVFD. To test the efficacy of such treatments, it is necessary to measure the presence and change of residual visual functions (RVCs), for instance blindsight, with high precision. We use the term RVCs to refer to all types of visual functions that are present within the HVFD irrespective of the patient's awareness for it. However, issues with the methods used to examine RVCs have not always received the attention they deserve. These methodological issues complicate the interpretation of findings, undermine some of the theoretical claims, and hamper the development of more effective treatments for patients with visual disorders. The first two manuscripts in this dissertation address two of those methodological issues.

Firstly, we investigated the methodological problem of light-scatter artefacts. Light from targets directed towards the HVFD can scatter into the seeing part of the visual field. This might lead to correct responses that are misinterpreted as RVCs even though the information from the HVFD is not processed. In the first part of the manuscript, we presented a comprehensive literature review showing that light scatter is reinforced by increasing target luminance and size as well as by reducing distance to the HVFD-border and room illumination. The most reliable way to test light-scatter artefacts is the blind-spot method. Light-scatter artefacts are present if targets lead to above-chance performance even though they are located within the natural blind spot. Results in the literature showed above-chance detection, localization, and orientation discrimination on the basis of light scatter. However, the review also uncovered that not all recent studies with experimental setups likely producing light-scatter artefacts applied such laborious control tests.

Following this, we aimed to develop light-scatter-free paradigms for RVC-research. Initially, we showed that our experimental setup is sensitive enough to detect light-scatter artefacts. Presenting white targets on a black background in a dark room led to above-chance detection (temporal 2AFC task) even if targets were located within the natural blind spot (N = 19). Such light-scatter artefacts were not present in the other paradigms tested in an illuminated room. Hence, we provided the following light-scatter-free paradigms: Temporal 2AFC with (1) white or (2) black targets on a grey background; (3) movement direction discrimination of black targets on a grey background; and (4) a redundant target paradigm (RTP) with black targets on a grey background.

Secondly, we addressed the issue of unclear diagnostic quality of RVC-tests. For this, we focused on one commonly used RVC-test: the RTP. The RTP is based on the redundant target effect (RTE) meaning reduced reaction times in response to two redundant targets compared to reaction times in response to a single target. To test RVCs in HVFD-patients, one target is presented in the blind visual field, the other in the sighted visual field. If reaction times are still reduced, RVCs should be present. We selected the RTP because of its indirect approach to testing RVCs. This indirectness allows us to avoid the problem of biased response criteria. Other advantages of the RTP are for instance the simplicity of the task and its instructions.

In the first part of the manuscript, we conducted a meta-analysis on the RTE in healthy participants. Analysis showed that experimental features used in RVC-research lead to a positive summary effect size on group level. Following this, we evaluated the diagnostic quality of the RTP based on a comprehensive literature review as well as based on our own empirical data. In detail, we measured a small sample of HVFD-patients at two points in time (N = 11) and a large group of healthy controls (N = 53). We estimated three diagnostic values in the context of RVCs. (1) The sensitivity indicates how good the RTP detects the presence of visual functions. Resulting values ranged between 18.18%-77.27% even if visual functions were present at the target locations in 100% of participants. (2) The specificity indicates how good the RTP detects the absence of visual functions. To estimate the specificity, we relied on data of the light-scatter manuscript. 10.53% of participants showed a significant RTE even if visual functions were absent within the natural blind spot. Thus, the RTP correctly indicated the absence of visual functions in 89.47% of cases. (3) The reliability indicates how good results correspond between test sessions if visual functions are constant. Regarding single-case analysis in the control group, 32.08% of healthy participants showed inconsistent results between redundant target conditions. Comparing results between test sessions in patients and between conditions in the control group showed low intra-class-correlations. Taken together, correspondence of RTP-results was poor.

Thus, we can conclude that the RTP has a reasonable specificity but poor sensitivity and poor reliability. This means that the presence of a RTE likely indicates the presence of RVCs, but its absence does not preclude the existence of RVCs. The first two manuscripts aimed to improve the methods that we can use to assess visual functions in patients with HVFDs. For the study that formed the basis of the third and last manuscript, the topic was still visual rehabilitation, but the focus shifted from assessment to treatment and from HVFDs to unilateral neglect.

In unilateral neglect, insight into the disorder is often lacking. We therefore focused on training approaches based on implicit learning of behavioral patterns. Current treatments, for instance prism adaptation, mainly influence the orientation bias in neglect. However, these treatments are not yet as successful as hoped for, especially regarding long-term effects or the generalization to activities of daily living. Hence, we proposed a new, gaze-contingent intervention that is similarly based on implicit learning but focuses on another major symptom of neglect: Disturbances in attentional allocation. Inspired by the premotor theory of attention (Craighero & Rizzolatti, 2005; Rizzolatti et al., 1987), we argue that a shift of eye movement patterns induces a shift in attentional allocation. Shifting the attentional allocation towards the neglected side could reduce symptoms in neglect patients.

The gaze-contingent intervention is based on a visual search task in which targets within the preferred, i.e. ipsilesional, side vanish as soon as eye movements reach this side of the screen. Thus, eye movements towards the preferred side are punished. In consequence, patients should restrain from exploring the preferred side and rather explore the neglected, i.e. contralesional, side.

We tested the gaze-contingent intervention in five experiments in healthy participants. During the intervention, eye movements shifted towards the non-punished side in all experiments. Importantly, awareness for the shift in eye-movements was not necessary for the intervention effect. Furthermore, the intervention effect generalized to two visual search tasks and persisted in the second half of both tasks. However, the intervention effect was not present in both experiments measuring a Posner paradigm with exogenous cues. Furthermore, the intervention did not influence behavior in a line-bisection task. Thus, it seems that the intervention effect is limited to overt attentional allocation. As the intervention effect did not require that observers were aware of the behavioral change, we hope for a high effectiveness in neglect patients.

In summary, the findings from this dissertation might help to improve the assessment and treatment of neurological patients suffering from visual deficits

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Abbreviations

ADL: Activities of daily living

CCT: Cerebral computer tomography

CI: Confidence interval

CVS: Caloric vestibular stimulation

EWB: Endpoint weighting bias

EWS: Endpoint weighting sum

(f)MRI: (Functional) magnetic resonance imaging

GVS: Galvanic vestibular stimulation

HIV: Human immunodeficiency virus

HVFD: Homonymous visual field defect

ICC: Intra-class correlation

IOP: Intra-ocular pressure

LGN: Lateral geniculate nucleus

M: Mean

MCC: Minimal configuration criterion

MDD: Movement direction discrimination

NMV: Neck muscle vibration

OKS: Optokinetic stimulation

PA: Prism adaptation

PGL: Pre-geniculate lesions

PI: Prediction interval

PTA: Premotor theory of attention

RG: Redundancy gain

RTE: Redundant target effect

RTP: Redundant target paradigm

RVC: Residual visual capacity

SC: Superior colliculi

SD: Standard deviation

SE: Standard error

SWM: Spatial working memory

TRD: Trans-synaptic retrograde degeneration

T-R (in)compatibility: Target-response (in)compatibility

VET: Visual exploration training

VRT: Visual restitution training

VST: Visual sensitivity training

V1: Primary visual cortex

2AFC: Two alternative forced choice

1. General Introduction

The current dissertation aims to provide a contribution to visual rehabilitation. Visual rehabilitation has for many years been at the center of attempts to introduce novel diagnostic procedures and evidence-based therapeutic approaches into the field of neurorehabilitation. Visual rehabilitation has benefited from the fact that almost every neuroscientific research technique was pioneered in the visual domain. As a consequence, we know more about the neuroscientific foundations of vision (both in its normal and pathological form) than we know about most other cognitive domains. Two disorders that have particularly benefitted from this intense research activity are homonymous visual field defects (HVFDs) and unilateral neglect. In both cases, neuroscientific research led to important discoveries which in turn led to new developments in the diagnosis and treatment of both disorders. HVFDs and neglect can therefore serve as key examples for the potential but also the difficulties that accompany the translation of neuroscientific findings into clinical praxis. In this dissertation we focused on three issues that have hampered the process of this translation process.

Regarding HVFDs, we addressed two methodological issues relevant for research and rehabilitation: Light-scatter artefacts and unclear diagnostic quality of visual tests. Regarding neglect, we proposed a new intervention that aims to avoid shortcomings of current treatments.

In the first manuscript, we investigated light-scatter artefacts in testing residual visual capacities (RVCs) within the HVFD of patients, for example blindsight (Weiskrantz et al., 1974). The term light-scatter artefact describes the phenomenon that light from targets directed towards the HVFD can stray into the sighted visual field increasing performance artificially (Campion et al., 1983). After reviewing the literature, we tested light-scatter artefacts in three frequently used RVC-paradigms in healthy participants. Our objective was to provide stimuli and procedures that avoid light-scatter artefacts. We hope that the availability of such paradigms will help to ensure that light-scatter-safe procedures will be employed more frequently in future research on RVCs.

In the second manuscript, we estimated the diagnostic quality of the redundant target paradigm (RTP) which has been widely used in RVC-research in HFVD-patients. The RTP is based on the redundant target effect (RTE) which describes reduced reaction times in response to two targets as compared to a single target (Raab, 1962). RVC is assumed to be present if the second, redundant target within the HVFD leads to reduced reaction times (Marzi et al., 1986). First, we calculated a meta-analysis to estimate the average size of the RTE in healthy participants. Next, we reviewed the literature to see how the RTP has been applied in RVC-research. On the basis of the literature review and on the basis of our own empirical data in healthy participants and in HVFD-patients, we estimated the reliability,

sensitivity, and specificity of the RTP. Furthermore, we evaluated whether the RTP could be used as test to determine whether the minimal configuration criterion (MCC) of RVCs is satisfied or put differently, if a positive outcome of the RTP can be seen as a necessary, albeit not sufficient, condition for the existence of RVC in any other visual task.

In the third manuscript, we presented a new intervention for neglect patients that should overcome several weaknesses of previous treatments. Past research presented trainings that were aversive (e.g. caloric vestibular stimulation; Been et al., 2007) or relied on the awareness of patients (e.g. compensatory trainings; Kerkhoff & Schenk, 2012), just to name some of the issues. In contrast, we created a new training task based on implicit learning of new gaze behavior. For this, we used a so-called gaze-contingent intervention to the treatment of neglect patients. When talking about the different hemispaces in the context of unilateral neglect, it can become quickly quite confusing. To avoid such confusion, we will use consistently the following terms: we will use the term *neglected side* to refer to the contralesional hemi-space and the term *preferred side* to refer to the ipsilesional hemi-space in the remainder of this dissertation. This intervention is intended to work as follows. Patients look for a tilted line (target) among vertical lines (distractors). Lines within the preferred side are removed each time patients make eye movements towards it. Lines in the neglected side are unaffected. Ideally, this gaze-contingent manipulation reduces the visual exploration of the preferred side and instead encourages the exploration of the neglected side. In this way the intervention should create a lateral imbalance that runs counter the existing neglect bias and might thus reduce neglect symptoms in daily life. We tested the effect of this training in five experiments on healthy participants as the initial step leading to the application in neglect patients.

1.1. HVFDs versus neglect: Similarities and differences

HVFDs occur after a post-chiasmatic lesion of the visual system (Zihl, 2010; Zihl & Kennard, 2003). The most frequent etiology are ischemic or hemorrhagic strokes which cause 69.7% of HVFDs (Zhang et al., 2006). As strokes are the most frequent cause of focal damage to the brain, HVFDs are a prevalent disorder. The ophthalmologic diagnosis of a HVFD is based on the results of a perimetry which measures the visual field. The extent of the HVFD depends on lesion size as well as location and can therefore vary considerably between patients: A hemianopia affects one hemifield, a quadrantanopia affects one quadrant, and a scotoma is a single defective area (Zihl & Kennard, 2003). Patients suffering from HVFD experience substantial impairments in activities of daily living (ADL), for instance regarding orientation, shopping, driving, and reading (de Haan, Heutink, et al., 2015). Spontaneous recovery of the HVFD is usually limited and happens only in about 10-20% of patients within the first months after the lesion (for a review see Zihl, 2010). Additionally, spontaneous

compensation by eye movements is insufficient. Patients exhibit a laborious visual exploration with a disorganized scanpath, a high number of fixations, making small, hypometric saccades towards the blind field (e.g. Pambakian et al., 2000; Zihl, 1995). To summarize, HVFDs are a common visual disorder that requires effective treatment.

Neglect '*designates a consistent, exaggerated spatial asymmetry in processing information in bodily and/or extrabodily space due to an acquired cerebral lesion'* (p. 320; Cubelli, 2017). In general, the center of exploratory behavior is shifted towards the ipsilesional, i.e. preferred, side (Karnath et al., 1998). In line with this, patients show reduced responses to contralesional targets, i.e. targets within the neglected side (Kerkhoff, 2001). This shift is also present in visual exploration, for instance Sprenger et al. (2002) showed hypometric saccades towards the neglected side and repeated fixations within the preferred side. Interestingly, the bias in fixations was stronger in more severe cases of neglect (Walle et al., 2019). Neglect usually occurs after brain damage to the right hemisphere (Cubelli, 2017), for instance after stroke. The incidence of neglect after right-hemisphere stroke varies from 13-82% (Bowen et al., 1999). The considerable range in incidence values comes mostly from methodological differences in neglect testing (Bowen et al., 1999). This variability can further be explained by the various types of neglect. Buxbaum et al. (2004) tested 166 rehabilitation inpatients and observed 1% personal neglect, 27% peripersonal neglect, 27% motor neglect, and 21% perceptual neglect. Moreover, neglect can manifest in different modalities, mostly in the visual, auditory, and tactile domain (for a review see Brozzoli et al., 2006). An additional factor for the incidence is the time since lesion onset. In the first 10 days, spontaneous recovery is pronounced, reaching a plateau at three months after the onset (Stone et al., 1992). Fortunately, a number of patients experiences full spontaneous recovery (Stone et al., 1992). However, some patients are still affected in the chronic stage showing symptoms more than one year after onset (Karnath et al., 2011). In daily life, patients are impaired, for example, regarding self-care, orientation, walking, and driving (for a review see Bosma et al., 2020). It is worth noting that the presence of neglect is associated with poorer outcome after stroke (Buxbaum et al., 2004). Consequently, neglect patients are in need of an effective treatment.

We have seen that HVFDs and neglect are two distinct disorders with differing disease mechanisms. Interestingly, HVFDs and neglect can occur simultaneously in one patient. A posterior parietal lesion relevant for neglect might also affect the neighboring fibers of the optic radiation leading to a HVFD (Karnath, 2001). But even if only one disease is present, HVFDs and neglect are frequently confused. Both, HVFD- and neglect patients omit targets within the impaired side. In neglect, perimetry results can thus look similar to HVFDs. This issue has been nicely illustrated in a case study by Walker et al. (1991). In perimetry, the neglect patient showed a HVFD but only when the target and the fixation symbol were

presented simultaneously. In another version of the perimetry, the fixation symbol extinguished shortly before target onset. Herein, the patient was able to respond to targets on the neglected side (Walker et al., 1991). This study illustrates that manipulations of task design can lead to differential effects in HVFDs and neglect (e.g. Müller-Oehring et al., 2003).

Regarding visual search, similar abnormalities in oculomotor exploration behavior can occur for HVFD- and neglect patients. In both cases, patients show hypometric saccades towards the impaired hemifield (Pambakian et al., 2000; Sprenger et al., 2002) as well as overall more fixations (Pambakian et al., 2000; Walle et al., 2019). Some studies compared visual search behavior between clinical groups directly. Gainotti et al. (2009) investigated neglect patients with or without HVFD. Results showed that the presence of distractors reinforced saccades towards the preferred side. In neglect patients with HVFD, this effect was more pronounced than in the neglect-only-group (Gainotti et al., 2009). Another prominent feature of neglect is a shift in the horizontal distribution of fixations (Karnath et al., 1998). This fixation pattern is also present in free-viewing of images of natural scenes (Fellrath & Ptak, 2015). Moreover, Fellrath and Ptak (2015) showed a similar but less pronounced horizontal shift of fixations in neglect patients with HVFD but not in the HVFD-only-group. Regarding the saliency of images, HVFD-patients did not differ from controls. In contrast, neglect patients with or without HVFD looked to areas with high saliency, local orientation, and intensity threshold on the neglected side (Fellrath & Ptak, 2015). In summary, shifts in the eye movement pattern are stronger in neglect patients than in HVFD-patients.

It is worth noting that spontaneous recovery and compensation have a different time course in HVFDs and neglect. HVFD-patients look more on the hemianopic side to compensate for their visual field defect (Ishiai et al., 1987). However, if neglect is present as well, such compensatory eye-movements are largely absent in visual exploration (Ishiai et al., 1987). Saj et al. (2012) compared patients with neglect and/ or hemianopia in four tasks at two points in time. In the subjective straight-ahead test, the presence of HVFDs *and* neglect led to the strongest deviation in the first session. In the second session, a few weeks later, the additive effect of HVFDs vanished leaving neglect as the crucial factor for a deviation. The same pattern was observed for the three clinical tests. Authors suggested that in the initial period after the lesion, HVFDs induce an ipsilesional bias, similar but smaller than in neglect. Via spontaneous, compensatory adaptation, this bias is reversed in the chronic stage of HVFDs. In neglect, such spontaneous behavioral compensation does not happen, leaving the patients with a strong ipsilesional bias (Saj et al., 2012). This is in line with other studies demonstrating a contralesional shift in chronic HVFDs (e.g. Lewald et al., 2009; Zihl et al., 2009). In summary, results suggest that in a given patient the strong neglect shift towards the

ipsilesional side might override the small contralesional HVFD-shift. Hence, neglect is the determining factor for the persistent bias in exploration behavior.

To conclude, symptoms of HVFDs and neglect can be similar in daily life, perimetry, and visual exploration. In general, HVFDs and neglect differ in the time course and extent of spontaneous recovery and compensation. In both diseases, there is an initial bias towards the ipsilesional side. But only in HVFDs, compensational adaptation reverses this bias in the chronic stage. If a patient shows both, a HVFD and neglect, neglect symptoms are prominent. Furthermore, manipulating certain aspects of tasks leads to differential effects.

Given the similarities between and the co-occurrence of HVFDs and neglect, it is not surprising that certain rehabilitation strategies were tested in both clinical samples. One approach aims to compensate for the visual deficit by improving visual exploration. Poppelreuter (1917) started visual search training in HVFDs. Later, this approach was adopted for neglect patients (Diller & Weinberg, 1977). Some training paradigms have been applied to both disorders (Kerkhoff et al., 1992; Szalados et al., 2021). Training tasks vary tremendously. In some trainings, patients were taught specific scanning strategies, for instance to scan the search display horizontally row by row (Kerkhoff et al., 1992). In other trainings, patients have to follow a ball from one side of the screen to the other (Szalados et al., 2021). However, in both disorders, there is yet no convincing evidence for long-term effects of visual exploration training (VET) and for its generalization to ADL.

Early neglect studies showed promising effects of VET. This led to a recommendation of VET as a practice standard for neglect after right-hemisphere stroke (Cicerone et al., 2000; Cicerone et al., 2019). However, the evidence is not as clear. The effects of VET in neglect were highly specific improving reading and visual search but not tactile search (Schindler et al., 2002). In another study, VET did not improve performance in neglect tests nor in reading and writing (Schröder et al., 2008). Interestingly, in both studies patient groups receiving VET combined with some other training factor showed more generalized training effects (e.g. neck muscle vibration in Schindler et al., 2002; optokinetic stimulation in Schröder et al., 2008). In a meta-analysis about neglect, the short- and long-term effects of VET were compared to other interventions. There were no differences between training types neither in standardized assessment of neglect nor in ADL (Bowen et al., 2013). Overall, there is still a lack of evidence in neglect-research for the generalization of VET-effects on ADL (Bowen et al., 2013; Cicerone et al., 2019).

The same problem is present in HVFDs. The generalization of training effects to other tasks is inconsistent. For instance, VET did improve reading abilities in Aimola et al. (2014) but not in Schuett et al. (2012). VET enhanced obstacle avoidance during walking (de Haan, Melis-Dankers, et al., 2015). In Ong et al. (2015), patients reported improvements in an

ADL-questionnaire in three of six scales. However, self-reported improvements might not correlate with behavioral outcome in ADL. Patients in Aimola et al. (2014) reported improvements in several domains. However, there were no improvements in tasks simulating ADL (Aimola et al., 2014). Hence, it is unclear to which degree VET effects generalize to ADL. It is worth noting that even after VET, performance in HVFD-patients did not reach the level of healthy controls (de Haan, Melis-Dankers, et al., 2015; Jacquin-Courtois et al., 2013; Nelles et al., 2001). Furthermore, there is a lack of studies investigating long-term effects of VET in HVFD-patients (Hanna et al., 2017). Several studies compared VET against other training types (for a review see Howard & Rowe, 2018). Some studies showed VET-effects to be superior compared to other trainings. Roth et al. (2009) showed that only VET but not flicker-stimulation training improved visual search. In Rowe et al. (2017), exploration training improved the subjective rating of ADL more than prism glasses or standard care. Results of Aimola et al. (2014) indicated that improvements after VET were significantly stronger than after an attention training. In contrast, Lane et al. (2010) showed that VET was not superior than attention training in improving visual search performance. A VET using audio-visual targets had greater effects on visual search, reading, and ADL than VRT (Keller & Lefin-Rank, 2010). Following this, VET seems to be superior in comparison to other training tasks and might be enhanced by audio-visual targets. Treatment studies found that the efficacy of VET is different for patients with HVFD as compared to neglect patients. Kerkhoff et al. (1992) showed that HVFD-patients improved significantly more than neglect patients. This finding has been confirmed in a recent study. Szalados et al. (2021) showed that their training improved search times in the HVFD-only-group as well as in the HVFD-and-neglect-group but not in the neglect-only-group.

To sum up, VET showed improvements in neglect and even stronger effects in HVFDs. Still, it is unclear if VET reliably leads to long-term effects and if effects generalize to ADL. Furthermore, in neglect-research there is yet no convincing evidence that VET is superior to other training types.

There is an important reason that could be responsible for weak or inconsistent effects of VET: Anosognosia, meaning the *"lack of awareness of having a disorder or disability"* (page 385; Mograbi & Morris, 2018). The positive outcome of compensatory trainings relies on the awareness of the deficit and on the commitment by the patient (Kerkhoff & Schenk, 2012). However, awareness for deficits after stroke is often lacking thus hindering rehabilitation and leading to a poorer prognosis (for a review see Jenkinson et al., 2011). As chronic anosognosia is associated with persistent neglect symptoms (Jenkinson et al., 2011), clinicians cannot assume awareness during rehabilitation. Similarly, awareness cannot be expected in HVFD-patients. Rowe et al. (2013) investigated a total of 479 patients with visual field loss in a multi-center study showing that 16% did not complain about this symptom.

In conclusion, compensatory trainings are cognitively demanding and the outcome is not as successful as hoped for. Other rehabilitation approaches are less strategy-based. They focus on implicit learning of behavioral patterns. Ideally, awareness and active application of instructions are not necessary. Rather, perceptual functions are made available for ADL. In the next sections, we will describe current implicit approaches in the rehabilitation of HVFDs and neglect. Furthermore, we will point towards methodological problems and how we addressed some of these issues in our studies.

1.2. Current visual rehabilitation of HVFDs

Regarding HVFDs, training approaches based on implicit learning occurred after findings of RVCs within the HFVD. If some visual functions were still present, it seemed possible to restore the visual field with training (Zihl & von Cramon, 1979). Patients themselves usually describe their visual experience within the HVFD as '*blind'*. In contrast, some patients perform above-chance in response to target presented within the HVFD. Weiskrantz et al. (1974) termed this phenomenon blindsight. Decades before, there were the first descriptions about RVCs in soldiers of World War I (Holmes, 1918; Riddoch, 1917). But only in the 1970s, strong interest in RVCs arose due to studies in monkeys. As an example, monkeys with bilateral ablation of the striate cortex could be retrained to discriminate area, brightness, shape, and color (Pasik & Pasik, 1971). Thorough investigations in human HVFD-patients followed (e.g. Pöppel et al., 1973). From the case study of patient DB, Weiskrantz et al. (1974) derived a dissociation between '*acknowledged awareness*' (page 720) and visual performance. On this basis, researchers aimed to discover the neuronal correlate of visual consciousness. If consciousness is affected without disrupting visual performance, the lesion has to affect the brain area specifically responsible for consciousness (Weiskrantz, 1999).

Nonetheless, descriptions of visual perceptions within the HVFD by patients were inconsistent with this dissociation. Patients reported visual stimuli within their HVFD as '*dark shadows*' (Barbur et al., 1980) or as '*pin-prick'* and '*a prickling*' (Richards, 1973). Even the first blindsight-patient *DB* described the target X as '*jagged'* and the target O as '*smooth'* when urged to report his perception (Weiskrantz et al., 1974). However, it is unclear how visual consciousness should be measured best (Overgaard, 2011). What is clear is that the awareness scale is crucial. When patient *SL* responded on a dichotomous scale (*'seen'* versus *'guessed'*) the pattern of results fitted to the original definition of blindsight (Mazzi et al., 2016). On the contrary, when patient *SL* responded on a four-level scale, performance was above-chance only when patient *SL* perceived at least a '*brief glimpse*' of the target (Mazzi et al., 2016). In a subsequent study, awareness ratings of patients were related to findings in electroencephalography (Mazzi et al., 2018). As there is no agreement yet on how to measure and classify awareness for targets within the HVFD of patients, it is reasonable to

use a broader term. In the current dissertation, we will use the term residual visual capacities (RVCs) to encompass all variants of visual awareness.

From the perspective of a clinician, the awareness-problem is only of secondary importance. The most important point is that patients with HVFDs perform above chance in response to targets presented within the blind field. This discovery together with reports about spontaneous recovery in HVFD-patients led to studies that aimed to restore visual functions (Zihl & von Cramon, 1979). In the time course of spontaneous recovery, light sensation reappeared first (Poppelreuter, 1917; Riddoch, 1917). Consequently, Zihl and von Cramon (1979) focused on the stimulation of the blind field with light targets to extend the sighted field. These early attempts of visual restitution training (VRT) were very promising (e.g. Kasten et al., 1998; Zihl & von Cramon, 1985). Later, researchers applying more rigorous methods could not replicate VRT-effects (Reinhard et al., 2005). In brief, there is yet no compelling evidence that stimulation with light targets significantly enlarges the sighted field in HVFD-patients (for a review see Pollock et al., 2011).

A second line of restoration trainings aimed to improve responsiveness for certain stimuli within the blind visual field. In the first place, the goal was to increase the sensitivity for specific target features like motion. Hence, we will use the term visual sensitivity training (VST) to refer to this type of treatment. VST was based on frequent reports of RVCs for motion perception (e.g. Riddoch, 1917; Weiskrantz et al., 1974). Starting with promising results in cats (Huxlin, 2004; Rudolph & Pasternak, 1996), a training to discriminate motion direction was also successful in human HVFD-patients (Huxlin et al., 2009). Subsequent studies from this research group replicated the findings and characterized the regained motion perception (e.g. Cavanaugh et al., 2017). Importantly, the effectiveness of this VST was confirmed by other researchers conducting motion discrimination training (e.g. Vaina et al., 2014). Motion was not the only target feature of interest. Sahraie et al. (2006) successfully trained patients to detect gratings reducing the contrast over the course of the intervention. Although not originally aimed for, VST also enlarges the sighted visual field (Ajina et al., 2021; Cavanaugh & Huxlin, 2017). Interestingly, changed sensitivity through VST was recently confirmed by fMRI analysis (Ajina et al., 2021). Furthermore, effects of VST were superior to spontaneous recovery (Saionz et al., 2020). However, to our knowledge, none of the studies included a follow-up measurement nor questionnaires or tasks about ADL. Hence, it is unclear how long training effects persist after the end of the intervention and if they generalize to ADL.

To summarize, restoring visual functions is a promising approach for rehabilitation of HVFD-patients. Still, methodological problems cast doubt on some of the findings on RVCs and on restoration trainings. In the following discussion, I will focus on four methodological

problems that have to be addressed in HVFD-research: Insufficient eye movement control, light-scatter artefacts, biased response criteria, and low diagnostic quality.

Firstly, artefacts due to insufficient eye-movement control have been made responsible for some of the RVC-findings and training effects (Campion et al., 1983; Reinhard et al., 2005). In RVC-tasks and in restoration trainings (VRT and VST), it is necessary to reassure that targets are presented at specific positions within the blind visual field. Thus, paradigms usually require fixation. If patients move their eyes nevertheless, target positions shift within the visual field even reaching the sighted part. High performance could hence be based on visual capacities of the sighted visual field. Following this, fixation quality is highly important. Still, eye movements have not been controlled adequately in a number of studies. Controlling eye movements manually by experimenters is one method that has been frequently used (e.g. Ross et al., 2018; Zihl & von Cramon, 1979). However, only few studies described the quality of fixation control by experimenters (e.g. Schärli et al., 1999; Wüst et al., 2002). The quality of the method was the research topic of Hooge et al. (2018, 2021). Authors showed that experimenters had considerable inter- and intra-rater variability (Hooge et al., 2018, 2021). Other studies used eye-tracking devices but did not describe criteria for fixation breaks (e.g. Bertini et al., 2019). In both cases, it is unclear to what extend targets could be shifted within the visual field. In short, multiple studies used insufficient control of fixation behavior.

The issue of fixation control is especially crucial in VRT that presents targets at the border zone between blind and sighted visual field (Marshall et al., 2010; Zihl & von Cramon, 1979). Herein, small shifts in fixation are enough to bring targets towards the sighted visual field. Reinhard et al. (2005) could not find effects of VRT with precise fixation control. Marshall et al. (2010) using another, but similarly precise, eye-tracking device found a visual field enlargement. Although results for VRT were inconsistent, these studies further highlight the relevence of thoroughly monitoring fixation behavior in RVC-research and in clincal studies. Importantly, eye-tracking devices with high temporal and spatial resolution and automated eye-movement analysis are available and already used in HVFD-research (e.g. Portengen et al., 2021; Reinhard et al., 2005). We will use precise eye-tracking devices and suitable analysis of gaze behavior in all experiments of the three manuscripts.

A second issue is light-scatter artefacts casting doubt on effects of restoration training and on RVC-results. Light that is emitted by targets presented within the HVFD scatters and can reach retinal areas corresponding to the sighted visual field (Campion et al., 1983). Campion et al. (1983) used the blind spot in healthy participants to investigate light scatter. As humans are physiologically blind within this area of the visual field, targets cannot be directly processed (Jonas et al., 1991). Any above-chance performance must hence be attributed to

extra- or intra-ocular sources of light scatter. In a blind-spot experiment with healthy participants, visual information from light scatter was sufficient for target localization and discrimination of target orientation (Campion et al., 1983). Target localization on the basis of light scatter was also possible in a HVFD-patient (Danckert & Culham, 2010). These examples illustrate that it is necessary to differentiate between light-scatter artefacts and true RVCs.

Light scatter gets stronger, the brighter a target is and the closer targets are located at the border to the sighted visual field (Barbur et al., 1994; Campion et al., 1983). Hence, VRT applying border zone stimulation with light targets are especially prone to light scatter. During training, patients could learn to utilize light scatter rather than improve visual functions. Still, a number of studies did not control for light-scatter artefacts in recent restoration training studies (e.g. Bergsma & van der Wildt, 2010; Larcombe et al., 2018). Possible reasons for this methodological weakness are that light-scatter testing is time-consuming, laborious, and not easily transferrable from one experimental setup to another. Hence, light scatter is an ongoing issue in RVC-testing and in the evaluation of restoration trainings. As a consequence, we addressed this issue in the current dissertation.

Thirdly, biased response criteria are a problem when patients classify their perception (Cowey, 2010). Responding on a scale, for instance '*yes*' versus '*no*', patients make implicit boundaries between response levels. Having the same percept, a patient with a liberal criterion responds '*yes*', whereas a patient with a conservative criterion responds '*no*' (Cowey, 2010). These criteria vary depending on scales and on experimental paradigms. This has been illustrated, for instance, by Stoerig et al. (1985). The detection rate changed depending on the ratio of target trials and blank trials (Stoerig et al., 1985). Similarly, performance of patient *GY* could be explained by differences in response criteria depending on target type and paradigm (Azzopardi & Cowey, 1998). Another example, already mentioned above, is patient *SL* whose response criteria got obvious when comparing responses between the two-level and four-level scale (Mazzi et al., 2016). The issue of biased response criteria is relevant not only in RVC-tests but also in VRT using simple detection paradigms (e.g. Zihl & von Cramon, 1979). During training, patients might change the response criteria to be more liberal resulting in increased detection rates. In this case, the visual perception itself might be unmodified (Cowey, 2010).

Following this, it is necessary to use paradigms in which response criteria are not or less decisive. In Azzopardi and Cowey (1998), the bias in response criteria was considerably weaker in the forced-choice task than in the '*yes'* versus '*no'* task. Hence, forced-choice tasks should be preferred against dichotomous scales (Cowey, 2010). Furthermore, response biases are abolished in indirect measurements of RVCs. Such paradigms have

been applied in studying affective blindsight, i.e. RVCs for emotional stimuli (for a review see Celeghin, de Gelder, et al., 2015). For instance, Bertini et al. (2019) showed reduced response times to Gabor patches within the sighted visual field if fearful faces were simultaneously presented within the blind visual field. Another, frequently used indirect RVC-test is the RTP (Raab, 1962). Herein, RVC should be present if reaction times are reduced by targets within the HVFD (Marzi et al., 1986). To conclude, the problem of biased response criteria can be avoided using adequate experimental paradigms.

The intention to avoid biased response criteria and the simplicity of the RTP convinced us to focus our study on this task. However, the diagnostic quality of the RTP is unknown. This issue applies to a number of RVC-tests which led us to formulate the forth methodological problem of RVC-research: The diagnostic quality of RVC-tests is usually not evaluated. This means that it is unclear how good a test can differentiate between a HVFD-patient with or without RVCs. Several values are of interest. The sensitivity indicates how good a test detects the presence of RVCs (Lalkhen & McCluskey, 2008). The specificity indicates how good a test detects the absence of RVCs (Lalkhen & McCluskey, 2008). Moreover, the reliability indicates how good test results agree between multiple testing if the RVCs are stable (Koo & Li, 2016). A test with high sensitivity, specificity, and reliability is crucial to evaluate treatment effects. This can be illustrated with a simple example: In a post-test, patients show no RVCs despite intensive treatment. On the one hand, the absence of RVCs could be based on the true lack of visual functions and an ineffective intervention. On the other hand, it could be based on low sensitivity of the RVC-test. Hence, high diagnostic quality is decisive for the development of effective treatments.

To evaluate the diagnostic values, it is necessary to know if HVFD-patients truly have RVCs or not. A gold standard measuring RVCs must include the diversity of functions that can be preserved, for instance the discrimination of wavelength or emotions (Danckert et al., 2019). It is worth noting that one patient can show high performance for certain RVCs but not for others (e.g. Corbetta et al., 1990). To complicate it even further, within one patient RVCs might be only present at specific areas within the HVFD (e.g. Wüst et al., 2002). Importantly, all these variants of RVCs have to be taken into account. However, in the clinical and scientific practice, it is not feasible to test all variants in each HVFD-patient. As a solution, a gold standard for RVCs could test whether a given patient fulfills the neuronal and behavioral precondition, i.e. the minimal configuration criterion (MCC), underlying all types of RVCs. Currently, no reliable MCC-test for RVCs is available. This means we need to assess potential tests and their diagnostic features based on conditions where we know for certain that vision is either reliably present or reliably absent. Vision is reliably present in the visual fields of healthy participants and in the sighted field of HVFD-patients. A RVC-test with perfect sensitivity should detect the presence of visual functions in both cases. This means

that all of these participants have to show the performance or the effect of interest. In Ajina et al. (2015) detection performance of healthy participants and within the sighted field of patients was at 100% even for the most difficult condition. Hence, sensitivity for visual function in this test was 100% (Ajina et al., 2015). However, the pattern is less clear in continuous measurements like reaction times in the RTP (Schärli et al., 1999) or in obstacle avoidance (Ross et al., 2018). In both studies, most but not all healthy participants showed the effect of interest (Ross et al., 2018; Schärli et al., 1999). Following this, low performance in patients could be due to a lack of RVCs or due to a poor sensitivity of these tests.

As the diagnostic quality is not yet tested regularly in RVC-studies, this is a continuing topic in RVC-research. In the current dissertation, we started filling this research gap by estimating the diagnostic quality of the RTP.

1.3. Improving methods for visual rehabilitation of HVFDs

In the current dissertation, we addressed the two methodological issues that are an ongoing problem in RVC-research and HVFD-rehabilitation: Light-scatter artefacts and the diagnostic quality of RVC-tests.

Regarding light-scatter artefacts, we first conducted a literature review to pool the available knowledge about sources and influencing factors of light scatter. Furthermore, we reviewed current studies about RVCs and restoration trainings to assess whether light-scatter artefacts are controlled for in all studies with conspicuous stimulus conditions. However, results of light-scatter tests cannot easily be generalized between experimental setups because different pieces of equipment used in different paradigms and tasks have different light emission properties (e.g. CRT- vs. LCD-monitors; Menozzi et al., 1999). Furthermore, paradigms often vary in target size, stimulus luminance, as well as distance between target and blind field border. Such factors increase or decrease the light scatter strength and hence its influence on behavior (Barbur et al., 1994; Campion et al., 1983). As a consequence, light-scatter needs to be tested for every new experiment. The best way to do this is the blind-spot test (Cowey, 2010). However, this procedure requires precise testing of the blind-spot borders and the same high methodological standards as the RVC-test. These additional measurements are laborious. This may explain why they were not applied in a number of recent studies (e.g. Larcombe et al., 2018). We argue that it is possible to solve the light-scatter problem by establishing default experimental setups that are light-scatter-free.

For this, we selected three paradigms that have been used frequently in RVC-testing and in the evaluation of restoration trainings. In each experiment, we applied the blind-spot method to control for intra- and extra-ocular sources of light scatter. Firstly, we used a temporal two-alternative-forced-choice test (2AFC). This paradigm measures the detection of targets

but is robust against biased response criteria (Azzopardi & Cowey, 1998). 2AFC paradigms have been used for example in VST (Sahraie et al., 2006) or in studies investigating the neuronal correlate of RVCs for emotional faces (Ajina et al., 2020). In the first experiment, we tested whether we could produce light-scatter artefacts in our experimental setup by presenting white targets on a black background in darkness. Additionally, we measured two luminance versions in an illuminated room: (1) white targets on a grey background and (2) black targets on a grey background. We hypothesized that the latter condition should be light-scatter-free. Hence, we used the condition with black targets on a grey background in the subsequent experiments. In the second experiment, we measured light-scatter in a movement direction discrimination task. The target was a random dot cloud similar to stimuli used in VST (Huxlin et al., 2009; Vaina et al., 2014) or fMRI studies measuring RVCs for motion (Ajina & Bridge, 2018). In the third experiment, light-scatter was tested in a RTP. As the RTP measures RVCs indirectly, biased response criteria are circumvented. RTP has not only been used to measure RVCs in HVFD-patients (e.g. Marzi et al., 1986; Ross et al., 2018) but also in a number of other clinical populations, for instance split-brain patients (e.g. Savazzi & Marzi, 2004) or bipolar disease (Florio et al., 2013).

In summary, we aimed to provide light-scatter-free versions of these paradigms for RVC- and rehabilitation research. Excluding light-scatter artefacts as a potential explanation for results in RVC-tests does also improve the diagnostic quality of such tests.

This brings us to the second topic of the current dissertation. So far, the diagnostic quality of RVC-tests is unknown. To fill this research gap, we evaluated the diagnostic quality of one frequently used RVC-test: The RTP. The RTP is a simple detection paradigm based on the RTE. The RTE refers to the finding that reaction times are shorter in response to two identical targets compared to one target (Raab, 1962). Marzi et al. (1986) introduced the RTP as a RVC-test presenting the second redundant target within the HVFD. If reaction times of patients are still reduced in this condition, RVC is present (Marzi et al., 1986). We chose this test because it has several advantages. As it measures RVCs indirectly, it is free of biased response criteria. For patients, the instruction is easy: '*Press a button as fast as possible if you see a target*'. As patients always perceive a target within the sighted visual field, the task does not lead to frustration. Furthermore, researchers used the outcome of the RTP as a predictor for other types of RVCs (Striemer et al., 2009, 2018) making it a promising candidate for a MCC-test.

Initially, we conducted a systematic literature review to select all relevant RTP-studies. All studies that measured the RTP in healthy controls were included in a meta-analysis. Calculating the meta-analysis, we evaluated the average effect size of the RTE in healthy participants and defined which experimental features led to the strongest RTE. All studies

measuring the RTP in HVFD-patients were summarized in a comprehensive review. Besides the literature research, we acquired data of the RTP in a big sample of healthy participants as well as in a small sample of HVFD-patients. The patient group was tested at two points in time. Using the reports in the literature and the results of our empirical data, we estimated the diagnostic quality of the RTP. In particular, we estimated its sensitivity, specificity, and reliability. Additionally, we evaluated whether the RTP indicates the MCC of RVCs.

Knowing the diagnostic quality of the RTP allows researchers to re-evaluate previous RTP-results and use the RTP validly in future studies. Ultimately, we aim for a RVC-test with high diagnostic quality measuring whether the MCC of RVCs is satisfied in a given patient. In this regard, an optimal RVC-test could be used to predict different types of RVCs, to recruit suitable patients for research, and to measure the prevalence of RVCs. Regarding the application in the clinical context, such a RVC-test could be used to plan individual rehabilitation strategies and to improve clinical trials. A better outcome of visual rehabilitation means improved quality of life for HVFD-patients.

1.4. Current visual rehabilitation of unilateral neglect

Similar to HVFDs, compensatory trainings in unilateral neglect are not as effective as previously expected (Kerkhoff & Schenk, 2012). Following this, several trainings aimed to improve neglect symptoms by implicit learning. So far, none of these trainings had a resounding success due to unpleasant side effects or a lack of convincing evidence. Still, implicit learning seems to be the most promising approach.

Current treatments aim to counteract the orientation bias by sensory stimulation of, for instance, the vestibular or visual system (Karnath & Dieterich, 2006). Caloric as well as galvanic stimulation affect the vestibular system. Applying caloric vestibular stimulation (CVS), water of different temperature is input to the ear canals leading to a vestibular nystagmus. This treatment led to multimodal effects reducing neglect symptoms (Kerkhoff & Schenk, 2012). A recent study showed that CVS also improves representational neglect (Holé et al., 2020). To our knowledge, long-term effects of CVS have not yet been investigated. Importantly, CVS can produce unpleasant side effects for instance vertigo or nausea (Been et al., 2007). Galvanic vestibular stimulation (GVS) shows effects similar to CVS in the acute stage (e.g. Utz et al., 2011). Using repetitive stimulation, researchers attempted to produce long-term effects. Schmidt et al. (2013) found significant effects on tactile symptoms lasting for one year. However, a randomized control trial testing repetitive GVS in combination with standard eye movement therapy showed no significant effects in any therapy group (Volkening et al., 2018). In summary, there is not yet enough evidence for long-term effects of CVS and GVS.

Neck muscle vibration (NMV) does affect the proprioception. Depending on the setup, participants report that the trunk is rotated in relation to the fixed head or the head is rotated in relation to a fixed trunk (Kerkhoff & Schenk, 2012). NWV reduces neglect symptoms in the short-term (e.g. Karnath et al., 1996). Long-term effects have been shown in few studies (Johannsen et al., 2003; Pettorossi et al., 2015; Schindler et al., 2002). NMV produced significant effects (Johannsen et al., 2003) and improved outcome of VET (Schindler et al., 2002). Pettorossi et al. (2015) combined NMV with asymmetric whole-body rotation and showed aftereffects lasting more than 72 hours. Furthermore, authors showed that the long-lasting effect depended on duration of vibration, on vibration frequency, and on muscle status (Pettorossi et al., 2015). Following this, NWV is a promising treatment option but it is still unclear which combination of parameters produces the best outcome.

Regarding the visual system, the most popular approaches are prism adaptation (PA) and optokinetic stimulation (OKS). In CVS, GVS, and NMV patients are stimulated while patients are passive. In contrast, PA requires active participation of patients. Wearing prisms, everything patients see is shifted to the right. Initially, patients point on the right side of the target. While making pointing movements, they adapt by shifting the movement endpoint to the left. Taking the glasses off leads to an aftereffect in which patients point on the left side of the target. Like this, the rightward-bias in neglect patients was significantly reduced (for reviews see Panico et al., 2020; Redding & Wallace, 2006). With ten or more PA-sessions, effects were significantly stronger than in a sham-group (Serino et al., 2009). In the sham-group, participants pointed while wearing goggles with flat lenses that produced no perceptual shift. In this study, effects lasted until one month after the end of the intervention (Serino et al., 2009). In contrast, a recent trial applying PA in an inpatient rehabilitation setting found no benefit of PA compared to a sham-group (Vilimovsky et al., 2021). Importantly, both studies used similar treatment protocols (10 sessions during 2 weeks) with Serino et al. (2009, 90 trials per session, 10° prism shift) having more trials but a slightly smaller perceptual shift than Vilimovsky et al. (2021, 60 trials per session, 11.4° prism shift). The most conspicuous difference between studies was the time since lesion onset. In Serino et al. (2009), mean time since lesion onset was five months in the sham-group and ten months in the PA-group (values based on the table). In Vilimovsky et al. (2021), time since lesion onset was two months at the first session (PA-group: 76 days; sham-group: 70 days). Hence, studies fell into different stages of spontaneous remission in which a plateau is usually reached at three months after lesion onset (Stone et al., 1992). In summary, PA is a promising intervention but further research is needed to determine the decisive factors that lead to the treatment effects.

In OKS, patients view a visual display with stimuli moving to the left (Kerkhoff & Schenk, 2012). If the display is large enough, OKS induces the perception of a rightward body

rotation. Using smaller displays, for instance common PC-monitors, OKS induces optokinetic nystagmus. In both cases, patients reorient themselves to the left which should alleviate neglect symptoms (Kerkhoff & Schenk, 2012). Interestingly, Kerkhoff (2002) showed that OKS improves neglect in the visual as well as the auditory domain. This effect was still present two weeks after the training (Kerkhoff, 2002). A recent study investigated the neuronal correlate of the OKS-effect (von der Gablentz et al., 2019). Their results suggest that patients having less severe neglect symptoms in the chronic stage are more suitable candidates for an OKS-training than strongly impaired patients in the acute stage (von der Gablentz et al., 2019). During training, it is important that patients are allowed to make pursuit eye movements. If patients had to keep eyes fixated, OKS showed no significant effect (Pizzamiglio et al., 2004). Task instruction as well as the presence of a fixation symbol are a current matter of debate (Pitteri et al., 2015).

To summarize, the described treatment approaches showed promising but usually inconsistent results. In addition, researchers still disagree on the optimal training parameters. Furthermore, there is a lack of studies investigating generalization and endurance of training effects. The four described neglect treatments all assume that the core-deficit in neglect is the orientation bias. Hence, patients receive stimulation that counteracts this bias. However, it is not clear that the orientation bias is truly the core-deficit in neglect. As current interventions are not as successful as expected, it is worth considering other approaches.

1.5. Proposal for a new, gaze-contingent intervention for unilateral neglect

Besides the orientation bias, unilateral neglect has been described as a disturbance of attention control. Disturbances of attention are often coupled with disturbances in eye movement patterns (e.g. Craighero et al., 2001). Following this, an intervention aiming to bias the eye movement pattern to the left side could likewise modify attentional distribution and thus reduce neglect symptoms. In particular, the premotor theory of attention (PTA) links covert attentional orientation and (eye) movement planning (Craighero & Rizzolatti, 2005; Rizzolatti et al., 1987). Interestingly, the PTA makes specific predictions about the relation between covert attentional orientation and movement planning, for instance that they have the same neuronal correlate. Smith and Schenk (2012) reviewed evidence for each of these predictions. Evidence in favor of the PTA-predictions was inconsistent with one exception: Exogenous attention is dependent on movement planning (Smith & Schenk, 2012). In particular, studies showed that covert attentional allocation was not possible if eye movements could not be planned to this area of the visual field (Craighero et al., 2004; Smith et al., 2010). This principle could be used as a neglect treatment. If eye movements are impossible towards the preferred side, attentional allocation should shift towards the neglected side and hence reduce neglect symptoms. In our training tasks, we use a

gaze-contingent visual search paradigm. As it is not possible to make eye movements towards the preferred side unfeasible, we rather make them useless. As soon as eye movements reach the preferred side, i.e. right side on the screen, targets disappear. This should stop patients from exploring the preferred side and promote exploration of the neglected side.

Importantly, the proposed intervention has major advantages compared to previous treatments. Firstly, our intervention does not rely on awareness but corrects the exploration bias implicitly. Particularly, there is no need for a specific instruction about a visual-exploration strategy. To comply with such strategies, patients need insight into their deficit which is often lacking (Grattan et al., 2018; Robertson & Manly, 2002). Secondly, our intervention could directly counteract the disengage deficit. The disengage deficit describes the problem of neglect patients to disengage their attention from targets within the preferred side (Losier & Klein, 2001). As a consequence, patients have problems relocating attention to targets within the neglected side. Other studies showed that neglect symptoms reduced when there were no targets on the preferred side (e.g. Schnider et al., 2011). In our gaze-contingent intervention, both findings come together. Targets on the preferred side disappear when looking on them. Accordingly, it is not necessary to actively disengage from them thus facilitating relocation of attention to targets within the neglected side.

In the current dissertation, we tested the effect and feasibility of the proposed intervention in healthy participants. It has been shown that healthy participants have a so-called pseudoneglect (Bowers & Heilman, 1980). This term describes a small preference to the left, i.e. in the opposite direction of the neglect-typical right bias. Pseudoneglect is apparent in visual search tasks (Nuthmann & Matthias, 2014) and in line bisection (Bowers & Heilman, 1980). Hence, we adapted the paradigm to counteract the inherent bias in healthy participants. Like this, targets disappeared as soon as eye movements reached the left side of the screen. To measure the training effect, we conducted five experiments with four different paradigms comparing performance before and after the intervention. In the first experiment, we measured whether the training effect endures in a visual search task identical to the intervention but without removing targets. Secondly, we measured the generalization of the training effect to a conjunction search task. In the third and fourth experiment, we tested a Posner paradigm evaluating the effect of the intervention on covert attentional allocation. Last, the training effect was measured using a line bisection task which is used in clinical diagnosis of neglect.

In summary, we aimed to show that our new, gaze-contingent intervention has a short-term effect counteracting the pseudoneglect-bias in healthy participants. Furthermore, we wished to show that the effect of the intervention generalizes to other tasks. In subsequent studies,

we plan to evaluate the long-term effect of our training in healthy participants before conducting studies in neglect patients. Reaching our aim, we could provide an intervention based on implicit learning that overcomes several problems of previous treatments.

1.6. Objectives

In the current dissertation, we provide tools and techniques for visual rehabilitation.

In the first manuscript, we presented a comprehensive review on light-scatter artefacts in RVC-research. With that, we emphasized the need for light-scatter tests and informed about factors and precautionary measures. On this basis, we tested light-scatter artefacts in three frequently used RVC-paradigms. Using high methodological standards and a medium-size sample, we aimed to provide light-scatter-free experimental paradigms. As outcome, future researchers will be able to use these experimental paradigms for their studies thereby avoiding the light-scatter problem.

In the second manuscript, we evaluated the diagnostic quality of the RTP. Initially, we conducted a meta-analysis about the RTE in healthy participants. Next, we reviewed literature about the RTP in RVC-research. Lastly, we tested the RTP in a large group of healthy participants and in a small sample of HVFD-patients. Merging information from the review and from our own empirical data, we estimated the sensitivity, specificity, and reliability of the RTP. Furthermore, we evaluated whether the RTP indicates if the MCC of RVCs is given in a certain patient. Knowing the diagnostic quality of the RTP allows to re-evaluate previous RTP-results and use the RTP validly in future studies.

Taking the first and second manuscript together, we improved the methodology in measuring RVCs in HVFD-patients. In particular, our results enable future studies to measure RVCs with light-scatter-free stimuli and apply the RTP validly. Hence, we approximated the goal of testing RVCs with high diagnostic quality allowing a sound evaluation and thus advancement of treatment strategies.

In the third manuscript, we created a new gaze-contingent intervention for neglect based on an attentional framework. In the task, targets vanish within the preferred side if patients make eye movements towards it. In a first step, we tested the short-term effects of the intervention in healthy participants. Therefore, we conducted five experiments measuring the effects on overt and covert attentional allocation. Ultimately, we hope to successfully apply this intervention in patients counteracting the neglect symptoms.

To summarize, we evaluated, improved, and created methods and paradigms used to study and/or treat patients with HVFD or neglect.

2. Manuscripts

I. How to test blindsight without light-scatter artefacts?

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Abstract

The present study had two components. Firstly, we reviewed the methodological problem of light-scatter artefacts in testing residual visual capacities (RVCs), for instance blindsight, in patients with homonymous visual field defects (HVFD). The term light-scatter artefact describes the phenomenon that light from targets directed towards the HVFD can stray into the sighted visual field. This might enable an observer to respond correctly to information directed at her blind field despite the fact that she is unable to process that information in the blind field itself. Light scatter was shown to be sufficient for above chance detection, localization, and orientation discrimination. Furthermore, contamination of performance by light scatter is exacerbated by high target luminance, large targets, use of darkened room and targets presented close to the visual field border. Presenting targets within the blind spot is the most reliable way to test for light-scatter artefacts as it controls for intra- and extra-ocular sources of light scatter. Unfortunately, experiments on light scatter effects are laborious and therefore frequently neglected even in recent studies with stimulation likely to produce light scatter.

Consequently, the second part of this study aimed at developing stimuli and procedures for RVC-testing that will avoid light-scatter artefacts. To this end, we investigated 21 healthy young participants in three frequently used RVC-paradigms: (1) Temporal 2AFC task, (2) movement direction discrimination, and (3) redundant target paradigm. For each paradigm, we applied the blind-spot method. But first, we had to establish that our testing paradigm was sufficiently sensitive to detect light-scatter artefacts. For this, we used conditions that are known to produce strong light-scatter effects and a paradigm that is very sensitive to such effects. Specifically, we presented white targets on a black background in a dark room. The stimuli were presented to observers' blind spot. To check for light-scatter effects, we used a target-detection task in a temporal 2AFC format. We obtained clear light-scatter effects. Participants produced reliably above-chance detection performance under these conditions. The other two luminance conditions, measured in an illuminated room, did not produce light-scatter artefacts. Accuracy in the temporal 2AFC task was at chance level for white targets on a grey background at the blind-spot position. Additionally, black targets on a grey background avoided light-scatter artefacts in all three RVC-paradigms.

In future, researchers can use these stimulus and illumination conditions when using one of the three above paradigms in their studies. Using these conditions, they will be able to avoid light-scatter artefacts without having to perform their own blind-spot tests.

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I.1. Introduction

The present study had two aims. Firstly, the study reviews the methodological problem of light scatter in blindsight testing. The term blindsight describes residual visual capacities within the blind field of patients with homonymous visual field defect (HVFD, Weiskrantz et al., 1974). HVFD occurs due to a post-chiasmal lesion of the visual system, for instance due to a stroke (Zihl & Kennard, 2003). Light scatter is a potential artefact in the search for blindsight capacities. Light scatter describes the phenomenon that light from targets directed towards a blind portion of the visual field can stray into the preserved, seeing part of the visual field. Light scatter can thus lead to the misleading conclusion that signals from within the blind area are still processed and can form the basis of visual responses when in reality the responses are based on signals that reach the visual system via light that has fallen onto seeing portions of the visual field (Campion et al., 1983). Hence, high performance of patients could be based on visual information from light scatter and not on blindsight capacities. In the current article, we will use the term light-scatter artefact to refer to this problem. In our review, we will describe sources of light scatter and factors that influence the impact of light scatter. Additionally, we will present precautionary measures and tests that have been used to control for light scatter in recent blindsight studies. Unfortunately, experiments about light scatter have only been tested in small sample sizes and with few paradigms. Hence, the results are not generalizable and not applicable to the vast majority of blindsight tests. Furthermore, tests for light scatter are time-consuming and not all recent studies with conspicuous target-background luminance combinations took the necessary actions to rule out light-scatter artefacts.

Consequently, the second aim of this study was to provide stimuli and procedures for blindsight testing that can avoid contamination of results by light scatter. Therefore, we will present a thorough investigation of the possible influence of light scatter in three frequently used paradigms in a group of heathy participants. As a result, these stimuli and procedures can be used in future blindsight studies without worrying about light-scatter artefacts.

In Europe in 2017, 7.06 million life years were lost due to death or disability following stroke (Wafa et al., 2020). Besides other impairments, visual field defects are a common consequence of strokes. Numerically, 26.1% of persons with a first-in-a-lifetime stroke show a visual field defect (Lawrence et al., 2001). Following this, there are a high number of stroke survivors who need a sound diagnosis and treatment of their visual field defects. However, early studies already revealed that patients with post-chiasmal lesions were not completely blind but still responded surprisingly well to certain targets presented within their blind visual field (Holmes, 1918; Riddoch, 1917). Later, several case studies showed that above chance performance is possible without acknowledged awareness (Pöppel et al., 1973; Weiskrantz et al., 1974). This phenomenon has been called blindsight (Weiskrantz et

al., 1974). On the basis of this dissociation, researchers tried to uncover the neuronal correlate of consciousness. They argued that if visual performance is present but visual consciousness is absent, the lesion has to affect the neuronal correlate of visual consciousness (Weiskrantz, 1999). With this idea, blindsight became one of the most hotly debated topics in cognitive neuroscience. Interestingly, critical voices emphasized that some patients reported feelings about targets presented within their HVFD (Campion et al., 1983). Even patient *DB,* whose results led to the term blindsight, characterized the target O as '*smooth*` and the target X as '*jagged*' when urged to describe his perception (Weiskrantz et al., 1974). Another example is patient *G* in Barbur et al. (1980) who stated seeing '*dark shadows'*. Later studies showed that the measurement of visual awareness itself is a matter of debate (Mazzi et al., 2016). Using a dichotomous scale (*'seen'* versus *'guessed'*) patient *SL* showed a response pattern fitting to the original definition of blindsight, meaning above chance performance without visual awareness. Contradicting results occurred when a four-level scale was used: Patient *SL* showed above chance performance only when reporting at least a '*brief glimpse'* about the target (p.901; Mazzi et al., 2016). These results were supported by a subsequent study in four patients (including *SL*) showing that performance was above chance only for levels 2 ('*almost clear*') and 3 ('*clear*') (Mazzi et al., 2018). Furthermore, their results pointed to a relationship of the awareness ratings with event related potentials in electroencephalography (Mazzi et al., 2018). As a consequence, the authors recommend using a continuous scale to differentiate between pure blindsight and degraded vision in patients with HVFD (Mazzi et al., 2018). Due to the ongoing debate about the presence, absence, and quality of visual awareness in blindsight patients, it is reasonable to apply a broader term encompassing all variants of visual awareness in this clinical population. Following this, we will use the term residual visual capacities (RVCs) in the remainder of this article.

How to assess visual awareness is only one of several issues that plaques research on RVCs. Another major problem concerns biased response criteria (Cowey, 2010). In detection paradigms, patients have to decide whether a target was present or not ('*yes'* versus '*no'*). This classification is based on implicit boundaries between response alternatives. With identical perception, a patient with a conservative criterion would respond '*no'* whereas another patient with a liberal criterion would respond '*yes'* (Cowey, 2010). Furthermore, these response biases might change between paradigms or due to variations of task design. For instance, Stoerig et al. (1985) varied the ratio of target trials and blank trials and thus changed the detection rate. Azzopardi and Cowey (1998) showed that patient *GY* had varying response criteria depending on task type ('*yes-no'* versus forced choice paradigm) and target type (static versus moving). The same issue holds true for effects of classical visual restitution trainings (VRT) in which patients detect salient targets within the blind visual

field (e.g. Marshall et al., 2010). Patients might change their classification to a more liberal criterion leading to increased detection rates without changes in the perception (Cowey, 2010). The problem of response biases is reduced in forced choice tasks (Cowey, 2010) and can be avoided completely by indirect measurements of RVCs like the redundant target effect (RTE; Marzi et al., 1986). The RTE describes reduced reaction times in response to two targets in comparison to a single target. RVC is present if the second redundant target located within the blind visual field still decreases reaction times. In this task, patients are instructed to press a button as fast as possible if they see one or two targets (Marzi et al., 1986). As one target is always present within the sighted visual field, there is no need for response criteria. In conclusion, the issue of biased response criteria can be solved by adequate experimental paradigms.

Another methodological issue that influences results of RVC-tests are eye movements in tasks that require fixation. If eye movements are controlled insufficiently, RVCs are overestimated. Target locations are positioned within the blind visual field to test RVCs. If patients move their eyes, targets might be shifted to sighted parts of the visual field. Thus, results show an increased performance. Under proper fixation control, trials with eye movements can be excluded (Alexander & Cowey, 2013; Pavan et al., 2011). However, in multiple studies investigating RVCs fixation was only controlled manually by examiners (e.g. Bergsma & van der Wildt, 2010; Ross et al., 2018). Unfortunately, the method of manual fixation control has been called into doubt. Hooge et al. (2018, 2021) showed substantial differences between researchers who classified eye movements manually. In detail, researchers applied different implicit thresholds of saccade velocity and minimum saccade amplitude. As a consequence, the number of fixations and fixation durations varied tremendously between raters. Besides this inter-rater variability, there was also an intra-rater variability meaning that thresholds changed over the course of the rating task. Furthermore, classification of eye movements was done offline with an especially designed interface (Hooge et al., 2018, 2021). Consequently, it is likely that classification of eye movements online during an experiment might inherit even greater inter- and intra-rater variability. Following this, we conclude that this method of fixation control is insufficient for RVC-tests.

Other studies used eye tracking devices but without defining criteria for a fixation break (e.g. Carey et al., 2012; Mazzi et al., 2016). The issue of eye movements is especially crucial in studies investigating VRT as targets are often presented at the border between sighted and blind visual field (Marshall et al., 2010; Reinhard et al., 2005). If the border zone is stimulated, minimal eye movements are enough to shift part of the target towards the sighted visual field leading to a correct detection. Following this, critics emerged that the training might not restitute the visual field itself. Instead, minimal eye movements or a shifted fixation position could enlarge the visual field in the sense of compensation (Reinhard et al., 2005).

When fixation was controlled precisely during perimetry with a scanning laser ophtalmoscope, no visual field enlargement was found after restitution training (Reinhard et al., 2005). However, a later study measuring eye movements at a similar precision with a fundus-controlled microperimetry, presented contradicting evidence (Marshall et al., 2010). Unfortunately, the latter study did not include a control group. Thus, currently there is no compelling evidence to suggest that VRT significantly reduces the blind area in patients with visual field defects (Pollock et al., 2011). Furthermore, this research on the topic has made it abundantly clear that without precise fixation control, an evaluation of this type of training is not possible.

VRT aims to reduce the extent of the blind area and it does so by presenting targets at the border between the sighted and blind field. Another training approach aims to make certain portion within the blind field more responsive to visual stimulations. For this visual sensitivity training (VST), the monitoring and prevention of eye-movements are as important as in the case of VRT. Studies showed that preserved or trained RVCs can be highly location specific (Huxlin et al., 2009; Trevethan et al., 2012; Wüst et al., 2002). If the eye-position is changed, the target will no longer land at the same location on the retina and no RVC or training effect may be detected. Thus, without reliable fixation control the detection of position-specific training-induced RVCs will be very difficult. Moreover, if eyes change position during training, not just one but several positions will be stimulated, it thus becomes unclear at which position we should expect to see training-induced effects (Reinhard et al., 2005). It is worth noting that precise eye tracking devices and automated eye movement analysis are available to ensure precise fixation control or gaze-contingent designs (e.g. Portengen et al., 2021; Reinhard et al., 2005).

So far, we have demonstrated that problems related to response biases and eye movements can be avoided by using adequate experimental paradigms. For both methodological problems, there were good experimental tests and convincing solutions are available (Cowey, 2010; Marzi et al., 1986; Reinhard et al., 2005). However, in the case of light-scatter the situation is less satisfactory. Most studies on this effect use very small samples and can therefore not provide representative and reliable estimates for methods and target parameters that will avoid light scatter in most observers. The situation is further complicated by the fact, that some of the studies are by now 20 to 50 years old and used equipment that today is no longer in use. For this reason, we decided that it is important to provide reliable estimates for light-scatter-safe stimuli that can be implemented with current equipment. The idea that the effect of light scatter can mimic RVCs dates back at least to the studies of Cowey and Weiskrantz (1963). Since then, different sources of light scatter have been discovered, factors determining the extent of light scatter have been identified, and procedures to avoid light scatter have been suggested. To our knowledge, no

comprehensive review on light scatter is currently available. Therefore, we will start with a review on what is currently known about light scatter in RVC-research and also examine whether recent studies on RVCs have taken note of those insights into light scatter, its role and origins. We will conclude that light scatter is an avoidable methodological complication but one that is still prevalent in many recent studies. We suspect that the absence of readily available and reliable information on light-scatter-safe target parameters for commonly used RVC-paradigms is responsible for the inconsistency with which light scatter is addressed in recent RVC-studies. We, thus, decided to address this issue by developing and evaluating light-scatter-safe stimuli for three commonly used RVC-tests.

I.2. Review

I.2.1. Sources and factors of light scatter

On the way from the light source to the eye, light scatters and can thereby stimulate a wide region on the retina. In the case of a target directed to the blind field, particularly if it is directed towards the border between blind and sighted parts of the visual field, light scatter might reach the sighted part and thereby allow detection of light (Campion et al., 1983). Besides, light could be reflected by other objects, e.g. by the participants nose (Weiskrantz, 1980). Such extra-ocular sources are complemented by intra-ocular sources of light scatter. Light entering the eye is strayed by specular reflection from the retina (Faubert & Diaconu, 2001; Faubert et al., 1999). Thereby, light is reflected mirror like rebounding in a perpendicular angle (Faubert & Diaconu, 2001). Furthermore, Lambertian scattering happens within the eye while the light travels from the cornea to the retina (Campion et al., 1983). In the process, light is distributed in all directions synchronously (Faubert & Diaconu, 2001). Importantly, Lambertian scatter is enhanced by increasing target size as more energy enters the eye (Faubert et al., 1999). Authors showed that Lambertian scatter under photopic conditions was sufficient to explain blindsight results in hemidecorticate patients (Faubert & Diaconu, 2001). Importantly, they emphasized that the effect of intra-ocular light scatter is increased under scotopic conditions (Faubert et al., 1999). To summarize, light strays outside and inside the eye. Consequently, methods to test the potential impact of light scatter need to consider both sources of light scatter.

Therefore, we will not present results of experiments investigating light scatter with eye patches covering parts of the visual field in patients (Campion et al., 1983; King et al., 1996) or in healthy participants (Campion et al., 1983) because such methods only control for extra-ocular sources of light scatter.

The most powerful method to investigate light scatter is the presentation of targets within the natural blind spot (Cowey, 2010). The natural blind spot corresponds to the optic disc (Jonas

et al., 1991). As there are no photoreceptors at the optic disc (Curcio et al., 1990), humans have a physiological, absolute scotoma within their visual field (Jonas et al., 1991). Hence, if visual stimulation of the blind spot leads to above chance performance, the reason must be that light strays onto the retinal area surrounding the blind spot. Thus, RVC-results are valid if performance is high for targets within the HVFD but at chance level for targets within the blind spot (Stoerig et al., 1985). Like this, intra- and extra-ocular light scatter can be excluded as an explanation.

Early studies used the blind-spot method to investigate factors that increase or decrease light scatter. These factors are important to evaluate the potential of light scatter in recent studies.

Wilson (1968) measured the detection of targets on the basis of light scatter within the natural blind spot and within the blind visual field of four HVFD-patients. Results of the blind-spot experiment showed that the luminance threshold for detection decreased with increasing target size. On the basis of their results, Wilson (1968) presented a formula (see formula I.1) applicable to experimental settings with a minimum background luminance of 75 cd/m^2, a target duration of 1s and a target position at least 3° from the visual field border. Importantly, this formula (I.1) is independent of the luminance unit. If the resulting value of the left side is smaller than 2.8, light scatter is unlikely to be detected. This threshold that holds for a minimum distance of 3° between light target and sighted field increases to 53 when that distance is increased to 15° (Wilson, 1968).

$$\frac{Luminance\ Stimulus}{Luminance\ Background} \times (Stimulus\ diameter\ in\ °)^2 < 2.8 \qquad \text{(I.1)}$$

Campion et al. (1983) extended this study on light scatter. Three healthy participants localized targets at three positions within the blind spot. After a short training period with feedback, participants localized targets with reasonable accuracy. Thereby, accuracy was higher for target positions nearer to the fixation position. Moreover, participants could discriminate between vertical and horizontal orientation of a bar within the blind spot in the bright (100 cd/m^2) but not in the dim condition (5 cd/m^2). However, it is not always necessary to have such a bright target for light scatter to provide sufficient means for a reliable visually guided decision. For example, in the case of simple detection of light targets, above chance performance could be achieved with medium luminance targets (34 cd/m^2 on a 3 cd/m^2 background). With the latter targets, size was relevant as well. Reducing the diameter from 1°40’ to 1° led to detection rates at chance level (Campion et al., 1983).

The effects of target luminance, size, and eccentricity on light scatter were replicated by Barbur et al. (1994) in patient *GY* and in a healthy participant. In this experiment, the luminance of a test target was adapted until the flicker of the light-scatter source (peak: 100 cd/m^2) could be no longer detected. For the smallest distance between light-scatter source

and sighted visual field (distance between fixation and target: 3.5°), a target luminance at or below 7 cd/m^2 was required to avoid flicker detection.

Zihl and Werth (1984) tested whether light scatter could be used for saccadic target localization within the blind field of two HVFD-patients. They also measured the amount of light scatter at the visual field border using a photometer. Light scatter had a maximum value of 1.420 cd/m^2 when targets were at the position closest to the visual field border (distance 8°) in the high contrast condition (background: 0.032 cd/m^2; target: 320 cd/m^2). In the low contrast condition (background: 3.2 cd/m^2; target: 32 cd/m^2) both patients never reported any visual sensation but showed significant correlations between saccade endpoint and target eccentricity. Under high contrast condition, both patients reported seeing a diffuse light but performance did not differ from chance level. Hence, patients could not differentiate the location, nor the size or brightness of targets when perceiving the diffuse light scatter. Practicing this condition did not lead to an improvement in one patient. Reducing the contrast slightly (background: 3.2 cd/m^2; target: 320 cd/m^2) in the other patient did not improve saccadic localization but led to an almost perfect detection of target onset (Zihl & Werth, 1984).

Regarding colors, Stoerig and Cowey (1991) measured wavelength sensitivity within the natural blind spot within the blind visual field of two HVFD-patients. Under photopic conditions, accuracy was at chance level in both patients. In the scotopic condition after dark adaptation, the natural blind spot of both patients and of two healthy participants were tested. Furthermore, targets were measured at 10° eccentricity within the blind visual field of patients. Detection thresholds could be measured and the perception for targets within the blind spot was reported as a '*large halo of unidentifiable color'* (page 1505, Stoerig & Cowey, 1991). In patients, sensitivity measures for the blind spot and for the 10° target were similar. However, results for both conditions were considerably lower than in the force-choice procedure measuring sensitivity in the blind visual field (Stoerig & Cowey, 1991). As the light-scatter experiment used another experimental paradigm as the RVC-test, the results are not directly comparable. However, it seems that light scatter could not fully explain RVCs.

Studies with human participants have been complemented by research in monkeys (Cowey, 2004; Cowey & Stoerig, 1999). The monkeys *Wrinkle* and *Dracula* localized targets with an accuracy of about 90% in their impaired hemifield (Cowey, 2004). If the target was presented within the natural blind spot, accuracy dropped to 1% (*Dracula*) and 27% (*Wrinkle*) respectively (Cowey, 2004). The target was a white square (1.3°, 10 cd/m^2) on a grey background (1.2 cd/m^2). Monkeys were trained extensively to respond to this target within the blind visual field before light-scatter testing. Improvement during training might have reflected improved use of RVCs or improved use of light scatter. However, since performance dropped

substantially with blind-spot presentation, we can safely conclude that light scatter was not a major factor in the improvement observed after training.

To summarize, light scatter increases with increasing target-background luminance, increasing size, and decreasing distance to the visual field border. Light scatter is elicited by targets of varying wavelengths. Light scatter was shown to be sufficient for above chance detection and orientation discrimination. Information from light scatter can suffice for localization of targets within the blind spot in healthy participants (based on verbal report) but saccadic localization within the blind visual field in HVFD-patients was not possible.

Consequently, it is known which stimuli and which paradigms are more prone to light scatter and how this issue can be avoided. Back then, Campion et al. (1983) reviewed the measures against light scatter taken by authors of the early RVC-studies and came to a scathing verdict: '*None of the studies reviewed has provided adequate control procedures for light scatter*' (page 437, Campion et al., 1983). Campion et al. (1983) had several points of criticism. The most important criticism was that the effectiveness of experimental procedures, like flooding the sighted field with light (Weiskrantz, 1980), were not confirmed by psychophysical experiments. Furthermore, Campion et al. (1983) stated that the formula (I.1) by Wilson (1968) which was computed on the basis of psychophysical experiments, was applied wrongly in other studies. However, even if we would follow the instructions of Campion et al. (1983) or Wilson (1968) for light-scatter-free experiments, there is another issue. Most of the studies investigating factors of light scatter were conducted with equipment that is not in use anymore.

Since 1983, there were significant developments in experimental methods. Wilson (1968) used an illuminated concave surface and controlled target durations with an electro-mechanical shutter. Other studies used custom-made perimetry apertures with incandescent bulbs (Campion et al., 1983) or adjusted perimetry devices (Stoerig & Cowey, 1991; Zihl & Werth, 1984) for their light-scatter investigations. In contrast, recent studies investigating RVCs present stimuli on CRT (e.g. Saionz et al., 2020) or LCD monitors (e.g. Grasso et al., 2020). Importantly, results for light scatter of one device cannot be generalized to other devices as the properties of light emission differ. More generally, it is known that switching equipment, e.g. from CRT devices to LCD devices, can affect performance in visually-guided behavior (see for example findings on visual search: Hollands et al., 2002).

This means that modern studies on RVCs cannot simply use stimulus parameters that proved light-scatter-safe in the past and hope for the best. Instead, the light-scatter safety has to be demonstrated again for new stimuli, new paradigms and new equipment. In the following section, we review the relevant literature on RVCs for the last 10 years to examine whether these precautions have been taken.

I.2.2. Light scatter in recent studies

Many recent studies investigating RVCs used a target-background combination that aimed to reduce the potential for light scatter. For example, Das et al. (2014) chose targets to be dark dots on a bright background to avoid light-scatter artefacts. Hence, these studies usually did not address the light-scatter problem. Other studies used precautionary measures or pre-testing to rule out the influence of light scatter. However, these procedures, like blind-spot testing, require extensive testing and are time-consuming. Hence, not all studies investigating RVCs with critical target-background combination did address the issue of light scatter.

The following precautionary measures and tests have been used to avoid a bias of results due to light scatter. Several studies used methods avoiding only extra-ocular light scatter. For example, Cowey et al. (2013) as well as Danckert and Culham (2010) used hemifield patches covering the blind visual field. Other studies used a viewing tunnel enveloped in black felt (Sahraie et al., 2010) or covered all surrounding surfaces with non-reflective black felt (Sahraie, Trevethan, MacLeod, Urquhart, et al., 2013). Stoerig (2010) placed the monitor within a black felt-lined box. In the training study of Elshout et al. (2016), the training setup was places into a black container. As we have described above, applying only these methods is not sufficient as intra-ocular light scatter might still play a role. Many but not all (exceptions: Elshout et al., 2016; Sahraie et al., 2010) also used further techniques to minimize the effects of light scatter such as blind-spot testing (Danckert & Culham, 2010) or equiluminant target and background (Sahraie, Trevethan, MacLeod, Urquhart, et al., 2013).

Some studies used methods that were explicitly selected to deal with both extra- and intra-ocular forms of light scatter. Tamietto et al. (2010) surrounded targets, namely chromatic squares, with achromatic squares changing luminance at 20 Hz (1.1-20.1 cd/m^2). This method should ensure that targets can only be detected by their color.

Carey et al. (2012) used stimuli where targets and background had equal luminance and argued that this method prevented that the task could be solved on the basis of information provided by light scatter. The same method was applied by several other studies (coarse orientation discrimination tasks in Das et al., 2014; Sahraie, Trevethan, MacLeod, Urquhart, et al., 2013; Trevethan et al., 2012). Remarkably, none of these studies presented psychophysical evidence that equiluminant stimuli do not produce light-scatter artefacts. Although, it is possible to extrapolate from previous results to an equiluminant condition (Barbur et al., 1994; Wilson, 1968), these conclusions would only hold true for the exact same experimental parameters. Hence, the use of an equiluminant stimulus condition to avoid light-scatter artefacts has to be re-evaluated.

Trevethan et al. (2012) suggested that a potential effect of light scatter can be excluded by testing and training patients with complete cortical blindness. As there is no sighted visual field left, light scatter in their view cannot account for above chance performance in visual tasks. Both patients with complete cortical blindness showed behavioral improvements due to a training with moving gratings (Trevethan et al., 2012).

Danckert and Culham (2010) presented a thorough investigation of the effect of light scatter. Patient *DC* showed a significant negative correlation between pointing and target location if targets were white targets on a black background. This reversed relationship indicated that patient *DC* pointed closer to the center of the screen if targets had a higher eccentricity. However, this was also true if targets were located within the blind spot of the blind visual field. This relationship vanished only when colors were reversed (black targets on a white background). Furthermore, the negative nature of the relationship could be explained by light-scatter differences. When the largest target was presented, patient DC selected the most peripheral position. In the case of smaller targets, patient DC chose more central positions. As luminance was identical, the size difference led to a change in light scatter (similar to Barbur et al. (1994) and Campion et al. (1983)). In conclusion, this patient had a response criterion based on light scatter (Danckert & Culham, 2010)

Other studies used the blind spot as a method to test light scatter. Bergsma and van der Wildt (2010) trained patients using a Goldman perimeter in which target brightness increased (4-318 cd/m^2). To monitor fixation, they also tested targets within the blind spot regularly. Incidentally this technique for fixation monitoring could have also been used to exclude light-scatter artefacts. The same holds true for Bergsma et al. (2014). Unfortunately, authors of neither study did report details about the procedure, for instance the number of blind-spot trials, nor a statistical analysis of the blind-spot results. In other studies, blind-spot testing was used explicitly with the intent to avoid light scatter. Stoerig (2010) showed that detection was at chance level for grey disks (16 cd/m^2) presented on a white background (65 cd/m^2) in three HVFD-patients. In Savina and Guitton (2018) both hemispherectomized patients were unable to detect a light spot (0.8 cd/m^2) flashed on a dark background when presented to the blind spot even though the room was completely dark.

Other studies used blind-spot testing in healthy volunteers to select light-scatter-free stimuli for use in later investigations with patients. For instance, Huxlin et al. (2009) tested light scatter for random dot targets in two healthy participants. Movement direction discrimination was at chance level within the blind spot for grey dots (33 cd/m^2) presented on a lighter grey background (45 cd/m^2). Importantly, participants could detect target onset and offset reliably. The same pattern was present if luminance values were reversed (dots: 45 cd/m^2, background: 33 cd/m^2). Additionally, one of the healthy participants was trained over 17 days

with the blind-spot target. Results showed no improvement in performance. Authors concluded that light scatter is no sufficient explanation for training successes within the blind visual field of patients with HVFD (Huxlin et al., 2009). It is worth noting that apertures were considerably smaller in blind-spot testing (2°, 2.5°) than in patients (6°, 8°,12°). As targets were up to six times larger in patients, the generalization of the blind-spot testing to the training in patients should be treated with caution. Later studies used similar random dot targets with grey (0.5 cd/m^2 in Das et al. (2014)) or black dots (Cavanaugh et al., 2017; Saionz et al., 2020).

Notably, few studies still disregarded the potential impact of light scatter even though the choice of target-background luminance seems conspicuous. In their first experiment, Azzopardi and Hock (2011) tested illusory motion with white rectangles of different height presented subsequently on a black background in patient *GY*. In the following experiments, they replicated their effect with black-and-white targets on a grey background. The latter luminance combination seems to be less prone to light scatter. However, all testing has been done in a dimly lit room which increases the potential impact of stray light (Faubert et al., 1999). Alexander and Cowey (2013) tested two patients with a temporal two-alternative forced-choice (2AFC) paradigm in which they had to detect the presence of motion. Random dot targets were either moving or static and presented in various colors and luminance ratios (targets: 0-180 cd/m^2, background 5-10 cd/m^2). Performance of patient *GY* was above chance if targets were brighter or darker but at or below chance when tested under equiluminant conditions. Patient *MS* showed best performance for the brightest targets. Authors conclude that the '*the chief factor in determining motion detection was luminance contrast*' (p. 150, Alexander & Cowey, 2013). Surprisingly, authors did not discuss whether those results might have been influenced by light scatter. Grasso et al. (2016) used bright LEDs in a light-attenuated room for training and testing detection. Larcombe et al. (2018) tested and trained their patients with a white random dot target on a black background. The impact of light scatter should also be considered in studies using functional magnetic resonance imaging (fMRI). Barleben et al. (2015) reported that none of their patients showed RVCs in pre-testing without giving further details about the type of tests. Still, some of the same patients showed neuronal activation elicited by bright white moving bars presented on a darker background (Barleben et al., 2015). In principle, within the typically dark environment of a MRI scanner the stimuli from pre-testing re-employed during MRI-testing may have produce more reliable light-scatter signals, thereby creating the observed fMRI activation. Remarkably, none of these studies mentioned the problem of light scatter. It is unclear whether in these studies light scatter might have affected the results. In our view the above review suggests that while the problem of the light-scatter artefact is well known, the

problem is not always addressed and consequently findings on RVCs reported in recent studies may still be contaminated by light-scatter artefacts.

To summarize, authors used a number of different approaches to deal with the light-scatter problem. The most frequent methods were an equiluminant target-background combination and blind-spot testing. For unequal luminance combinations, blind-spot testing is the most reliable method to measure the effect of light scatter on performance in a given task. However, the described studies also show that blind-spot testing is time-consuming and laborious. There are several reasons for this. Firstly, the exact blind-spot border has to be measured with high precision. Unfortunately, standard static perimetry often does not measure the borders of the blind spot by default. Hence, it is necessary to run additional perimetry programs or custom-made procedures. Secondly, RVC-targets have to be tested within the blind spot with the same paradigm as the RVC-test. Of course, for the blind-spot trials the same high methodological standards have to apply: precise fixation control, a sufficient number of trials, a reasonable sample size, and appropriate statistics. This procedure requires additional time and effort from examiners and participants. For neurological participants, prolonged testing time can lead to fatigue, loss of motivation and hence reduced performance. For examiners, preparation of experiments, data acquisition and analysis are extended considerably (see for example Danckert & Culham, 2010). On the basis of these considerations, it is not surprising that blind-spot testing is not always performed even in studies where target configurations are chosen likely to produce light-scatter artefacts. Moreover, studies conducting blind-spot tests used very small sample sizes, ranging from just one to four participants. In the literature about RVCs, the spectrum of experimental paradigms is quite impressive ranging from the saccadic localization of dots (Weiskrantz et al., 1974) to the discrimination of emotional faces (Ajina et al., 2020). However, only few paradigms, mostly simple detection, have been tested for light-scatter artefacts. This means that currently we have no reliable estimates for light-scatter-safe stimulus conditions for many of the most commonly used RVC-paradigms. In the absence of published reliable light-scatter-safe procedures, each researcher is forced to test the light-scatter propensity for their own chosen stimulus configuration. This is laborious and time-consuming and therefore frequently neglected. In our current study, we wish to address this problem by developing and evaluating light-scatter-safe procedures for three RVC-paradigms.

I.3. Testing light scatter

The aim of the current study was to measure the impact of light scatter in three paradigms used frequently to test RVCs in patients with HVFD. For each paradigm, we applied the blind-spot method to control for intra- and extra-ocular sources of light scatter. All testing was done in a medium-sized sample of healthy participants using contemporary devices and employing reliable measures for monitoring and controlling eye-movements. We hope to provide useful experimental paradigms and target-background combinations that will allow other researchers to carry out RVC-examinations without having to worry about light-scatter artefacts.

Initially, we carried out a temporal two-alternative forced choice (2AFC) task. Participants indicated the interval in which a target was presented (e.g. Ajina et al., 2015). Next, we measured movement direction discrimination (MDD) of a random dot target which is often used in recent restoration trainings (e.g. Saionz et al., 2020). Last, we acquired data of a redundant target paradigm (RTP). Thereby, reaction times in response to two targets are compared to reaction times in response to one target. The redundant target effect is present if reaction times are shorter in the condition with two stimuli (Raab, 1962). RVC is present when the second redundant target is presented within the blind visual field of HVFD-patients and reaction times are still reduced (Marzi et al., 1986).

For the current study, we controlled the before mentioned methodological issues as best as possible. Response biases are most critical in simple detection paradigms (Cowey, 2010). Hence, we chose a temporal 2AFC task which also measures detection but is less affected by response criteria (Cowey, 2010). As the RTP measures RVC indirectly, there are no biases due to response criteria. Furthermore, we recorded gaze behavior precisely and repeated all trials in which gaze position deviated more than 1° from the center of the fixation symbol.

In each paradigm, we compared performance in the sighted field with performance in the natural blind spot. For the temporal 2AFC task and the MDD task, we tested accuracy against chance level. If performance is above chance for targets presented in the blind spot, light scatter was sufficient to solve the task. Regarding the RTP, if reaction times are reduced, even though the redundant target is presented within the blind spot, light scatter influenced the performance.

On the basis of the literature reviewed above, we started with two assumptions: (1) bright targets on a dark background are prone to light scatter; (2) this effect is enhanced in a dark room. To find the optimal light-scatter-free target conditions, we varied the target-background contrast and also the room-illumination conditions. We first used the temporal 2AFC task to look for light-scatter artefacts. To test the suitability of our task for detecting light-scatter

artefacts, we started with white targets on a black background in darkness (WB). To allow dark adaptation of the eyes, we included a pause of 15 minutes in the dark room prior to the experiment. Using this condition, we expected to see clear light-scatter artefacts, i.e. effects of light scatter that were strong enough to influence behavior in our experimental setup. Next we opted for an intermediate target, i.e. a white target presented on a mid-grey background in an illuminated room (WG). Finally, as a target with low light-scatter probability we chose a black target presented on mid-grey background in an illuminated room (BG). The first two conditions were used only in the temporal 2AFC task. The last condition was examined in all three paradigms.

I.3.1. General Methods

I.3.1.1. Sample

Participants were recruited via flyer, notice boards, emails and personal contacts at the LMU Munich. Exclusion criteria were diagnosis of psychiatric, neurological or ophthalmologic diseases. Participants got a compensation of 8€ per hour or course credit. We invited 25 healthy participants to our study. Due to problems with calibration, two participants were excluded (*so*, *zk*). Another participant was excluded due to an illness between test sessions (*dk*). Moreover, one participant dropped-out after the first perimetry (*jd*). The resulting sample of 21 participants had a mean age of 25.48 years (SD = 4.27) and 6 participants were male. 19 participants were right handed and 16 participant's dominant eye was the right eye. The sample consisted mostly of students (N = 18). From the initial perimetry, the borders of the blind spot were retrieved by two raters. If raters disagreed, the more conservative value, i.e. the value leading to smaller size of the blind spot, was chosen. Following this, the blind spots had on average a width of 5.29°±0.83° and a height of 6.82°±1.03°.

I.3.1.2. Procedure

First, participants read the study information, signed the consent sheet and filled out the demographic questionnaire. Second, the dominant eye of each participant was tested using the whole-in-card test. The dominant eye was used for testing. If there were issues with calibrating the eye tracker, the non-dominant eye was used. The other eye was covered with an eye patch. Initially, the area of the blind spot and hence the individual target positions were defined via a custom-made perimetry. Testing was done in two sessions and the perimetry paradigm was conducted each time at the beginning of the session. In the first session, the long version of the perimetry was used in which all test points within the blind spot were measured. In the second session, a shorter perimetry version which tested only positions at the border zone of the blind spot was administered. Each participant carried out five tasks: the MDD task, the RTP, and three versions of the temporal 2AFC task. The versions of the temporal 2AFC test were: White targets on black background tested in

darkness (WB); white targets on grey background in an illuminated room (WG); black targets on grey background in an illuminated room (BG). Before the WB-version, participant's eyes were dark adapted for 15min. Therefore, the WB-version was tested last in the second session. All other tasks were conducted in a pseudorandomized order.

I.3.1.3. Aperture

All tasks were programmed and run with Matlab (Version R2016b) using the Psychophysics Toolbox (Version 3.0.13; 6. Juli 2016; Brainard, 1997; Kleiner et al., 2007). Stimuli were presented on a BenQ LCD-Screen with a frame rate of 144 Hz, a size of 532.3 x 298.8 mm and a resolution of 1920 x 1080 pixels. To keep a distance of 725 mm between the nasion and the center of the screen, the head was stabilized via a head- and chinrest. This setting lead to a screen size of 32.8° x 18.5°. Responses were made via a PST Serial Response Box. All sizes of the stimuli are given in degrees of visual angle (°) using the distance of the nasion to the center of the screen as a reference (1° = 45.67 pixel = 12.65mm). As the distance from the nasion to stimuli with a higher eccentricity increases, there is a small bias. Colors had the following luminance values: black = 0.0 cd/m^2, grey = 58 cd/m^2, white = 247 cd/m, blue = 24 cd/m, red = 63 cd/m.

The fixation symbol in all experiments was of the *abc* type adapted from Thaler et al. (2013) which is composed of a bull's eye and a cross hair (outer diameter: 1°; inner diameter and line width: 0.2°). If not otherwise stated, this fixation symbol was black and presented at the center of the screen during the whole course of the tasks. Participants were instructed to fixate continuously on the fixation symbol. Fixation behavior was controlled monocularly with an EyeLink 1000 Plus (SR Research) recording with 2000Hz. At the beginning of each experiment, the eye tracker was calibrated and validated with a 9-point-pattern. The calibration and validation was repeated if participants moved the head during the pauses. Additionally, there were fixation checks implemented during the tasks indicated by a blue fixation symbol (800ms). The program calculated if gaze positions were within the fixation window (maximum distance of 1° from the center of the screen) during the fixation checks. If not, the experimenter had the possibility to recalibrate. Deviations of fixation could happen because of drift, slight head movements, unstable fixation or blinks. Analysis of saccades, fixations, and blinks was done by the EyeLink parser. Saccade onset was determined by either a velocity of 30°/s or by an acceleration of 8000°/s^2 and an eye movement of at least 0.1°.

I.3.1.4. Analysis

Descriptive and inference statistics were calculated using R (R version 3.6.1 (2019-07-05). Assumption of normality distribution was tested with the Shapiro-Wilk test. If data was not normally distributed, non-parametric tests were used. To test if accuracy in the blind-spot

conditions was at the chance level of 50%, we used the exact Wilcoxon signed rank test with correction for tied observations (function '*wilcox.exact*' in R package '*exactRankTest*', Hothorn and Hornik (2015)).

To compare two conditions, we used paired t-tests or the exact Wilcoxon signed rank test as the non-parametric alternative. To compare multiple conditions, a repeated measures analysis of variance (ANOVA; non-parametric alternative: Friedman ANOVA) with pairwise comparisons was calculated. Mauchly's test was used to check the assumption of sphericity. If the assumption of sphericity was violated, we applied the Greenhouse Geisser correction. We will report partial eta-square as effect size for ANOVAs, Cohens' d for t-test and r for Wilcoxon test (estimated by transforming the p-value into a z-value and then using the formula r = z/sqrt(N) with N = total sample size; Field et al., 2012, page 665). Values in brackets always refer to arithmetic mean and standard deviation (M±SD).

I.3.2. Experiment 1: Temporal 2AFC task

I.3.2.1. Methods

At the beginning of the test, there were 10 practice trials which could be repeated if necessary. Pauses were included every 50 trials with a self-determined duration. Participants were instructed to indicate in which time interval a target was present. A trial started with a one-second pause. Every 20 trials, a fixation check followed (see section I.3.1.3). Subsequently, there were two target intervals of 993.6ms defined by the fixation color: 1. interval with red fixation target, 2. interval with blue fixation target. Additionally, there were acoustic signals with a duration of 100ms. The beep at the beginning of the first and at the end of the second interval had a carrier frequency of 800Hz. The beep between the intervals had a carrier frequency of 500Hz. In one of the intervals, the target (filled circle, 2° diameter) was presented for 151.8ms with a random onset time between 300-700ms. After the second interval, participants had a maximum of 10000ms to respond. The first key indicated the first interval and the second key indicated the second interval. There were three individually defined target positions. The first target position was located within the blind spot. Next the center of the control positions was set 2° above and 2° below the border of the blind spot (Figure I.1). Control positions were at the same horizontal coordinate as the blind-spot position. In total, there were 120 trials, 80 for the blind-spot position and 20 trials per control position. The order of trials was randomized. After each trial, the recorded gaze behavior of both intervals was tested for stable fixation. If the gaze data was outside the fixation window for more than 250ms, the trial was repeated at the end of the experiment. The test was administered in three color versions: White targets on black background tested in darkness (WB); white targets on grey background in an illuminated room (WG); black targets on grey

background in an illuminated room (BG). The WB-version contained a 15-minute dark adaptation period before the test.

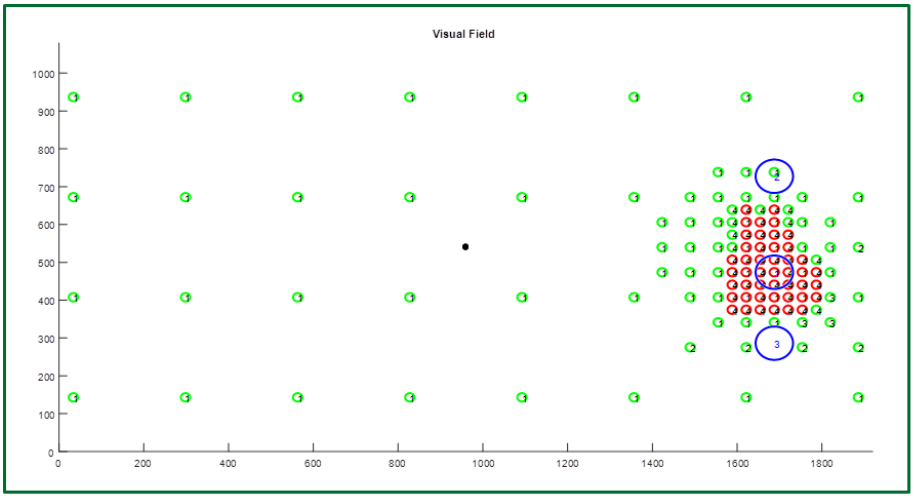
I.3.2.2. Results

Concerning the temporal 2AFC task, we had to exclude four participants in the WB-version and one participant in the BG-version due to issues with eye tracking calibration. Additionally, participant *vn* had to be excluded due to input errors for target coordinates. For the same reason, we excluded participant *ca* from the analysis of the WB-version and participant *qa* from the analysis of the BG-version. Moreover, there was only one dataset for participant *ip* for the BG-version of the task.

As a result, there was a sample of 14 participants for the WB-version (age: 27.14±4.24 years), 18 participants for the BG-version (age: 25.61±4.49 years), and 19 participants for the WG-version (age: 25.79±4.35 years). On average, the blind-spot position was at a horizontal eccentricity of 16.32±1.29° and 1.32±0.68° below the horizontal midline. The upper control position was on average at 4.18±1° above the horizontal midline. The lower control position was on average at -6.59±0.96° below the horizontal midline. The number of repeated trials due to fixation break were 53.07±48.70 (range: 1 to 142) for the WB-version, and 32.37±27.91 (range: 1 to 98) for the WG-version, and 33.00±25.59 (range: 1 to 79) for the BG-version. Excluding trials with fixation break left all participants with 120 trials per luminance version of the task.

Figure I.1

Example for target positions in the temporal 2AFC task



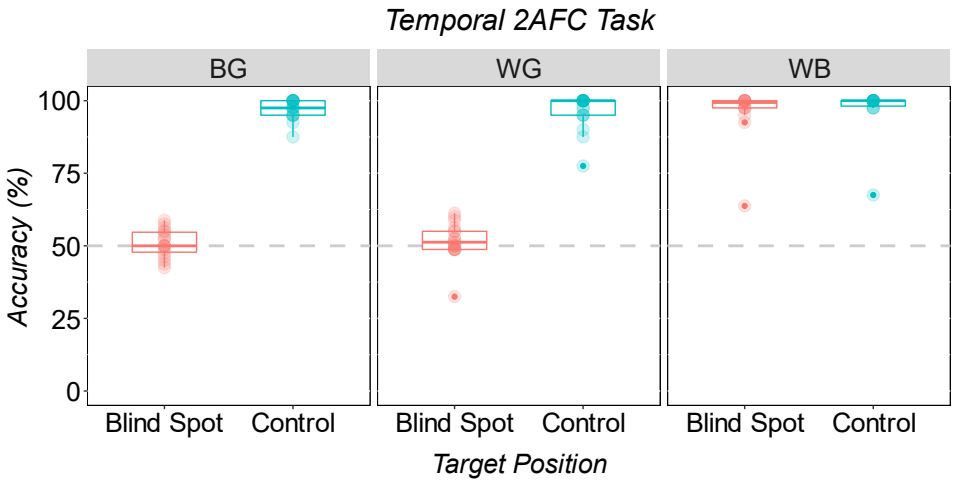
Note. Coordinates indicated in pixels; Green circles: Perimetry targets detected correctly; Red circles: Perimetry targets missed; Blue circles: Target positions of temporal 2AFC task; Black numbers: Numbers of perimetry step; Blue numbers: Numeration of target positions; 2AFC = Two alternative forced choice.

Results (Figure I.2) showed significant differences from the 50% chance level for the following conditions: WB blind-spot condition (V = 105, p <.001, r = -1.03); WB control condition (V = 105, p <.001, r = -1.03); WG control condition (V= 190, p <.0001, r = -1.06); BG control condition (V = 171, p <.0001, r = -1.05). Differences were not significant for WG blind-spot condition (V = 95, p = .170, r = -0.31) and BG blind-spot condition (V = 65, p = .452, r = -0.18). The pattern of results shows high accuracy values for the control position in all luminance conditions. When white targets were presented on a black background in darkness, accuracy values were also high in the blind-spot position. In contrast, accuracy was at chance level when black or white targets on a grey background were presented within the blind spot.

To sum up, the task was very easy when targets were presented at control positions reaching almost ceiling at 100% accuracy. Light scatter in the WB-version for targets within the blind spot was strong enough to increase performance to the same level as at the control position. These results illustrate that light scatter is a highly important factor that could lead to behavioral artefacts. In contrast, performance was at chance level for targets within the blind spot in the BG- and WG-version of the task. Hence, there are no light-scatter artefacts if targets are black or white on a dark background in an illuminated room.

Figure I.2

Accuracy values in the temporal 2AFC task



Note. Boxplots of accuracy values per luminance condition and target position. BG: Black targets on a grey background; WG: White targets on a grey background; WB: White targets on a black background in darkness with previous dark adaptation. 2AFC = two alternative forced choice.

I.3.3. Experiment 2: Movement direction discrimination

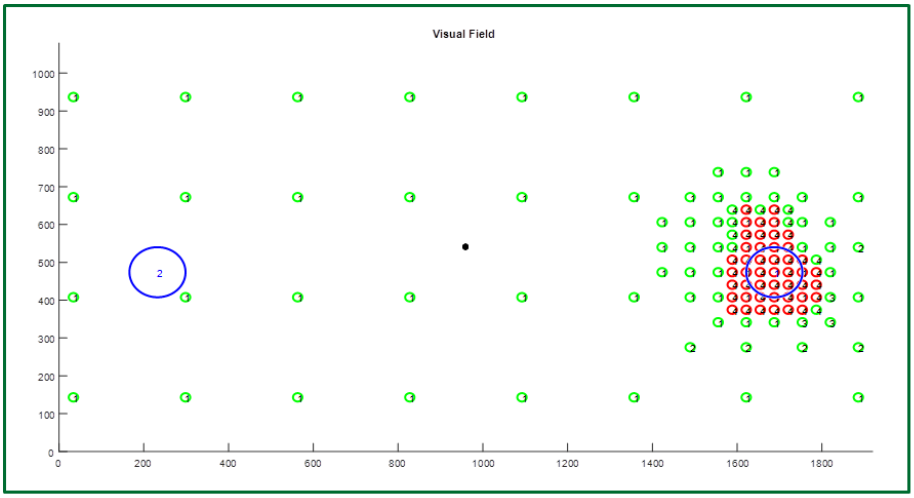
In experiment 2, we wanted to test whether changes in luminance are enough to discriminate moving targets within the blind spot. All 21 participants were included in the analysis of this task (see section I.3.1.1).

I.3.3.1. Methods

There were 10 practice trials at the beginning of the task. Practice trials could be repeated if necessary. A pause was suggested every 50 trials with a self-paced duration. Participants were instructed to report the movement direction of a random dot cloud (100% coherence). The dots were black on a mid-grey background (BG). Movement direction of the random dot cloud (aperture 3° diameter) was either up (first key) or down (second key). There were three dots per square degree with a dot diameter of 0.1°, a life time of 250ms, and a speed of 15° per second. Positions of the random dot cloud were set individually: (1) within the blind spot and (2) mirrored horizontally to the other hemifield (Figure I.3). There were 80 trials for the position in the blind spot and 40 trials for the control position. Order of trials was randomized. Every 20 trials, there was a fixation check. Between trials, there was a short pause of 1s. Start (800Hz carrier frequency) and end (500Hz carrier frequency) of the target interval were indicated by an acoustic signal (duration = 100ms). One trial consisted of an initial time period of 248.4ms, the target presentation for 500ms, and another time period of 248.4ms. Afterwards, participants had a maximum of 5000ms to respond.

Figure I.3

Example for target positions in the movement direction discrimination task



Note. Coordinates indicated in pixels; Green circles: Perimetry targets detected correctly; Red circles: Perimetry targets missed; Blue circles: Target positions for movement direction discrimination task; Black numbers: Numbers of perimetry step; Blue numbers: Numeration of target positions.

Participants were instructed to press the first key for the upward and the second key for the downward direction. During the target interval, the fixation symbol color was black, otherwise it was blue. After each trial, the program checked whether the gaze position during the target interval was within the fixation window. If not, the trial was repeated at the end of the test.

I.3.3.2. Results

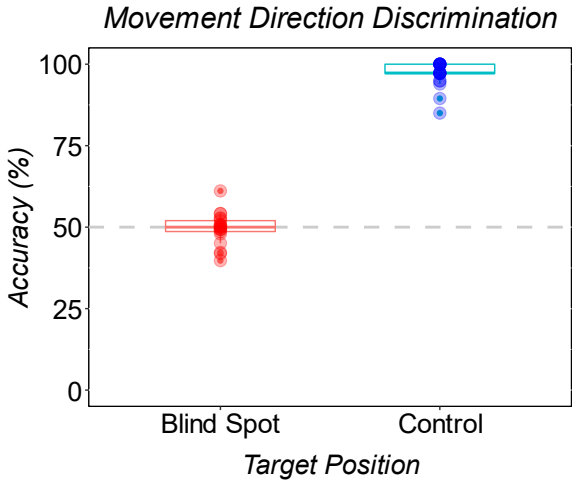
In 16 out of 21 participants, the right eye was tested (blind spot in right hemifield). The blind-spot position was at a mean horizontal eccentricity of 16.22°±1.24° and on average 1.40°±0.86° below the horizontal midline. Due to fixation breaks, an average of 56.10 (SD = 45.21, range 1-144) trials had to be repeated. Excluding fixation broken trials led to 120 trials per participant.

Next, we analyzed the accuracy values per target position averaged across movement directions (Figure I.4). The accuracy in the blind-spot position (49.65±4.68%, median = 50%) was significantly lower than in the control position (97.09±3.88%, median = 97.30%; t(20) = -37.41, p<.0001, d = -8.16). Following this, we tested whether accuracy values per target position were above 50% chance level. Accuracy for targets within the blind spot was not significantly different from 50% (V = 87, p = .479, r = -0.15). In contrast, accuracy for targets at the control position was significantly higher than 50% (V = 231, p <.0001, r = -1.10). Results indicate that participants had an accuracy at ceiling when responding to targets at the control position and guessed when targets were at the blind-spot position.

Hence, potential changes in luminance or light scatter were not enough to discriminate the movement direction of a black random dot cloud within the blind spot.

Figure I.4

Accuracy values in the movement direction discrimination task



Note. Boxplots of accuracy values per target position.

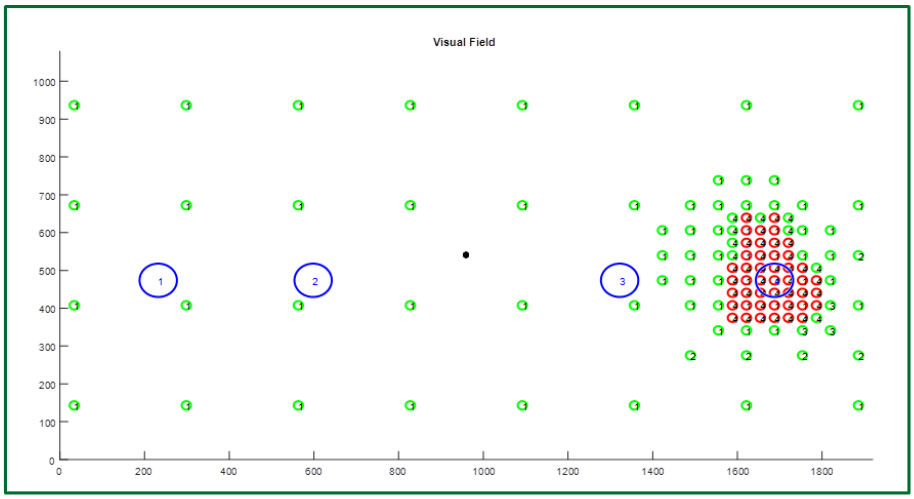
I.3.4. Experiment 3: Redundant target paradigm

I.3.4.1. Methods

The task started with 10 practice trials which could be repeated if necessary. There were pauses included every 50 trials. The duration of pauses was self-paced. Targets were black circles with a diameter of 2°. There were four target positions individually defined by the area of the blind spot. The first position was centered within the blind spot. The second position had the same vertical coordinate and half the horizontal coordinate in reference to the center of the screen. Mirroring the first and second position to the other horizontal hemifield produced the third and fourth positions respectively (Figure I.5). The target configurations were as follows: Double unilateral without blind spot, double unilateral with blind spot, double bilateral without blind spot, double bilateral with blind spot, and three single positions except the blind-spot position. These were combined to double, blind spot, and single target conditions (Figure I.6). The experiment consisted of 180 trials. Each double configuration was tested in 30 trials and each single configuration was tested in 20 trials resulting in 60 trials for each target condition. The order of the tested target configurations was randomized. Between trials, there was a 1000ms pause. Every 20 trials, there was a fixation check. A trial started with an acoustic signal (100ms, 800Hz carrier frequency). After a variable time interval of 100-500ms, targets were presented for 151.8ms. Afterwards, participants had another 1350ms to respond. Participants were instructed to press the first button as fast as possible if they detected one or two black circles. After a trial, the gaze data starting from 100ms before to 100ms after target presentation was tested for a stable fixation. If there was gaze data outside the fixation window, the trial was repeated at the end of the experiment.

Figure I.5

Example of target positions for the redundant target paradigm



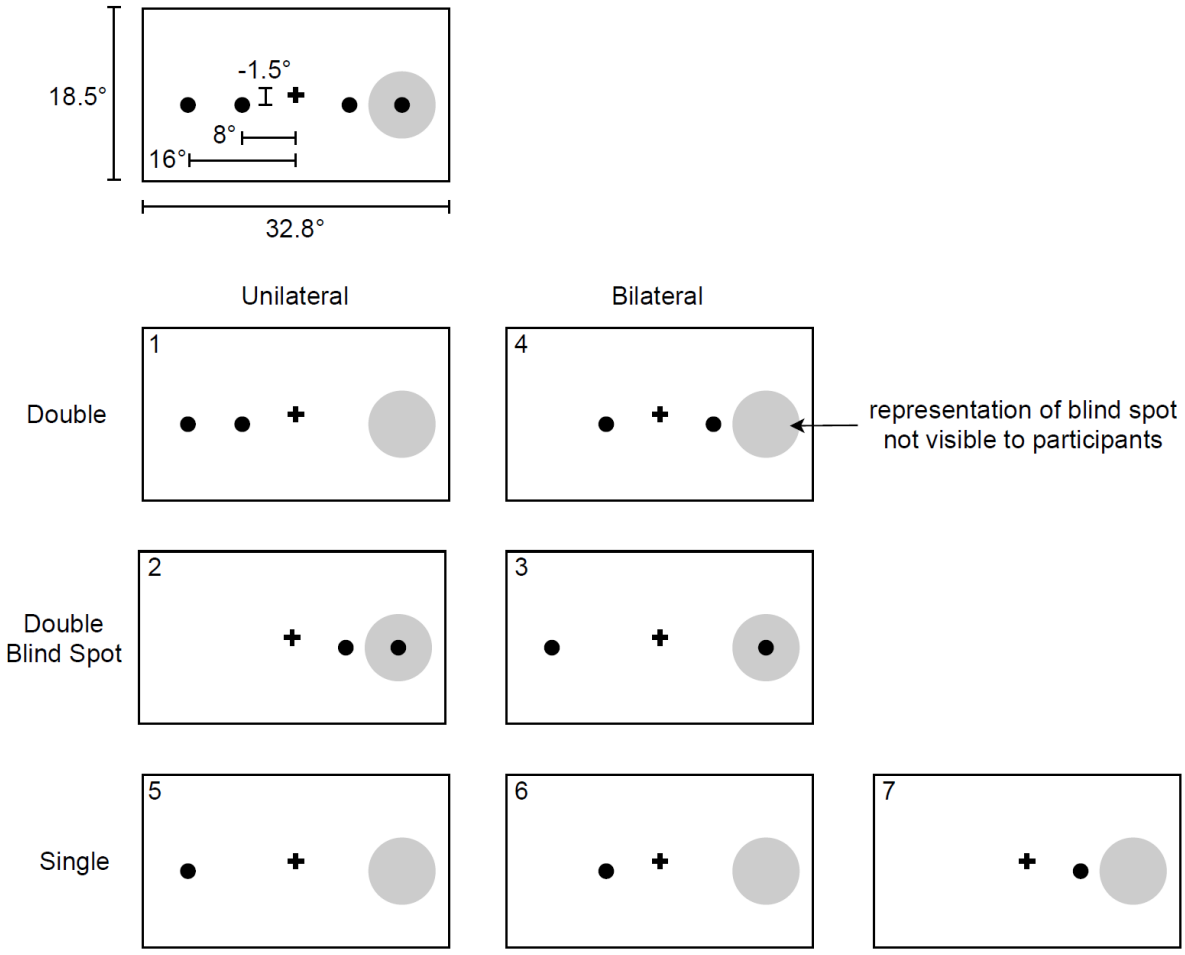
Note. Coordinates indicated in pixels; Green circles = perimetry target detected correctly; Red circles = perimetry target missed; Blue circles = target positions; Black numbers = numbers of perimetry step; Blue numbers = numeration of target positions.

I.3.4.2. Results

For the redundant target paradigm, there was no data of one participant (*pj*). In one participant (*ss*), there was a particularly high number of misses (83 trials). Hence, we excluded this participant from analysis resulting in a sample of 19 participants (age: 25.37±4.41 years). In four participants, the blind spot was in the left hemifield (left eye tested). The individually defined target position within the blind spot had a mean horizontal eccentricity of 16.08°±1.17° and was on average 1.44°±0.86° below the horizontal midline. The number of trials repeated due to fixation breaks ranged between 0-100 (19.85±25.24). Trials with fixation breaks as well as trials without a response (miss trials) were excluded. Participants had a very low number of misses (1±1.11 trials; max = 3 trials). Subsequently, we excluded false positive trials (responses before target onset, 3.74±4.29 trials, max = 15 trials) and trials with reaction times below 100ms (2.79±3.07 trials, max = 9 trials) and above mean + 2.5*SD per participant (3.63±1.57 trials, max = 7 trials). This resulted in an average number of 93.80±3.89% of 180 planned trials (minimum = 83.89%) with at least 75% of trials per target configuration.

Figure I.6

Example of target positions and target configurations of the redundant target paradigm



Note. Numbers at the upper left side refer to the numeration of target configurations and were not visible to the participants. The fixation symbol has been the *abc* symbol (Thaler et al., 2013). The fixation symbol is simplified in the figure for better visibility. Sizes are indicated in degree of visual angle.

Starting with the statistical analysis, we calculated the mean reaction time per participant per target configuration. Target configurations were then averaged for the three target conditions: Blind spot, double, or single. First, we tested whether we could replicate the classical redundant target effect to validate our experimental manipulation with the blind spot. Reaction times to double targets (267.58±37.33ms) were significantly faster than reaction times to single targets (274.24±33.99ms; one-sided paired t-test: $t(18) = 2.31$, $p = .016$, $d = 0.53$; Figure I.7). Hence, we replicated the redundant target effect.

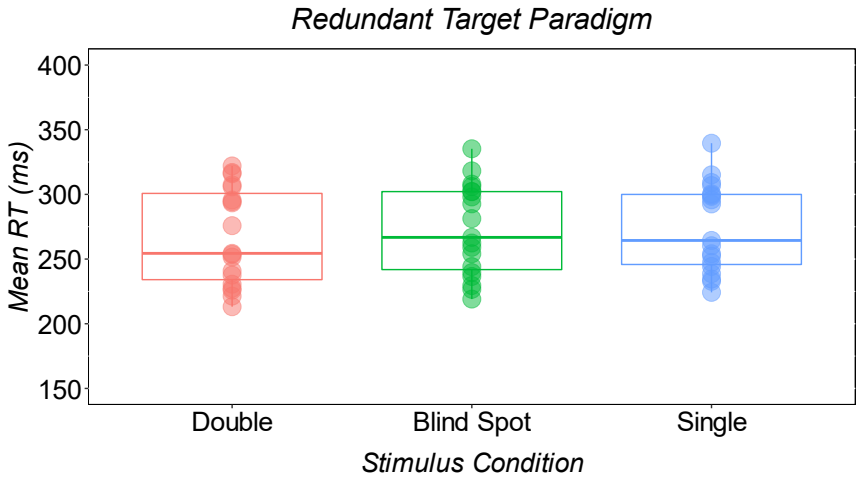
Next, we calculated a three-way ANOVA with factor target condition including the blind-spot condition. The main effect target condition was significant ($F(2, 36) = 4.02$, $p = .027$, $p\text{-eta}^2 = 0.18$). Pairwise comparisons with Bonferroni correction showed marginal significant differences between the double and single condition ($t(18) = 2.31$, $p = .098$) and between

double and blind-spot condition (t(18) = 2.50, p = .070). Reaction times for the blind spot and the single condition were not different (t(18) = 0.64, p = 1). Results showed that the target condition influenced reaction time and that this effect is driven by the reduced reaction time in the double condition. Importantly, there was no difference in reaction times between the blind spot and single condition indicating that the second target in the blind spot was not processes and did not influence response behavior.

Our results showed, as expected, a replication of the redundant target effect. Furthermore, we see that a target in the blind spot does not reduce the reaction times.

Figure I.7

Mean reaction times in the redundant target paradigm



Note. Box plots of mean reaction times per stimulus condition. RT = reaction time; ms = millisecond.

I.4. Discussion

Light scatter is a methodological problem in testing residual visual capacities (RVCs) in the blind visual field of patients with homonymous visual field defect (HVFD) following an acquired brain injury (Campion et al., 1983). If targets are presented within the blind visual field, light could stray to retinal parts corresponding to the sighted field. The visual information from light scatter can be used for behavioral responses and hence increase performance. The most powerful way to test light scatter is presenting targets within the blind spot (Cowey, 2010). Using the blind-spot effects of intra- and extra-ocular light scatter can be measured. In the review, we showed that the strength of light scatter is increased by increasing target luminance, increasing target size and decreasing distance between target position and visual field border. For many paradigms, including detection, orientation discrimination and localization of targets, light scatter can suffice to solve the task. Unfortunately, up to now the influence of light scatter has been measured in very small

samples (at most four participants) and often with experimental equipment that is no longer in use. This means the findings from such studies are not representative and cannot be transferred to current psychophysical setups and new samples of observers. Even though it is known that light scatter is an issue (particularly when bright targets on a dark background are used) a number of recent studies did not address the issue. One reason for this might be that testing light scatter is laborious and time-consuming.

Hence, it would be helpful for future studies to have a pool of stimuli and paradigms which demonstrably do not elicit light-scatter artefacts. We started this pool by testing three paradigms often used to study RVCs in HVFD-patients. To investigate light scatter, we used the natural blind spot in a group of young, healthy participants.

First, we established that our testing paradigm could detect the effects of light-scatter. For this, we used a temporal 2AFC task and white targets presented on black background in a dark room (WB). In this condition, the detection rate reached almost ceiling at 100% (temporal 2AFC). In patients with HVFD, such a high accuracy within the blind visual area could be misinterpreted as RVC. However, we know that humans are physiologically blind within the natural blind spot (Jonas et al., 1991). Following this, any above chance performance must be attributed to light scatter. As a consequence, we thereby provided further evidence that light scatter is a crucial confound in studies on RVCs.

Fortunately, there are also luminance conditions that do not produce light-scatter artefacts. White (WG) as well as black targets (BG) on a grey background were tested in an illuminated room. For WG presented to the blind spot, detection accuracy was at chance level. For BG presented to the blind spot, accuracy was at chance level for detection as well as for the discrimination of movement direction. Furthermore, BG did not reduce reaction times in the redundant target paradigm. Thus, the results confirmed that the BG condition avoids light scatter in all three of our RVC-paradigms.

While the findings from our study is in line with previous reports (see for example: Danckert & Culham, 2010; Huxlin et al., 2009), it goes beyond those studies in several respects. We did not only measure single participants but a group of 21 healthy young controls. While designing the study, we chose three paradigms frequently used to investigate RVCs in HFVD-patients to offer a broad application for future research. As we conducted the experiments on a modern LCD monitor that is quite typical for the kind of setup currently used in most psychophysics labs, the findings from our study should also transfer to experiments run in most modern perception labs. Furthermore, we selected paradigms reducing or avoiding the problem of biased response criteria (Cowey, 2010). Also, during testing, eye movements were recorded with high temporal and spatial resolution excluding all

trials with a gaze deviation of more than 1° from the center of the fixation symbol. This ensured that our targets were restricted to the blind spot.

Our study also has some limitations. We measured light scatter only for three luminance conditions and only for three paradigms. Regarding the luminance condition, we chose two extremes: White targets on a black background in darkness and black targets on a grey background in an illuminated room. Clearly there are lots of other conditions and other possible combinations. Consequently, we can only make claims about these three luminance conditions. If studies use other parameters, they have to re-evaluate the impact of light scatter.

Furthermore, we tested only young healthy participants. In RVC-studies, participants are usually above 50 years. However, we argue that our results are generalizable to the higher age group. Young participants have full vision and high attentional capacities. If healthy, young participant show no light-scatter artefacts, it is unlikely that older patients with a neurological disease and other age-related impairments are able to use the weak visual information coming from light scatter for their responses.

Besides, the blind-spot method itself has certain limits. The natural blind spot can only be measured monocularly. In contrast, most tests for RVCs are conducted binocularly. Additionally, the size of testable targets is limited to the size of the blind spot. In our experiment, the size of the blind spot was 6.8° vertically and 5.3° horizontally. This was slightly bigger than in previous studies. Cowey (2010) stated that the blind spot subtended approximately 6° x 4° in his monkey (Cowey & Weiskrantz, 1963) and human studies (Stoerig & Cowey, 1991). Importantly, in our measurement of the blind spot, its shape was often irregular being broader in certain parts and far from a perfect circle. Hence, the maximum size of a symmetric target fitting within the blind spot is often smaller than the maximum height and width of the blind spot. In addition, due to the inherent inaccuracy of blind-spot testing, it is advisable to keep a safe distance between the border of the target and the border of the blind spot. In our study, this inaccuracy resulted from an eye tracking imprecision of up to 1.5°, a fixation window of 1°, and from the spatial resolution of test points with a maximum of 0.5°.

Consequently, targets need to be relatively small to test light scatter with the blind spot. In the current study, we successfully used target diameters of 2° and 4°. In contrast, targets for RVCs are often bigger, for instance 10° squares in Persaud et al. (2011) or a 20° window with random dots in Alexander and Cowey (2013). Training studies used circular targets with a diameter of 6° (Sahraie, Trevethan, Macleod, Weiskrantz, et al., 2013) or 6° to 12° (Huxlin et al., 2009). Importantly, the size of targets can be crucial for RVCs. Weiskrantz et al. (1974) varied the size of targets within the blind visual field systematically in patient *DB*. Only if

letters (X versus O) or lines (horizontal versus vertical) had a size of 12° or better, accuracy for discrimination was above chance level. Importantly, targets were black on a white background in each case making light scatter an improbable explanation for the size effect. Similarly, color discrimination depended on the target size (Brent et al., 1994). With a 40° diameter colored field, patient *GY* discriminated wavelength by only 30nm in the best case. However, if the diameter was reduced to 10°, the discrimination was at chance level even for large wavelength differences. Interestingly, there was a white field from the edge of the colored target into the ipsilesional half-field making an influence of light scatter unlikely (Brent et al., 1994).

Early studies used control patients with pre-geniculate lesions (PGL) having extensive visual field defects to measure light-scatter artefacts (e.g. Perenin & Jeannerod, 1978). At first glance, this could be a solution to test light-scatter artefacts of larger targets. It was hypothesized that the neuronal correlate of RVCs are *intact*, extrastriate pathways bypassing the primary visual cortex (V1), e.g. the pathway from superior colliculus to inferior pulvinar (Perenin, 1978). A lesion solely damaging V1 would not affect these pathways allowing RVCs. In contrast, a pre-geniculate lesion does affect these pathways. Hence, visual field defects due to pre-geniculate lesions were thought to be absolute scotomas, like the natural blind spot. However, it has been shown later that PGL-patients can also have RVCs, meaning that surviving fibers can be sufficient to mediate RVCs (Wüst et al., 2002). Interpreting the result of the light-scatter test would hence have the same problem as in HVFD patients. If there is a negative finding in the light-scatter test, light scatter is unlikely. However, if there is a positive finding, it could be evidence for RVCs or for light scatter. This insecurity makes it less conclusive than blind-spot testing. Furthermore, recruiting and testing suitable PGL-patients is even more laborious than blind-spot testing in healthy participants.

To conclude, limitations of target size due to blind-spot testing have to be considered and balanced against its advantages. Clearly, whenever possible light-scatter artefacts should be avoided in RVC-studies since this improves the validity of research results, thereby leading to more reliable experimental data and more effective treatment approaches.

The role of light scatter in experimental work on blindsight seems obvious. Research on blindsight and RVCs is of great theoretical importance. It can inform us about the functional organization of the visual system, the nature of visual awareness, the brain structures associated with awareness and the functional role of visual awareness in the control of behavior (e.g. Celeghin et al., 2015; Mazzi et al., 2019; Weiskrantz, 1999). However, unless an experiment can clearly distinguish between RVCs (i.e. responses based on signals from the blind area) and light-scatter artefacts, findings from such studies will shed no light on any one of those issues. However, it may be less obvious that light scatter or rather the failure to

take light scatter into account can seriously limit the relevance of studies aimed at developing training procedures to help patients with visual field defects. To be more specific, if light scatter during training is not prevented, patients might come to rely on light-scatter information. Rather than learning how to interpret signals from their blind field, they might learn to interpret the light straying from their blind into their sighted visual field. But as we have seen above, the usefulness of light-scatter information is very dependent on certain conditions, such as target-background contrast, illumination condition, size of targets, distance between target and blind-field border. Given this condition-dependency, it can be expected that when light-scatter interpretation contributes to training benefits, those benefits are unlikely to transfer to untrained tasks and untrained observation conditions.

Regarding treatment options, it is possible to distinguish between several approaches (for a review see Howard & Rowe, 2018). One approach attempts to restore visual functions. In the classical visual restitution training (VRT), targets are static and the training aims to increase the area of the sighted visual field (e.g. Marshall et al., 2010; Zihl & von Cramon, 1979). Another type of restorative training aims to improve sensitivity within the HVFD (visual sensitivity training, VST; e.g. Saionz et al., 2020; Trevethan et al., 2012), for instance by training the discrimination of moving targets. In both types of training, the probability for light-scatter artefacts is high if bright stimuli are presented on a dark background. In VRT, targets are usually bright white squares on a black background (Bergsma & van der Wildt, 2010; Marshall et al., 2010). In VST, light scatter is similarly problematic when, as moving targets, white dots on a black background are used (Larcombe et al., 2018). The issue of light scatter is aggravated in restitution trainings stimulating the border zone of the HVFD (e.g. Marshall et al., 2010) because light scatter increases with decreasing distance between target and sighted visual field. Following this, it would be necessary to control light-scatter artefacts in restorative training studies. But it is not clear that this problem is sufficiently addressed. Some studies simply do not test for light scatter (e.g. Larcombe et al., 2018). Other studies do test for light scatter but provide so little information about their test procedures and their analysis of the test findings that it is impossible to determine whether light-scatter has been avoided (e.g. Bergsma & van der Wildt, 2010). In yet other studies, it is simply not clear whether the procedures used for testing restored visual function are vulnerable to light scatter artefacts (e.g. Marshall et al., 2010). When patients improve in the training task, it is thus not possible to distinguish between a true restoration of sight and an improved utilization of light-scatter information. If improvement would only be based on better utilization of light scatter, the training effects are unlikely to improve performance in activities of daily living (ADL). Interestingly, there are only few reports describing the transfer of restoration training effects to ADL (Howard & Rowe, 2018). For instance, Gall and Sabel (2012) measured transfer to reading abilities. However, there was no control group making it

unclear whether the improved reading reflects the effects of training or the effects of spontaneous recovery (Gall & Sabel, 2012).

In brief, light scatter is particularly critical in the area of restorative trainings. On the one hand, restorative trainings often used stimuli likely to elicit light scatter. On the other hand, control procedures for light-scatter artefacts are largely missing. The existence of light-scatter artefacts in training procedures and the adaptation to such signals during training might explain why patients fail to improve in ADL despite impressive improvements found during the training.

I.4.1. Conclusion

In summary, light scatter can influence behavioral results of RVC-tests in patients with HVFD after an acquired brain injury. As a consequence, studies intended to measure or improve RVCs have to test light scatter to rule out a potential bias. Unfortunately, this is still no default procedure in RVC-research. To avoid light-scatter artefacts, authors have to invest time and effort for every new experimental setup. In this study, we described and evaluated a stimulus configuration that reliably avoids light scatter in three commonly used RVC-paradigms. In future, researchers may use these stimulus and illumination conditions for their studies, thereby avoiding light-scatter artefacts without the need to perform their own blind-spot tests. We hope that the availability of such paradigms will help to ensure that light-scatter-safe procedures will be adopted more widely in future research on RVCs.

I.5. References

Ajina, S., Pestilli, F., Rokem, A., Kennard, C., & Bridge, H. (2015). Human blindsight is mediated by an intact geniculo-extrastriate pathway. *Elife*, *4*. https://doi.org/10.7554/eLife.08935

Ajina, S., Pollard, M., & Bridge, H. (2020). The Superior Colliculus and Amygdala Support Evaluation of Face Trait in Blindsight. *Frontiers in neurology*, *11*, 769. https://doi.org/10.3389/fneur.2020.00769

Alexander, I., & Cowey, A. (2013). Isoluminant coloured stimuli are undetectable in blindsight even when they move. *Experimental brain research*, *225*(1), 147-152. https://doi.org/https://doi.org/10.1007/s00221-012-3355-6

Azzopardi, P., & Cowey, A. (1998). Blindsight and visual awareness. *Consciousness and Cognition*, *7*(3), 292-311. https://doi.org/10.1006/ccog.1998.0358

Azzopardi, P., & Hock, H. S. (2011). Illusory motion perception in blindsight. *Proceedings of the National Academy of Sciences*, *108*(2), 876-881. https://doi.org/10.1073/pnas.1005974108

Barbur, J., Harlow, A. J., & Weiskrantz, L. (1994). Spatial and temporal response properties of residual vision in a case of hemianopia. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *343*(1304), 157-166. https://doi.org/10.1098/rstb.1994.0018

Barbur, J., Ruddock, K., & Waterfield, V. A. (1980). Human visual responses in the absence of the geniculo-calcarine projection. *Brain: a journal of neurology*, *103*(4), 905-928. https://doi.org/10.1093/brain/103.4.905

Barleben, M., Stoppel, C. M., Kaufmann, J., Merkel, C., Wecke, T., Goertler, M., Heinze, H. J., Hopf, J. M., & Schoenfeld, M. A. (2015). Neural correlates of visual motion processing without awareness in patients with striate cortex and pulvinar lesions. *Human Brain Mapping*, *36*(4), 1585-1594. https://doi.org/10.1002/hbm.22725

Bergsma, D. P., Baars-Elsinga, A., Sibbel, J., Lubbers, P., & Visser-Meily, A. (2014). Visual daily functioning of chronic stroke patients assessed by goal attainment scaling after visual restorative training: an explorative study. *Topics in stroke rehabilitation*, *21*(5), 400-412. https://doi.org/https://doi.org/10.1310/tsr2105-400

Bergsma, D. P., & van der Wildt, G. (2010). Visual training of cerebral blindness patients gradually enlarges the visual field. *British Journal of Ophthalmology*, *94*(1), 88-96. https://doi.org/10.1136/bjo.2008.154336

Brainard, D. (1997). The Psychophysics Toolbox. *Spatial Vision*, *10*(4), 433-436.

Brent, P., Kennard, C., & Ruddock, K. H. (1994). Residual colour vision in a human hemianope: spectral responses and colour discrimination. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *256*(1347), 219-225. https://doi.org/https://doi.org/10.1098/rspb.1994.0073

Campion, J., Latto, R., & Smith, Y. (1983). Is blindsight an effect of scattered light, spared cortex, and near-threshold vision? *Behavioral and Brain Sciences*, *6*(3), 423-448. https://doi.org/10.1017/S0140525X00016861

Carey, D. P., Trevethan, C. T., Weiskrantz, L., & Sahraie, A. (2012). Does delay impair localisation in blindsight? *Neuropsychologia*, *50*(14), 3673-3680. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2012.08.018

Cavanaugh, M. R., Barbot, A., Carrasco, M., & Huxlin, K. R. (2017). Feature-based attention potentiates recovery of fine direction discrimination in cortically blind patients. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2017.12.010

Celeghin, A., de Gelder, B., & Tamietto, M. (2015). From affective blindsight to emotional consciousness. *Consciousness and Cognition*, *36*, 414-425. https://doi.org/10.1016/j.concog.2015.05.007

Cowey, A. (2004). The 30th Sir Frederick Bartlett lecture. Fact, artefact, and myth about blindsight. *Quarterly Journal of Experimental Psychology Section A*, *57*(4), 577-609. https://doi.org/10.1080/02724980343000882

Cowey, A. (2010). The blindsight saga. *Experimental brain research*, *200*(1), 3-24. https://doi.org/10.1007/s00221-009-1914-2

Cowey, A., Alexander, I., & Ellison, A. (2013). Modulation of cortical excitability can speed up blindsight but not improve it. *Experimental brain research*, *224*(3), 469-475. https://doi.org/10.1007/s00221-012-3327-x

Cowey, A., & Stoerig, P. (1999). Spectral sensitivity in hemianopic macaque monkeys. *European Journal of Neuroscience*, *11*(6), 2114-2120. https://doi.org/https://doi.org/10.1046/j.1460-9568.1999.00635.x

Cowey, A., & Weiskrantz, L. (1963). A perimetric study of visual field defects in monkeys. *Quarterly Journal of Experimental Psychology*, *15*(2), 91-115. https://doi.org/https://doi.org/10.1080/17470216308416561

Curcio, C. A., Sloan, K. R., Kalina, R. E., & Hendrickson, A. E. (1990). Human photoreceptor topography. *Journal of Comparative Neurology*, *292*(4), 497-523. https://doi.org/ https://doi.org/10.1002/cne.902920402

Danckert, J., & Culham, J. C. (2010). Reflections on blindsight: Neuroimaging and behavioural explorations clarify a case of reversed localisation in the blind field of a patient with hemianopia. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale*, *64*(2), 86. https://doi.org/https://doi.org/10.1037/a0017426

Das, A., Tadin, D., & Huxlin, K. R. (2014). Beyond Blindsight: Properties of Visual Relearning in Cortically Blind Fields. *Journal of Neuroscience*, *34*(35), 11652-11664. https://doi.org/10.1523/jneurosci.1076-14.2014

Elshout, J. A., van Asten, F., Hoyng, C. B., Bergsma, D. P., & van den Berg, A. V. (2016). Visual Rehabilitation in Chronic Cerebral Blindness: A Randomized Controlled Crossover Study. *Frontiers in neurology*, *7*, 92. https://doi.org/10.3389/fneur.2016.00092

Faubert, J., & Diaconu, V. (2001). Chapter 25 From visual consciousness to spectral absorption in the human retina. In *Progress in brain research* (Vol. 134, pp. 399-409). Elsevier. https://doi.org/https://doi.org/10.1016/S0079-6123(01)34026-8.

Faubert, J., Diaconu, V., Ptito, M., & Ptito, A. (1999). Residual vision in the blind field of hemidecorticated humans predicted by a diffusion scatter model and selective spectral absorption of the human eye. *J Vision research*, *39*(1), 149-157.

Field, A., Miles, J., & Field, Z. (2012). *Discovering statistics using R*. Sage publications.

Gall, C., & Sabel, B. A. (2012). Reading performance after vision rehabilitation of subjects with homonymous visual field defects. *PM&R*, *4*(12), 928-935. https://doi.org/https://doi.org/10.1016/j.pmrj.2012.08.020

Grasso, P. A., Ladavas, E., & Bertini, C. (2016). Compensatory Recovery after Multisensory Stimulation in Hemianopic Patients: Behavioral and Neurophysiological Components. *Frontiers in systems neuroscience*, *10*, 45. https://doi.org/10.3389/fnsys.2016.00045

Grasso, P. A., Pietrelli, M., Zanon, M., Ladavas, E., & Bertini, C. (2020). Alpha oscillations reveal implicit visual processing of motion in hemianopia. *Cortex*, *122*, 81-96. https://doi.org/10.1016/j.cortex.2018.08.009

Hollands, J. G., Parker, H., McFadden, S., & Boothby, R. (2002). LCD versus CRT displays: a comparison of visual search performance for colored symbols. *Human factors*, *44*(2), 210-221. https://doi.org/https://doi.org/10.1518/0018720024497862

Holmes, G. (1918). Disturbances of Vision by Cerebral Lesions. *British Journal of Ophthalmology*, *2*(7), 353-384. https://www.ncbi.nlm.nih.gov/pubmed/18167806

Hooge, I. T., Niehorster, D. C., Nyström, M., Andersson, R., & Hessels, R. S. (2018). Is human classification by experienced untrained observers a gold standard in fixation detection? *Behavior Research Methods*, *50*(5), 1864-1881. https://doi.org/https://doi.org/10.3758/s13428-017-0955-x

Hooge, I. T., Niehorster, D. C., Nyström, M., Andersson, R., & Hessels, R. S. (2021). Correction to:"Is human classification by experienced untrained observers a gold standard in fixation detection?". *Behavior Research Methods*, 1-2. https://doi.org/https://doi.org/10.3758/s13428-017-0955-x

Hothorn, T., & Hornik, K. (2015, 2015-02-20). *Exact Distribution for Rank and Permutation Tests*. http://ftp.uni-bayreuth.de/math/statlib/R/CRAN/doc/packages/exactRankTests.pdf

Howard, C., & Rowe, F. J. (2018). Adaptation to poststroke visual field loss: A systematic review. *Brain and behavior*, *8*(8), e01041. https://doi.org/10.1002/brb3.1041

Huxlin, K. R., Martin, T., Kelly, K., Riley, M., Friedman, D. I., Burgin, W. S., & Hayhoe, M. (2009). Perceptual relearning of complex visual motion after V1 damage in humans. *Journal of Neuroscience*, *29*(13), 3981-3991. https://doi.org/10.1523/JNEUROSCI.4882-08.2009

Jonas, J. B., Gusek, G. C., & Fernández, M. C. (1991). Correlation of the blind spot size to the area of the optic disk and parapapillary atrophy. *American journal of ophthalmology*, *111*(5), 559-565. https://doi.org/https://doi.org/10.1016/S0002-9394(14)73698-0

King, S. M., Azzopardi, P., Cowey, A., Oxbury, J., & Oxbury, S. (1996). The role of light scatter in the residual visual sensitivity of patients with complete cerebral hemispherectomy. *Visual neuroscience*, *13*(1), 1-13.

Kleiner, M., Brainard, D., & Pelli, D. (2007). What's new in Psychtoolbox-3? Perception 36 ECVP Abstract Supplement. In.

Larcombe, S. J., Kulyomina, Y., Antonova, N., Ajina, S., Stagg, C. J., Clatworthy, P. L., & Bridge, H. (2018). Visual training in hemianopia alters neural activity in the absence of behavioural improvement: a pilot study. *Ophthalmic and Physiological Optics*, *38*(5), 538-549. https://doi.org/https://doi.org/10.1111/opo.12584

Lawrence, E. S., Coshall, C., Dundas, R., Stewart, J., Rudd, A. G., Howard, R., & Wolfe, C. D. (2001). Estimates of the prevalence of acute stroke impairments and disability in a multiethnic population. *Stroke*, *32*(6), 1279-1284. https://doi.org/https://doi.org/10.1161/01.STR.32.6.1279

Marshall, R. S., Chmayssani, M., O'Brien, K. A., Handy, C., & Greenstein, V. C. (2010). Visual field expansion after visual restoration therapy. *Clinical Rehabilitation*, *24*(11), 1027-1035. https://doi.org/10.1177/0269215510362323

Marzi, C. A., Tassinari, G., Aglioti, S., & Lutzemberger, L. (1986). Spatial summation across the vertical meridian in hemianopics: a test of blindsight. *Neuropsychologia*, *24*(6), 749-758. https://www.ncbi.nlm.nih.gov/pubmed/3808284

Mazzi, C., Bagattini, C., & Savazzi, S. (2016). Blind-Sight vs. Degraded-Sight: Different Measures Tell a Different Story. *Frontiers in psychology*, *7*, 901. https://doi.org/10.3389/fpsyg.2016.00901

Mazzi, C., Savazzi, S., & Silvanto, J. (2019). On the "blindness" of blindsight: What is the evidence for phenomenal awareness in the absence of primary visual cortex (V1)? *Neuropsychologia*, *128*, 103-108. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2017.10.029

Mazzi, C., Tagliabue, C. F., Mazzeo, G., & Savazzi, S. (2018). Reliability in reporting perceptual experience: Behaviour and electrophysiology in hemianopic patients. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2018.01.017

Pavan, A., Alexander, I., Campana, G., & Cowey, A. (2011). Detection of first-and second-order coherent motion in blindsight. *Experimental brain research*, *214*(2), 261. https://doi.org/https://doi.org/10.1007/s00221-011-2828-3

Perenin, M. (1978). Visual function within the hemianopic field following early cerebral hemidecortication in man—II. Pattern discrimination. *Neuropsychologia*, *16*(6), 697-708. https://doi.org/https://doi.org/10.1016/0028-3932(78)90004-0

Perenin, M., & Jeannerod, M. (1978). Visual function within the hemianopic field following early cerebral hemidecortication in man—I. Spatial localization. *Neuropsychologia*, *16*(1), 1-13. https://doi.org/https://doi.org/10.1016/0028-3932(78)90037-4

Persaud, N., Davidson, M., Maniscalco, B., Mobbs, D., Passingham, R. E., Cowey, A., & Lau, H. (2011). Awareness-related activity in prefrontal and parietal cortices in blindsight reflects more than superior visual performance. *Neuroimage*, *58*(2), 605-611. https://doi.org/https://doi.org/10.1016/j.neuroimage.2011.06.081

Pollock, A., Hazelton, C., Henderson, C. A., Angilley, J., Dhillon, B., Langhorne, P., Livingstone, K., Munro, F. A., Orr, H., Rowe, F., & Shahani, U. (2011). Interventions for Visual Field Defects in Patients With Stroke. *Stroke*, *43*(4), e37-e38. https://doi.org/10.1161/strokeaha.111.639815

Pöppel, E., Held, R., & Frost, D. (1973). Residual visual function after brain wounds involving the central visual pathways in man. *Nature*, *243*(5405), 295-296. https://doi.org/https://doi.org/10.1038/243295a0

Portengen, B. L., Roelofzen, C., Porro, G. L., Imhof, S. M., Fracasso, A., & Naber, M. (2021). Blind spot and visual field anisotropy detection with flicker pupil perimetry across brightness and task variations. *Vision research*, *178*, 79-85. https://doi.org/https://doi.org/10.1016/j.visres.2020.10.005

Raab, D. H. (1962). Statistical facilitation of simple reaction times. *Transactions of the New York Academy of Sciences*, *24*, 574-590.

Reinhard, J., Schreiber, A., Schiefer, U., Kasten, E., Sabel, B. A., Kenkel, S., Vonthein, R., & Trauzettel-Klosinski, S. (2005). Does visual restitution training change absolute homonymous visual field defects? A fundus controlled study. *British Journal of Ophthalmology*, *89*(1), 30-35. https://doi.org/10.1136/bjo.2003.040543

Riddoch, G. (1917). DISSOCIATION OF VISUAL PERCEPTIONS DUE TO OCCIPITAL INJURIES WITH ESPECIALL REFERENCE TO APPRECIATION OF MOVEMENT. *Brain*, *40*(1), 15-57. https://doi.org/https://doi.org/10.1093/brain/40.1.15

Ross, A. I., Schenk, T., Billino, J., Macleod, M. J., & Hesse, C. (2018). Avoiding unseen obstacles: Subcortical vision is not sufficient to maintain normal obstacle avoidance behaviour during reaching. *Cortex*, *98*, 177-193. https://doi.org/https://doi.org/10.1016/j.cortex.2016.09.010

Sahraie, A., Hibbard, P. B., Trevethan, C. T., Ritchie, K. L., & Weiskrantz, L. (2010). Consciousness of the first order in blindsight. *Proceedings of the National Academy of Sciences*, *107*(49), 21217-21222. https://doi.org/10.1073/pnas.1015652107

Sahraie, A., Trevethan, C. T., MacLeod, M. J., Urquhart, J., & Weiskrantz, L. (2013). Pupil response as a predictor of blindsight in hemianopia. *Proceedings of the National Academy of Sciences*, *110*(45), 18333-18338. https://doi.org/10.1073/pnas.1318395110

Sahraie, A., Trevethan, C. T., Macleod, M. J., Weiskrantz, L., & Hunt, A. R. (2013). The continuum of detection and awareness of visual stimuli within the blindfield: from blindsight to the sighted-sight. *Investigative ophthalmology & visual science*, *54*(5), 3579-3585. https://doi.org/10.1167/iovs.12-11231

Saionz, E. L., Tadin, D., Melnick, M. D., & Huxlin, K. R. (2020). Functional preservation and enhanced capacity for visual restoration in subacute occipital stroke. *Brain*, *143*(6), 1857-1872. https://doi.org/10.1093/brain/awaa128

Savina, O., & Guitton, D. (2018). The primitive retino-tecto-reticular pathway is functional in hemidecorticate patients. *Current Biology*, *28*(20), R1184-R1186. https://doi.org/10.1016/j.cub.2018.09.006

Stoerig, P. (2010). Cueless blindsight. *Frontiers in human neuroscience*, *3*, 74. https://doi.org/10.3389/neuro.09.074.2009

Stoerig, P., & Cowey, A. (1991). Increment-threshold spectral sensitivity in blindsight: evidence for colour opponency. *Brain*, *114*(3), 1487-1512. https://doi.org/https://doi.org/10.1093/brain/114.3.1487

Stoerig, P., Hübner, M., & Pöppel, E. (1985). Signal detection analysis of residual vision in a field defect due to a post-geniculate lesion. *Neuropsychologia*, *23*(5), 589-599. https://doi.org/https://doi.org/10.1016/0028-3932(85)90061-2

Tamietto, M., Cauda, F., Corazzini, L. L., Savazzi, S., Marzi, C. A., Goebel, R., Weiskrantz, L., & de Gelder, B. (2010). Collicular vision guides nonconscious behavior. *Journal of Cognitive Neuroscience*, *22*(5), 888-902. https://doi.org/https://doi.org/10.1162/jocn.2009.21225

Thaler, L., Schütz, A. C., Goodale, M. A., & Gegenfurtner, K. R. (2013). What is the best fixation target? The effect of target shape on stability of fixational eye movements. *Vision research*, *76*, 31-42. https://doi.org/10.1016/j.visres.2012.10.012

Trevethan, C., Urquhart, J., Ward, R., Gentleman, D., & Sahraie, A. (2012). Evidence for perceptual learning with repeated stimulation after partial and total cortical blindness. *Advances in Cognitive Psychology*, *8*(1), 29-37. https://doi.org/10.5709/acp-0099-8

Wafa, H. A., Wolfe, C. D., Emmett, E., Roth, G. A., Johnson, C. O., & Wang, Y. (2020). Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke*, *51*(8), 2418-2427. https://doi.org/https://doi.org/10.1161/STROKEAHA.120.029606

Weiskrantz, L. (1980). Varieties of residual experience. *The Quarterly journal of experimental psychology*, *32*(3), 365-386. https://doi.org/https://doi.org/10.1080/14640748008401832

Weiskrantz, L. (1999). *Consciousness lost and found: A neuropsychological exploration*. OUP Oxford.

Weiskrantz, L., Warrington, E. K., Sanders, M. D., & Marshall, J. (1974). Visual capacity in the hemianopic field following a restricted occipital ablation. *Brain*, *97*(4), 709-728. https://www.ncbi.nlm.nih.gov/pubmed/4434190

Wilson, M. E. (1968). The detection of light scattered from stimuli in impaired regions of the visual field. *Journal of Neurology, Neurosurgery & Psychiatry*, *31*(5), 509. https://doi.org/10.1136/jnnp.31.5.509

Wüst, S., Kasten, E., & Sabel, B. A. (2002). Blindsight after optic nerve injury indicates functionality of spared fibers. *Journal of Cognitive Neuroscience*, *14*(2), 243-253. https://doi.org/https://doi.org/10.1162/089892902317236876

Zihl, J., & Kennard, C. (2003). Disorders of higher visual function. In *Neurological Disorders* (pp. 255-263). Elsevier.

Zihl, J., & von Cramon, D. (1979). Restitution of visual function in patients with cerebral blindness. *Journal of Neurology, Neurosurgery & Psychiatry*, *42*(4), 312-322. https://www.ncbi.nlm.nih.gov/pubmed/458478

Zihl, J., & Werth, R. (1984). Contributions to the study of "blindsight"—I. Can stray light account for saccadic localization in patients with postgeniculate field defects? *Neuropsychologia*, *22*(1), 1-11. https://doi.org/https://doi.org/10.1016/0028-3932(84)90002-2

II. Blindsight and residual vision: How reliable is the redundant target effect as a diagnostic tool?

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Abstract

Certain patients with homonymous visual field defects have residual visual capacities (RVCs) within their blind visual field. RVCs, for instance blindsight, have been tested with varying paradigms, including the redundant target paradigm (RTP). This paradigm is based on the redundant target effect (RTE) which describes a reduction in reaction times to a visual target that occurs when a second, redundant target is presented simultaneously. A significant RTE with the second, redundant target in the blind visual field of patients is an indication of RVCs in the blind field. In a meta-analysis of the RTE in healthy participants, we found that the RTP, when used with the stimulus configuration also used for RVC-testing, yields on average a positive effect. Thus, on group-level the RTE is a robust phenomenon in healthy observers.

Next, we evaluated the RTP as a diagnostic tool for RVCs in patients. We estimated sensitivity, specificity, and reliability of the RTP by reviewing the literature and analyzing our own empirical data (patients: N = 11; two samples of healthy participants, sample 1: N = 53, sample 2: N = 19).

Firstly, sensitivity defines how good the RTP detects the presence of visual functions. A literature review showed a broad range of sensitivity values (sighted field of patients: 41.67%-64.15%; healthy participants: 77%). Findings from our own samples confirmed that sensitivity of the RTP to detect available visual functions is surprisingly poor (sighted field of patients: 18.18%-25%; healthy participants of sample 1: 30.19%-32.08%).

Secondly, specificity defines how good the RTP detects the absence of visual functions. We addressed this issue by examining the RTE in the natural blind spot of healthy participants (sample 2) and found a high, although not perfect, value for specificity of 89.47%.

Thirdly, reliability defines how good multiple RTP-results in a given person correspond if visual functions are consistently present. In our samples, intra-class correlations between test sessions in patients as well as between redundant conditions in healthy participants (sample 1) revealed a low reliability on group level. Similarly, correspondence of single-case results in healthy participants (sample 1) was poor. Following this, reliability of the RTP is low.

In previous studies, a significant RTE has been considered as a precondition for the validity of other RVC-measurements. This presupposes first that there is one necessary visual function that must be retained for any other RVCs to be possible. We call this function the minimal configuration criterion (MCC). Secondly, the use of a positive RTE as a precondition for RVC-research also implies that the RTP provides an ideal and reliable tool to examine whether this function is preserved. However, our literature research has shown that RVCs can be found in the absence of positive RTP-findings. This shows that either MCC is a fiction or that RTP is a poor test for MCC.

Still the RTP has several advantages compared to other RVC-tests. The RTE can be easily implemented in vision laboratories, has a simple instruction, and avoids biased response criteria. Following this, it is worth trying to improve the diagnostic quality of the RTP in future studies.

In conclusion, the RTP has a reasonable specificity but poor sensitivity and poor reliability. This should be taken into account when interpreting results of previous and subsequent RTP-studies. In particular, the presence of a RTE likely indicates the presence of RVCs in patients. However, the absence of a RTE does not indicate the absence of RVCs.

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II.1. Introduction

The redundant target paradigm (RTP) is a simple detection paradigm. A visual target is presented and the observer needs to press a button as soon as they detect the target. Reaction time in this condition is then compared with a second condition. In the second condition, reaction times are measured in response to two identical targets presented at the same time. It turns out that the presence of a second, redundant target leads to shortened reaction times (Raab, 1962). This is called the redundant target effect (RTE). The RTE is an interesting effect in its own right and it has been explored and modelled in various research contexts (e.g. in spatial neglect in Ogourtsova et al., 2011; or in split-brain patients in Roser & Corballis, 2002). However, RTPs have risen to particular prominence due to its use as a diagnostic tool for residual vision in patients who suffer from partial cerebral blindness following brain damage (Leh et al., 2006; Striemer et al., 2009). Residual vision is present, if the reaction time is shorter even though the redundant target is presented within the blind visual field (Marzi et al., 1986). In this article, we wish to evaluate the diagnostic qualities of the RTP. For our evaluation, we relied on the one hand on a systematic analysis of published reports on the RTP and on the other hand on the examination of the RTE in a sample of healthy observers and a smaller sample of patients with partial cerebral blindness. However, before we present our research question in detail, we first need to introduce the context within which the RTP has been most prominent and most controversial: The study of partial cerebral blindness and the phenomenon of blindsight.

Following a post-chiasmatic lesion in the neuronal visual system, patients exhibit a homonymous visual field defect (HVFD), i.e. a visual field defect affecting the same field portions in both eyes. When asked about their visual experience, patients report that they see nothing within their scotoma. However, some patients perform above chance in response to visual targets within their blind field. These residual visual functions have been called blindsight (Weiskrantz et al., 1974). Residual visual functions after damage to the occipital lobe were already described in soldiers of World War I (Holmes, 1918; Riddoch, 1917). After several decades, studies in monkeys renewed the interest in this topic. For example, Pasik and Pasik (1971) showed that monkeys with bilateral ablation of the striate cortex could be retrained to discriminate area, brightness, shape, and color. Extensive investigations of human cases with HVFD followed (e.g. Pöppel et al., 1973; Weiskrantz et al., 1974; Zihl & von Cramon, 1980). The dissociation between visual performance and visual consciousness led to theoretical considerations. It was conjectured that if visual capacities are still present but consciousness is not, the lesion has to affect specifically the neuronal correlate of visual awareness (Weiskrantz, 1999). Put differently, the phenomenon of blindsight offered the promise of uncovering the process by which the brain creates consciousness. This hope of unravelling one of the greatest mysteries of the human mind

fueled research on this topic. This association of blindsight with the quest to identify the neural basis of consciousness explains why blindsight attracted interest from philosophers, neuro-, cognitive, medical and computer scientists. The same link that sparked interest also raised serious doubts among many neuropsychologists. From the very beginning, the claim of a stark dissociation between a patient's ability to use visual information in spite of complete absence of visual awareness was met with skepticism. It was reported that some patients could describe feelings about visual targets within their scotoma like '*pin-prick*' and '*a prickling*' (Richards, 1973), or '*dark shadow*' (Barbur et al., 1980). This led to the classification of blindsight type I and II (Weiskrantz et al., 1995). Blindsight type I describes the classical view of visual functions without '*acknowledged awareness'* (page 6126, Weiskrantz et al., 1995). Blindsight type II describes cases in which the patient can report feelings about visual stimuli. The distinction between these two types of blindsight seems to offer a reasonable compromise, but it cannot detract from the fact that we lack an objective criterion to establish the presence or absence of awareness. More specifically, the typical measures used to assess visual awareness are controversial and alternative measures have been suggested (e.g. Overgaard, 2011). Importantly, studies showed that how you measure awareness determines what you find. A number of studies found that the chosen response modality affects the report of visual awareness (Garric et al., 2019; Mazzi et al., 2016; Phillips, 2020). Mazzi et al. (2016) demonstrated that the number of report options affects the likelihood of finding signs of awareness. These authors examined patient SL. When a dichotomous scale was used ('*seen*' versus '*guessed*'), it appeared that SL showed clear signs of blindsight, e.g. above chance visual performance in the absence of visual awareness. In contrast, when a scale with four possible levels of visual awareness was used, it turned out that SL only showed above-chance performance for trials where SL reported at least a fleeting awareness of the target (Mazzi et al., 2016). An even more pervasive problem concerns biased response criteria (Cowey, 2010; Cowey & Weiskrantz, 1963). Participants classify their degree of awareness by making implicit boundaries between response alternatives. This is especially critical for yes/ no decisions about the detection of targets. Patients with a liberal criteria for a '*yes*' response have a lower chance for '*no*' responses for the same visual perception (Cowey, 2010). Azzopardi and Cowey (1998) investigated the difference between yes-no and forced choice detection paradigms in patient GY. In the forced choice detection test, patient GY had to indicate the time interval in which a target appeared. The dissociations in the behavioral results for motion targets could be explained by differences in response criteria (Azzopardi & Cowey, 1998). These findings demonstrate that awareness is difficult to measure. In the absence of a reliable criterion for visual awareness the distinction between blindsight type I and type II is of little help and the contribution of blindsight to our understanding of the neural substrate of consciousness

remains unclear. Following this, we will use the term residual visual capacities (RVCs) in the remainder of this article to refer to all remnants of visual functions within the HVFD independent of the level of awareness.

However, from a clinical perspective the awareness-problem is only of secondary importance. What counts is that some patients with HVFD show reliable signs of above chance-performance for targets presented to their blind visual field. It should be possible to use this residual vision to improve the lives of patients with HVFD.

HVFDs are surprisingly common. They are a frequent symptom of stroke. In fact 69.7% of all HVFDs are caused by an ischemic or hemorrhagic stroke (Zhang et al., 2006). With stroke being the most common cause of focal brain-damage, it follows that HVFDs are a prevalent disorder. In the Erlangen Stroke Project, the annual incidence of a first-in-a-lifetime-stroke was 127.3 for men and 117.1 for women per 100.000 population (adjusted for the European population, Kolominsky-Rabas et al., 2015). Additionally, the stroke mortality significantly decreased from 1995 to 2015 (Rucker et al., 2020). In 2015, the 5-year survival rate was at 54.4% (Rucker et al., 2020). Following this, there are more survivors with a need for treatment. Regarding the expenses, the lifetime treatment of newly diagnosed first ischemic strokes was estimate to cost 108.6 billion euro from 2006-2025 in Germany (Kolominsky-Rabas et al., 2006). Almost one third of those stroke victims, or to be more precise 26.1%, in a sample of first-in-a-lifetime suffer from visual field defects (Lawrence et al., 2001). An effective treatment of HVFDs would therefore help a great number of people and thereby lift a significant burden from society.

Early attempts to retrain affected patients were very promising. It was found that extensive visual stimulation along the border between the sighted and the blind field helped to extend the sighted field (e.g. Kasten et al., 1998; Zihl & von Cramon, 1985). However, later studies using more rigorous measurements failed to replicate the early successes (Reinhard et al., 2005). In recent years, a different approach was used. Particularly promising is a treatment that uses dynamic visual targets (e.g. Huxlin et al., 2009). Huxlin et al. (2009) found that extensive training with random-dot motion targets in the patients' blind field improved patients' ability to identify the direction of the presented movement pattern. This was found even in patients who did not betray signs of above-chance movement discrimination prior to the training (Huxlin et al., 2009; Saionz et al., 2020). Furthermore, the training leads to an expansion of the sighted visual field (Cavanaugh & Huxlin, 2017; Saionz et al., 2020) and to an increase in awareness for moving targets presented in the blind field (Huxlin et al., 2009; Saionz et al., 2020). Thus, it seems that rekindling RVCs offers a promising approach to treat patients with HVFD. But how many patients could benefit from such a treatment? How many patients possess RVCs in their blind field?

The presence of RVCs is not assessed on a routine basis. Furthermore, studies about RVCs are usually single case studies (e.g. Azzopardi & Cowey, 1998; Mazzi et al., 2016; Stoerig et al., 1985) or have only small sample size (Celeghin, Savazzi, et al., 2015, N=6; Corbetta et al., 1990, N=4). Investigations in bigger samples (N>10) of patients with HVFD showed a percentage of RVC-positive participants of 0% (Grasso et al., 2020, 0 out of 15), 20% (Marzi et al., 1986, 4 out of 20), 57% (Ajina & Bridge, 2018, 8 out of 14), 62% (Ajina et al., 2020, 8 out of 13), and 71% (Ajina et al., 2015, 12 out of 17). To summarize, the prevalence scores for RVCs range from 0-71%.

An obvious reason for this variability is the fact that most studies looked at small samples. The problem is further exacerbated by the fact that samples are often highly selective and it is unclear to what extent samples from different studies use overlapping sets of patients thereby potentially enriching their samples with previously confirmed RVC-patients. All of these problems are not insurmountably. Studies with large sample sizes using random-selection methods, thus creating representative samples, are certainly feasible. There is, however, another problem, that is more difficult to tackle: What is the best measure to detect RVCs?

An impressive range of different methods to explore potential RVCs have been employed in past studies. Here are just a few examples: Grasso et al. (2020) tested the detection and discrimination of a moving or stationary random dot cloud. Marzi et al. (1986) tested the influence of targets within the blind area on reaction times using the RTE. Ajina and Bridge (2018) tested the temporal detection of a moving random dot cloud. Ajina et al. (2020) tested the detection and discrimination of emotional faces. Ajina et al. (2015) tested the temporal detection of a drifting Gabor patch. This list of RVC-paradigms could be extended further by including other forms of RVCs, e.g. *action blindsight* or *affective blindsight*. Action blindsight describes the capacity of some patients to localize targets within their blind visual field by eye or hand movements (for a review see Danckert & Rossetti, 2005). In affective-blindsight paradigms, the discrimination or influence of emotional stimuli, like fearful faces, is tested within the blind visual field (for a review see Celeghin, de Gelder, et al., 2015).

This inconsistency in paradigms would not matter so much were it not already known that some methods are clearly better than others at detecting signs of RVCs. Light scatter is a frequently mentioned problem of RVC-paradigms (Campion et al., 1983). Light emitted by targets presented within the blind visual field can stray into the seeing parts of the visual field. Studies showed that visual information from light scatter is sufficient to solve tasks (Campion et al., 1983). The effect of light scatter can, however, be tested and thus avoided. One method is the use of the natural blind spot as a control location for RVC-studies (e.g. Stoerig et al., 1985). The natural blind spot corresponds to the optic disc (Jonas et al., 1991).

As there are no photoreceptors at the optic disc (Curcio et al., 1990), humans have a physiological, absolute scotoma within their visual field (Jonas et al., 1991). This means that if visual stimulation of the blind spot leads to above-chance performance, the reason must be that light strays into the seeing field surrounding the blind spot. Thus, RVC-results are valid if performance is high for targets within the HVFD but at chance level for targets within the blind spot (Stoerig et al., 1985). The problem of biased response criteria, mentioned above, is also relevant not just for the assessment of awareness but can also bias RVC-results unless forced-choice or criterion-free paradigms are employed (Campion et al., 1983).

To sum up, it is clear that some methods are better than others but there is no agreement on a standard method that should be used to test for RVCs. Without an agreement on what constitutes a good test for RVCs, no agreement on prevalence values can be expected. However, this is not the only problem. The lack of an agreed standard on what constitutes evidence of RVCs prevents also the resolution of scientific debates. We will illustrate this problem with a recent example.

Milner and Goodale (1995, 2008) proposed two cortical pathways transmitting *'vision for action'* in the dorsal and *'vision for perception'* in the ventral stream. Processing in the dorsal pathway is largely automatic with observers having little awareness of the visual information used for guiding their actions. In contrast, visual information processed in the ventral stream will typically enter our awareness. Accordingly, it is expected that a selective deficit of visual awareness, as in the case of blindsight (following the original definition of Weiskrantz et al., 1974), will have a more profound effect on perceptual processes in the ventral stream, while leaving visuomotor processes served by the dorsal stream largely unaffected. Striemer et al. (2009) provided dramatic proof of this prediction. They found that obstacle-avoidance, a classical dorsal-stream task (see for example Schindler et al., 2004), can be achieved in the complete absence of awareness of the obstacle placed in the patient's blind field. The original study reported by Striemer et al. (2009) was a single case study. Ross et al. (2018) tried to replicate this finding in six patients with HVFD with selective lesions to the primary visual cortex (V1) but found no reliable evidence of residual obstacle avoidance in any of their patients. Subsequently, there were detailed methodological discussions (Hesse et al., 2018; Striemer et al., 2018). One contentious issue concerned the suitability of the patients selected for the study by Ross et al. (2018). Striemer et al. (2018) argued that a failure to find residual obstacle avoidance is only relevant if it can first be established that the selected patients possessed the requisite functional systems that are needed to guide actions in the absence of input from V1. Put more simply, only patients with RVCs can be expected to show preserved performance in an obstacle-avoidance task. Specifically, Striemer et al. (2018) argued that '*one would never expect to see any evidence of obstacle avoidance in the*

blind field of a patient who did not demonstrate blindsight in some other test involving processing visual stimuli unconsciously in the blind field' (page 3).

This brings us to the more general issue. To test a neuropsychological hypothesis we make predictions about the behavioral deficits and behavioral capacities that are expected in specific patients. Those patients are either defined in terms of symptoms or neurological damage. In the case of RVCs such a characterization is lacking. A selective lesion to V1 confirmed in an CCT-image or in MRI might fit the profile, but studies suggest that confirming a lesion restricted to V1 on the basis of brain imaging is neither a sufficient nor a necessary condition for RVCs (Leh et al., 2006; Ross et al., 2018). Animal and human studies have shown that selective V1 lesions can create trans-synaptic retrograde degeneration (TRD) in the retino-geniculate pathway thereby disrupting pathways deemed critical for RVCs (e.g. Cowey et al., 2011; Millington et al., 2014; Yamashita et al., 2016). This means, we can expect to see patients with lesions apparently restricted to V1 who are still lacking RVCs. On the other hand, patients with extensive lesions going well beyond V1 have been demonstrated to show RVCs (for a review about RVCs in hemispherectomized patients see Ptito & Leh, 2007). As far as humans are concerned, we still do not know which pathways are critical for RVCs (for reviews see Ajina & Bridge, 2016; Fox et al., 2020).

A functional test for identifying RVC-patients might show more promise. Several researchers used the RTP as a diagnostic test and generalized the results to other RVCs (Leh et al., 2006; Striemer et al., 2009). Equipped with such a test, we could apply the RTP to all patients with visual field defects. Patient with a positive RTE would be diagnosed as RVC-patients. This would provide us with reliable figures for the prevalence of RVCs but also provide us with a reliable criterion to determine whether a given patient can be used to test a specific hypothesis about RVCs or not.

Is the RTP the ideal test for RVCs? The RTP certainly offers a number of advantages. Firstly, experimental settings for other RVC-paradigms often have high technical requirements like precise measurement of eye and hand movements in localization tasks (e.g. Ross et al., 2018). In contrast, measuring the RTE requires minimal experimental effort. Experimenters have to present two static, simple, visual targets in two conditions (single vs. double) and reaction times should be measured precisely. Moreover, fixation behavior has to be monitored closely. Thereby, a precise recording of saccade characteristics is not necessary. It is sufficient to reliably detect deviations from fixation. Following this, the implementation of a RTP is possible in most psychological laboratories. Secondly, the simplistic nature of the RTP also markedly reduces the demands on the participants. Patients only need to understand and memorize a very simple instruction: Press a button as fast as possible whenever you see a target. Hence, the task can be conducted in patients having

impairments in memory or executive functions. As targets can be big, high contrast, and achromatic, visual acuity can be low and color vision is not necessary. To accomplish a button press, the demands on the motor system are low. Thirdly, the fact that patients respond to targets within their sighted field solves a further problem: Frustration. If patients are urged to respond to targets they do not see consciously, they face a seemingly intractable task. As experiments often consist of hundreds of trials, patients lose motivation, get frustrated and tired. Consequently, patients have a reduced attention and RVCs could be underestimated. Fourthly, as explained above, response criteria are a huge problem in RVC-testing (Cowey, 2010). The RTP avoids this problem. The RTP does not require an explicit decision on the presence or nature of targets presented in the blind field. Thus, the RTP remains unaffected by response criteria. However, before we can recommend the RTP as a reliable test for RVCs, we first need to find answers to a number of questions.

The first issue is not specific to RTP but applies quite generally to the quest of finding a good RVC-test. It seems that this quest regards RVCs as a unitary phenomenon. However, as we saw above, RVCs come in all shapes and sizes. There are RVCs for motion, color, emotion, location, and there is action blindsight. It is likely that these different forms of RVCs rely on different neuronal pathways. For instance, RVCs for motion perception relies on a pathway connecting the lateral geniculate nucleus and V5 (Ajina & Bridge, 2018). In comparison, affective blindsight is probably transmitted via a pathway that runs from the superior colliculi to the amygdala (Ajina et al., 2020). Moreover, it is known that some patients with HVFD show RVCs in some tasks but not in others (e.g. Corbetta et al., 1990; Mazzi et al., 2016). This does not rule out the possibility that there are also brain structures that are common to all those different RVC-pathways. Thus, there is hope that one might find one test that probes the intactness of this one common part – a test that can reliably identify the presence or absence of the minimal configuration criterion (MCC) required for all forms of RVCs. The question is whether the RTP is that one test for the MCC. The MCC is met when we find that RVCs in other paradigms can only be found when the RTP yields a positive result.

The other questions that we seek to address in this study are issues that are relevant for any diagnostic test: Is the RTP sufficiently sensitive, specific, and reliable to act as diagnostic tool for RVCs? It is important to note that the questions are not independent of each other. For example, a test with poor sensitivity cannot be expected to satisfy the MCC because there is a good chance of finding another test with higher sensitivity. In this case the high-sensitivity test will in some cases reveal RVCs when the low-sensitivity test fails to detect signs of RVCs, and, thus, the MCC is violated for the low-sensitivity test. However, for the purpose of this manuscript, we will address the questions of MCC, sensitivity, specificity, and reliability as separate issues.

We investigated these main research questions in three steps. Firstly, we reviewed results presented in the literature. Secondly, we examined the research questions with data from healthy participants. Thirdly, we complemented our findings with examinations of patients with HVFD.

II.2. Study (1): Literature overview about the RTE

II.2.1. Introduction

In our first study, we reviewed the literature about the redundant target paradigm (RTP). Studies investigating healthy participants and patients with homonymous visual field defect (HVFD) were selected by means of a systematic literature research. As a basic requirement for the application of the RTP in patient studies, we tested whether the redundant target effect (RTE) is a replicable and robust effect on group level in healthy participants using meta-analytic procedures. Next, we reviewed patient studies qualitatively. Initially, we were interested in how the RTP has been used as a RVC-test. Following this, we investigated the main research questions about sensitivity, reliability, and the minimal configuration criterion (MCC) by combining results in the literature.

II.2.2. Systematic literature research

To find all relevant, published studies using the RTP, we ran a systematic literature review between 16.06.2020 and 24.09.2020 using databases of Web of Science, Psyndex, PsycInfo, PsyArticles, and PubMed. Search words were: (1) *redundant target effect*, *redundant signal effect*, *redundancy gain*, *spatial summation,* and *hemispheric summation* together with (2) *reaction time*, *hemianop*, Blindsight*, and *cerebral blindness*. Results of all possible combinations were screened in the following order: By title, by abstract, by full text. Screening was done by two persons. In the case of disagreement, the record was kept for further inspection. We aimed for studies presenting experimental data of the RTE that matched the design of previously known RVC-studies. Furthermore, inclusion criteria are described in the following. The studies must have used simple visual targets, for instance circles or letters, and measured reaction times. We included only studies that used inference statistics and compared single versus double target conditions. Importantly, targets in the double condition had to be identical and presented simultaneously. We excluded data from experiments in which targets triggering the response were presented together with distractors or non-targets. Non-targets were only allowed in the no-go condition (participants are instructed to withhold the response) of go/ no-go designs. Consequently, experiments using feature or categorical redundancy or redundant targets within a visual search array were not considered. In previous RVC-studies, different target configurations were used for testing RVCs (double *bilateral*: one target in the sighted and one target in the blind visual

field) and for testing the RTE in the sighted visual field (double *unilateral*: two targets in the sighted visual field). Hence, we were interested if the effect sizes are comparable for these two target configurations. Studies were excluded if the RTE was calculated with mixed target configurations. Furthermore, we included only studies in English language, published in peer-reviewed journals. We included studies with healthy participants and/ or patients with HVFD. HVFD could be caused by post-chiasmal lesions or by hemispherectomy. We did not include animal studies. For the meta-analysis, we selected only the RTEs in healthy participants. Studies investigating patients with HVFD were reviewed qualitatively in detail. An overview of the systematic literature search can be found in Figure II.1.

II.2.3. Meta-analysis: The RTE in healthy participants

II.2.3.1. Methods

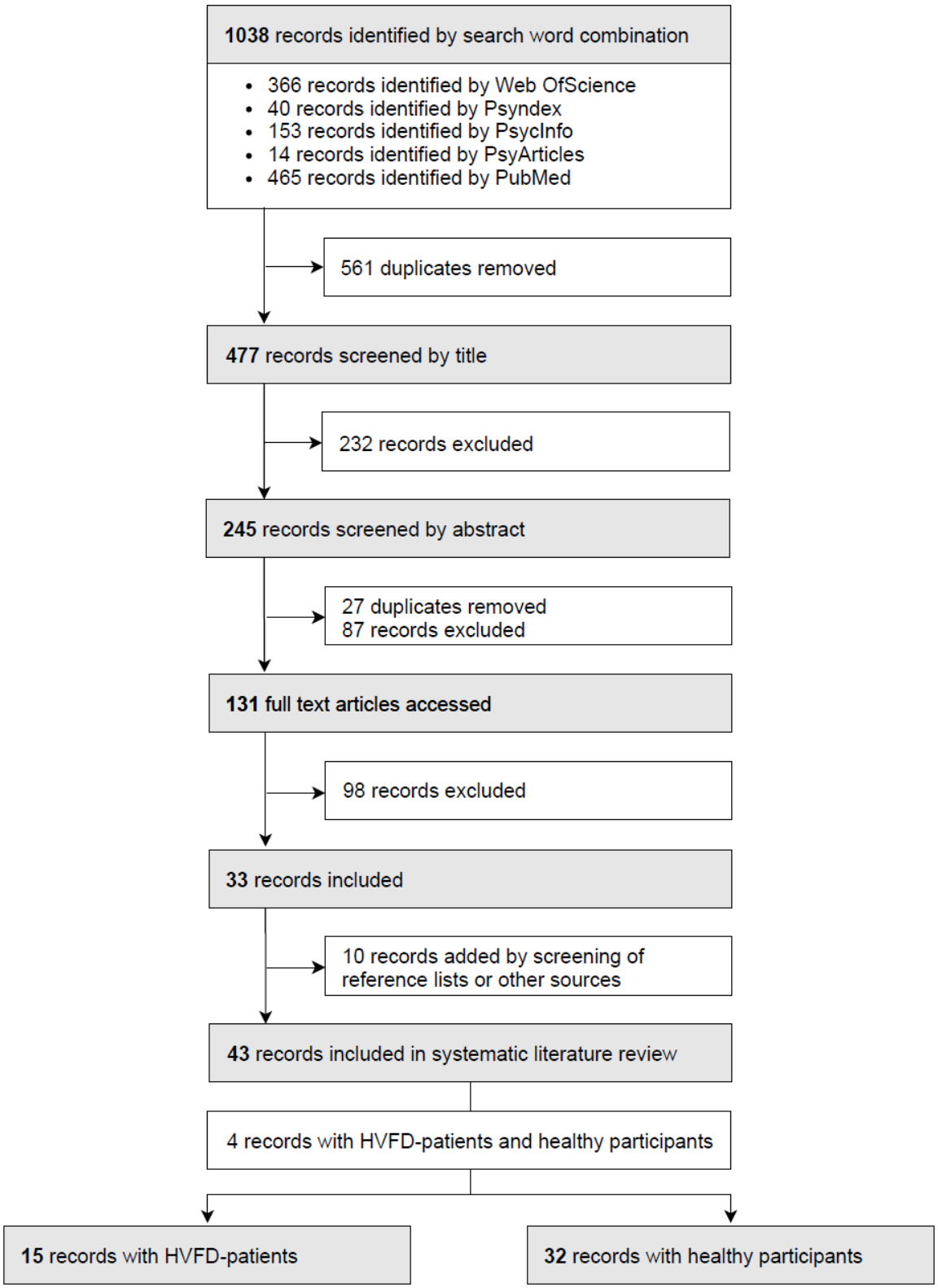
On the basis of the systematic literature research, we selected studies that tested the RTP in healthy participants. If studies contained multiple experiments with the same sample, we selected that experiment whose design was most similar to experimental designs used for patient studies. For the meta-analysis, we extracted the statistical test analyzing the RTE. These statistical tests will be called RTE-tests in the rest of this article. Analysis of one experiment sometimes contained multiple RTE-tests. Separate RTE-tests were only kept for one sample if target configurations were analyzed separately. Different target configurations are used for different research questions in RVC-research. Bilateral double stimulation tests RVCs. Unilateral double stimulation is used as a control condition. Hence, we kept the RTE-tests separate to evaluate if the summary effect size is comparable across these conditions. Some studies calculated separate RTE-tests for single target positions, for instance left vs. double and right vs. double. As there are no a-priori reasons for favoring one over the other, we calculated the average statistical value for this experiment (e.g. t- or F-statistic). This average statistical value was then used as the RTE-test. For each selected RTE-test, we extracted the following information: Experimental paradigm, descriptive statistics, and inference statistics. Furthermore, we extracted or calculated the size of the redundancy gain (RG), i.e. reaction time of the single minus reaction time of the double condition.

The calculations for the meta-analysis were run in R (version 4.0.3, 2020-10-10). For the meta-analytic procedure, we used the R packages *meta* (Schwarzer et al., 2015), *metafor* (Viechtbauer, 2010), and *dmetar* (Harrer et al., 2019b). Initially, we extracted the effect sizes reported in the studies. If Cohen's *d* was not provided, we estimated Cohen's *d* based on the reported test statistic (see appendix II.A for formulas based on Rosenthal (1993) and Cooper et al. (2009)). To correct for the population bias, we applied Hedges' *g* correction (Cooper et

al., 2009). If the experiment reported a negative RTE, meaning longer reaction times in the double compared to the single condition, we defined Hedge's *g* to be negative.

Figure II.1

Overview of the systematic literature research



Next, we estimated the standard error (*SE*) of each effect size. For within-subject designs, the calculation of the SE requires the correlation coefficient *r* between conditions (Cooper et al., 2009). However, the correlation was never reported in the studies. To solve this issue, we estimated the correlation based on the result of our own dataset of healthy participants (see section II.3.). Herein, the correlation between reaction times in response to one target and two redundant targets was $r_s = 0.97$, $p < .001$. As it is unlikely that all studies showed such a high correlation, we ran the meta-analysis once with $r = 0.97$, once with $r = 0.77$ and once with $r = 0.57$ to get a range of probable results.

The included RTE-tests differed with respect to several aspects. Firstly, RTE-tests used different paradigms: two choice, go/ no-go, and detection. In two-choice paradigms, participants press one button for the first target type and another button for the second target type. In go/ no-go paradigms, participants respond only to one of two target types. In detection paradigms, there is only one target type. Secondly, RTE-tests applied different target configurations: Bilateral, unilateral, and vertical. In vertical configurations, there is one target above and one target below the fixation cross. Thirdly, most RTE-tests were based on the mean reaction time of single conditions but some RTE-tests used the faster reaction time of the single conditions. Thereby, the latter variant is a more conservative measure of the RTE. In RVC-research, tasks were all detection paradigms using double bilateral stimulation to investigate RVCs and double unilateral stimulation as control condition. It is unclear which combination of experimental features (paradigm, target configuration, reaction time measure for single target condition) leads to the highest summary effect size. RVCs are remnants of visual functions. To increase the chances of finding RVCs in patients, it would be reasonable to use the combination of experimental features leading to the strongest possible RTE.

As we already expected differences in the effect size between experimental features, we ran a random effects model across all included experiments. For all meta-analytic models, we reported measures for heterogeneity: Parameter τ^2, the I^2 statistic and the χ^2 *Q*-statistic (Borenstein et al., 2009). To interpret I^2, we applied the categorization of Higgins et al. (2003) defining a heterogeneity of 25% as low, of 50% as moderate, and of 75% as high. Furthermore, we reported 95% confidence intervals (CIs) and 95% prediction intervals (PIs). Both CIs and PIs are interesting but provide answers to different questions (IntHout et al., 2016). CIs show the range within which the true mean of effect sizes can be expected. PIs show within which range an effect size of similar RTE-studies can be expected. Since we wish to establish the reliability with which a significant RTE can be expected in individual studies, the PI-estimate is the more relevant one (IntHout et al., 2016). On the basis of the overall random effects model, we calculated subgroup analysis in regard of the paradigm, target configuration, and mean versus faster single reaction time. Next, we selected RTE-tests that measured those conditions which are also typically used in RVC-studies

(detection, bilateral stimulation, mean single reaction time) and calculated the summary effect size. Importantly, experiments were all tested in healthy participants. Hence, we will refer to this selection of RTE-tests as the RVC-configuration subset. To test the RTE for the RVC-configuration subset most precisely, we applied an influence analysis based on the Leave-One-Out method (Viechtbauer & Cheung, 2010). This method provides us with an estimate for those RTE-tests that have the greatest impact on the summary effect size and the heterogeneity between RTE-tests. Influence measures were DIFFITS, Cook's distance, and the covariance ratio (Harrer et al., 2019a). Additionally, we used the Baujat plot to reveal RTE-tests contributing most to the heterogeneity (Baujat et al., 2002). Furthermore, we estimated the publication bias for the RVC-configuration subset using the small sample method (funnel plot; Egger's test; Egger et al., 1997). Lastly, we used Duval & Tweedie's trim-and-fill procedure to estimate the true summary effect size taking into account potential small studies that were not published due to the publication bias (Duval & Tweedie, 2000).

II.2.3.2. Results

To begin with, the RTE-tests reported in the studies were extracted and evaluated based on our inclusion criteria. From 32 studies registered in the systematic literature research, we extracted 39 RTE-tests. For 6 RTE-tests, we could not estimate Hedge's *g* because no test statistic was reported. Hence, these RTE-tests were not included in the meta-analysis. To evaluate how these RTE-tests would have influenced the summary effect size, we reviewed their direction and significance. Five RTE-tests were significant showing a positive RG (Leh et al., 2006; Ridgway et al., 2008; Savazzi & Marzi, 2008, Exp. 1: RG = 20.70ms & Exp. 2: RG = 21.14ms; Turatto et al., 2004, RG = 24.30ms). One of the RTE-tests was non-significant (Donkin et al., 2014, Exp. 1). In this latter study, authors manipulated a speed or accuracy emphasis which interacted significantly with the RTE. Under speed emphasis, there was a positive RG (8ms). In contrast, under accuracy emphasis, the RTE reversed (RG = -28ms; Donkin et al., 2014). Hedge's g could be calculated for the second experiment of Donkin et al. (2014) which contained the same experimental manipulation. Results showed a reversed redundancy gain. As this result was based on a main effect across both speed and accuracy emphasis conditions (Donkin et al., 2014), it was likely driven by the negative impact of the accuracy emphasis. Importantly, all other included RTE-tests in the meta-analysis and all patient studies emphasized speed (respond as fast as possible). Given the unusual manipulation and instruction, the RTE-tests of Donkin et al. (2014) are unrepresentative. Consequently, the RTE-test of the second experiment of Donkin et al. (2014) was also excluded from analysis.

From the 32 RTE-tests included in the meta-analysis, two were not significant (Grice & Gwynne, 1987, Exp. 5; Omura et al., 2004) and two RTE-tests were reversed showing longer

reaction times in the double condition (Grice et al., 1984, Exp. 1 & Exp. 2; see also Figure II.2). As these RTE-tests were in contrast to the other 28 positive RTE-tests, we looked for arguments or experimental manipulations that could lead us to unexpected sources of heterogeneity. Importantly, these RTE-tests were nevertheless kept in the meta-analysis because no predefined criterion was violated. Grice et al. (1984) interpreted their negative result in the first experiment as a distraction effect within the framework of target-response (T-R) compatibility. In the single compatible condition, the target is on the same side as the response hand. If a second redundant target is presented within the opposite hemifield, this target is incompatible with the response hand and hence prolongs reaction times. In Omura et al. (2004), the marginal RTE ($p<.10$) was calculated between bilateral redundant and incompatible single condition. Interestingly, Grice et al. (1984) reported also a negative RTE in the second experiment in which targets were presented vertically thereby eliminating a possible T-R incompatibility. For the analysis, Grice et al. (1984) chose the faster single condition to calculate the RTE and hence argue, that the less-preferred location in the redundant condition led to a distraction effect. The same explanation was used for the non-significant RTE with vertical stimulation of experiment five in Grice and Gwynne (1987).

The methodological problems identified in the previous paragraph might prompt us to consider the issue of T-R compatibility in general as a potential source of variability. Following this, we reviewed other studies included in the meta-analysis for results regarding T-R compatibility. Increased reaction times in T-R incompatible conditions have been replicated by three studies (Corballis, 2002; Fischer & Miller, 2008; Miller, 2007; Miller & Adam, 2006). However, these studies showed an overall positive RTE based on the average single reaction time (except Miller, 2007, who used the faster single condition). Other studies circumvented the T-R compatibility issues using different methodological approaches. Two studies solved the issue of T-R compatibility by a bimanual response (Fischer & Miller, 2008; Miller & Van Nes, 2007). Interestingly, bimanual responses led to a greater redundancy gain than unimanual responses (Fischer & Miller, 2008; Miller & Van Nes, 2007). Other studies counterbalanced trials with left or right response hand and averaged reaction times across both conditions (e.g. Schröter et al., 2011). Moreover, two studies centered the response button in reference to the body midline to avoid a T-R incompatibility (Miniussi et al., 1998; Murray et al., 2001).

Besides, a number of studies did not consider T-R compatibility. Several studies did not specify the response hand (e.g. Tamietto et al., 2010) and other authors instructed participants to use one specific hand (Müller-Oehring et al., 2009). As all these studies led to positive results, the T-R compatibility problem might be less critical than expected.

Similar to the second experiment in Grice et al. (1984), other studies applied vertical stimulation which avoids T-R compatibility issues. Importantly, these studies showed significant positive RGs even when the faster single condition was used for the analysis (e.g. Mordkoff et al., 1996, Exp. 2). The latter results contradict the argument of Grice et al. (1984) and Grice and Gwynne (1987).

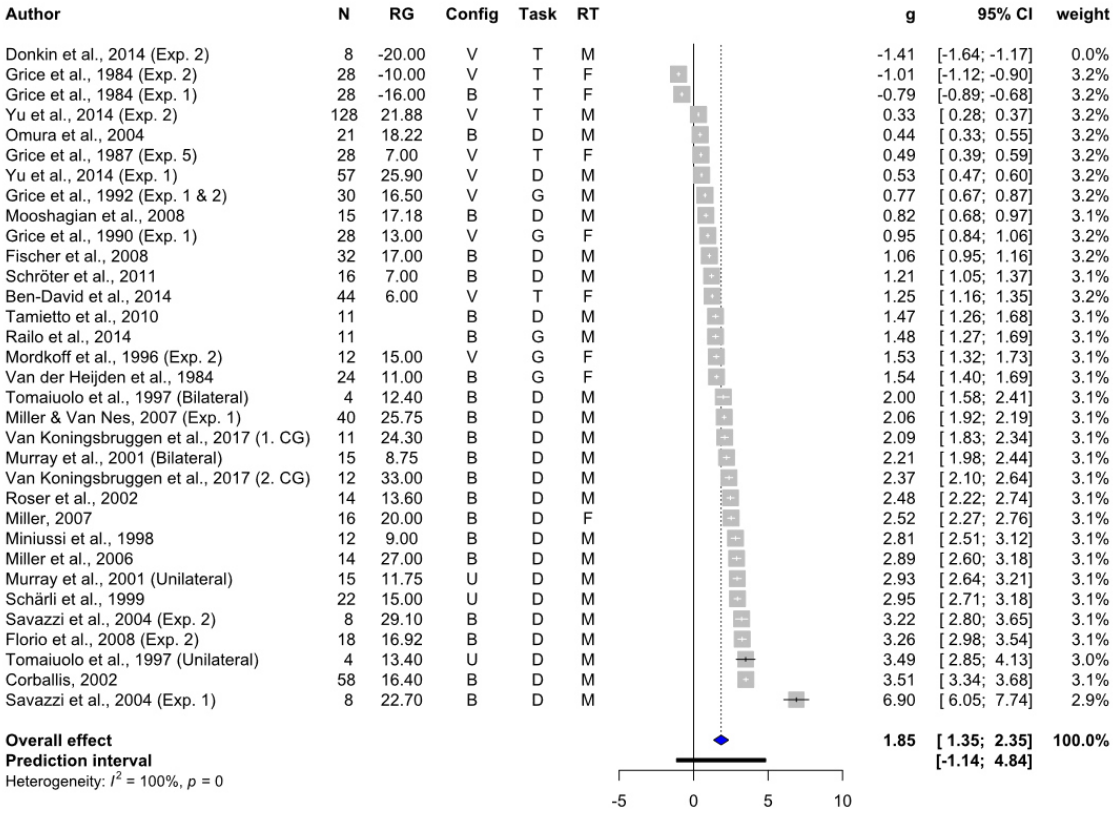
Regarding patient studies, it is worth emphasizing that the T-R compatibility cannot be manipulated in the majority of cases. The side of the single target is determined by the side of the HVFD and the choice for the response hand might be restricted by hemiplegia. Consequently, it is important for the application in HVFD-samples to test the RTE across all possible response modalities. Due to the variability in dealing with T-R compatibility subgroup analysis were not applicable for this parameter. In conclusion, we ran the meta-analysis with all 32 RTE-tests irrespective of T-R compatibility.

Results of the meta-analysis with $r = 0.97$ across all 32 RTE-test can be seen in Figure II.2 (results for $r = 0.77$ and r = 0.57 see Table II.A.1). All models ($r = 0.97$, $r = 0.77$, $r = 0.57$) were significant and showed a summary effect size of $g > 1.67$. Thereby the 95%-CIs never included zero. However, the lower borders of the 95%-PIs were negative in all three models showing that the range of true effect sizes in similar studies included zero. Measures of heterogeneity were high. All *Q*-statistics were significant and all I^2 were above 75% (Higgins et al., 2003). Importantly, the *SE*s increased with decreasing *r* ($r = 0.97$: $SE = 0.12 \pm 0.08$; $r = 0.77$: $SE = 0.32 \pm 0.24$; $r = 0.57$: $SE = 0.44 \pm 0.32$). Hence, the heterogeneity within the random effects models decreased with decreasing *r.* This was also true for the subsequent subgroup analysis and for the later analysis of the RVC-configuration subset.

As the pattern of results in subgroup analysis was similar for all three values of *r*, we present only the results of $r = 0.97$ in Table II.1 (results of $r = 0.77$ and $r = 0.57$ see Table II.A.2).

Figure II.2

Results of the random effects model (r = 0.97) across all studies



Note. The forest plot shows the effect size g with its associated 95% confidence interval for each included RTE-test and for the summary effect size at the bottom. The black bar at the bottom represents the 95% prediction interval of the summary effect size. N = Number of participants; RG = redundancy gain in milliseconds; Config = double target configuration; V = vertical; B = bilateral; U = unilateral; Task = experimental paradigm of study; T = two-choice, D = detection, G = go/ no-go; RT = reaction time measure of single target condition; M = mean reaction time across all single target configurations, F = faster/ fastest reaction time from all single target configurations; g = Hedge's g; 95% CI = 95% confidence interval of Hedge's g based on the calculation of the standard error with r = 0.97; weight = relative weight of each included RTE-test.

Table II.1

Results of subgroup analysis for random effects model with r = 0.97

model	*k*	*g*	*95% CI*	95% PI	*Q*	τ^2	I^2	*Q-G*
faster	8	0.81	[-0.03, 1.64]	[-2.31, 3.93]	2148.3	*1.44*	*99.7*	*7.43***
mean	24	2.20***	[1.65, 2.75]	[-0.69, 5.08]	4067.8	1.86	99.4	
bilateral	21	2.15***	[1.53, 2.77]	[-0.94, 5.23]	3626.4	2.07	99.4	
unilateral	3	2.98***	[2.81, 3.16]	[1.85, 4.12]	2.7	0.00	24.8	73.0***
vertical	8	0.60*	[0.07, 2.77]	[-1.38, 2.58]	1184.5	0.76	99.4	
detection	22	2.39***	[1.84, 2.95]	[-0.39, 5.18]	2890.4	1.71	99.3	
go/ no-go	5	1.24***	[0.92, 1.57]	[-0.02, 2.51]	113.9	0.13	96.5	23.6***
two-choice	5	0.06	[-0.77, 0.88]	[-3.22, 3.33]	1321.8	0.88	99.7	

Note. Model = Model of subgroup analysis: Faster single RT vs. mean single RT; k = number of included effects; g = estimate of summary effect size based on Hedge's g; 95% CI = 95% confidence interval of the summary effect size; 95% PI = the 95% prediction interval of the summary effect size; Q = Q statistic for statistical heterogeneity; τ^2 = estimate of the variance between RTE-tests; I^2 = percentage of the observed variance which is due to real differences in effect sizes; Q Groups= Q statistic for subgroup differences; * p<.05. ** p<.01. ***p<.001.

As expected, studies using the mean reaction time for the single condition had a higher summary effect size than studies using the faster reaction time. The 95%-CIs of the summary effect size based on the faster single reaction time included zero. Regarding target configurations, unilateral stimulation led to the highest summary effect size, followed by bilateral stimulation. Vertical stimulation led to a very small summary effect size. Comparing paradigms across studies, the results showed that two-choice tasks led to the smallest summary effect size (95%-CI includes zero). Detection paradigms had the highest summary effect size. Importantly, the number of included RTE-tests (*k*) varied considerably between subgroups, for example, $k = 5$ for go/ no-go and $k = 22$ for detection paradigms. These differences and the correlation coefficients *r* affected the measures of heterogeneity and hence the 95%-PIs. For $r = 0.57$ and $r = 0.77$, the 95%-PIs were above zero for the detection and the go/ no-go subgroup. Additionally, the lower border of the 95% PI was above zero for the unilateral subgroup at $r = 0.97$.

To test RVCs, studies used the mean single reaction time and a detection paradigm, both features leading to the highest summary effect size in their subgroups. Regarding target configurations, the unilateral stimulation led to the highest summary effect but was tested only in three RTE-tests (Figure II.2). Two of the three RTE-tests investigating unilateral

stimulation also tested bilateral stimulation in the same sample of participants (Murray et al., 2001; Tomaiuolo et al., 1997). For these two RTE-tests, the statistical results within the subgroups were dependent and differences should be interpreted with caution. Bilateral stimulation which is necessary to test RVCs led similarly to a high summary effect size.

To assess the summary effect size specifically for RVC-tests, we calculated a random effects model for the RVC-configuration subset. Importantly, RTE-tests investigated the RTE in healthy participants and we selected the experimental paradigms fitting to RVC-research. Regarding outliers, the RTE in Savazzi and Marzi (2004, Exp. 1) is apparently far above all other studies (Figure II.3). This is confirmed by the influence analysis showing extreme values for DIFFITS, Cook's distance, and the covariance ratio for $r = 0.97$ and $r = 0.77$ (Table II.A.3). For $r = 0.97$, the values are even above the cutoff proposed by Viechtbauer and Cheung (2010). In the Baujat plot, the RTE-tests of Omura et al. (2004) and Corballis (2002) were contributing most to the heterogeneity for all three values of *r*. Additionally, these two RTE-tests were conspicuous for some of the measures of influence but only when $r = 0.57$ and they did not exceed the cutoff value. Furthermore, Omura et al. (2004, N = 21) and Corballis (2002, N = 58) had a comparatively high number of participants compared to Savazzi and Marzi (2004, Exp. 1, N = 8). Consequently, we decided to keep Omura et al. (2004) and Corballis (2002) in the sample and only exclude Savazzi and Marzi (2004) from the RVC-configuration subset for all values of *r*.

The different kinds of meta-analysis yielded all significant summary effect sizes of $g \geq 2.03$ (see Figure II.3 for $r = 0.97$; see Table II.2 for all values of *r*). All 95%-CIs and 95%-PIs were above zero. Again, heterogeneity was high for all values of r with $I^2 > 75\%$ and significant *Q*-tests.

Funnel plots showed an asymmetric distribution of effect sizes and sample sizes indicating the presence of a publication bias for all values of *r* (Figure II.A.I). This asymmetry in the data was confirmed by significant Egger's tests (Table II.3) showing that there is a lack of RTE-tests having small sample sizes and small effects. However, with Duval & Tweedie's trim-and-fill procedure compensating for a publication bias, significant summary effect sizes were still obtained. However, with that correction the 95%-PIs included zero. This means that if all studies about the RTE would be published, the expected range of true effect sizes in similar studies could include zero.

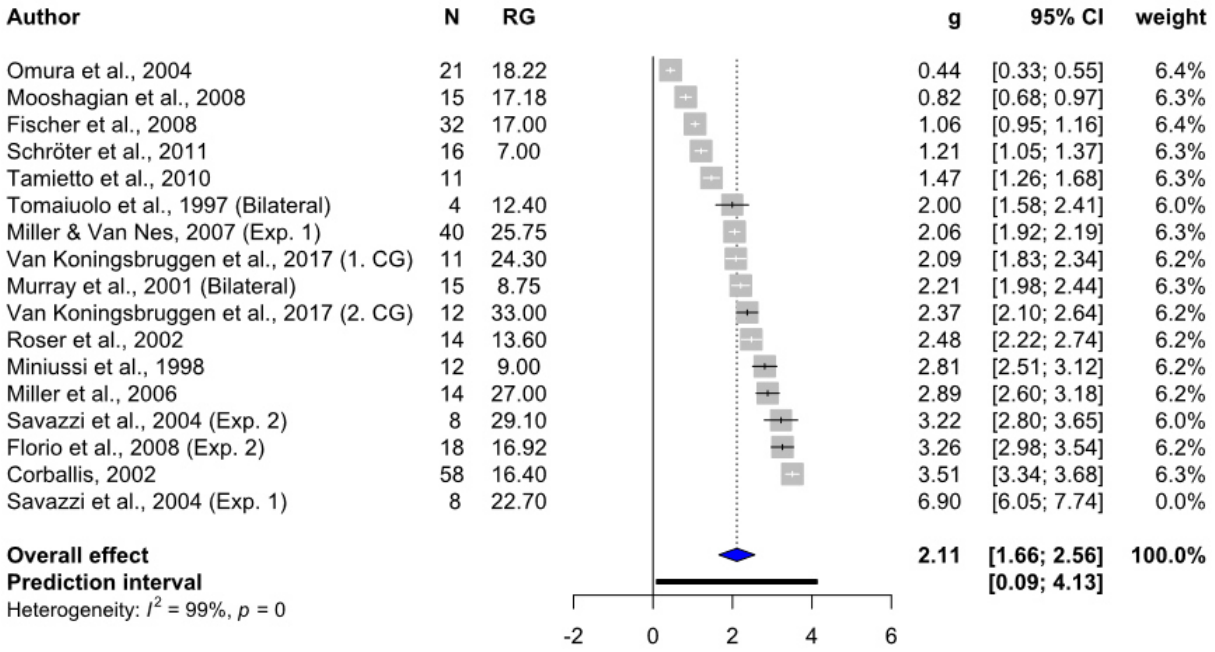
Lastly, we calculated the average RG for the RVC-configuration subset. Thereby, we included also RTE-tests that did not contribute to the meta-analysis but specified a RG in milliseconds. The average RG was 18.90±7.27ms.

To summarize, the RTE-tests included in the meta-analysis led to a significant summary effect size but revealed a high level of heterogeneity. This heterogeneity can be partly

explained by differences in the experimental designs. Thereby, the subgroups of mean single reaction time, detection paradigm and unilateral stimulation led to the highest summary effect sizes. A subset of experiments selected to fit the design of RVC-tests (RVC-configuration subset) led to a high and significant summary effect size. Importantly, the expected range of true effect sizes in similar studies was above zero but only if the publication bias was neglected.

Figure II.3

Results of the random effects model (r = 0.97) for the RVC-configuration subset with outlier correction



Note. The forest plot shows the effect size g with its associated 95% confidence interval for each included RTE-test and for the summary effect size at the bottom. The black bar at the bottom represents the 95% prediction interval of the summary effect size. The RVC-configuration subset included all RTE-tests using the mean single reaction time of a detection paradigm with a bilateral double stimulation. N = Number of participants; RG = redundancy gain in milliseconds; redundancy gain is the difference in reaction times between double and single stimulation; g = estimation of effect size based on Hedge's g; 95% CI = 95% confidence interval of Hedge's g based on the calculation of the standard error with r = 0.97; weight = relative weight of each included effect; Outliers that are excluded have a weight of 0.0%.

Table II.2

Results of meta-analysis for the RVC-configuration subset

r	*k*	*g*	*95% CI*	95% PI	*Q*	τ^2	I^2
0.97	16	2.11***	[1.66, 2.56]	[0.09, 4.13]	1643.4***	0.83	99.1
0.77	16	2.07***	[1.60, 2.53]	[0.10, 4.04]	214.4***	0.79	93.0
0.57	16	2.03***	[1.55, 2.51]	[0.11, 3.96]	114.7***	0.75	86.9

Note. r = correlation coefficient used to estimate the standard error of the effect size for each RTE-test; k = number of included RTE-tests; g = estimate of summary effect size based on Hedge's g; 95% CI = 95% confidence interval of the summary effect size; 95% PI = the 95% prediction interval of the summary effect size; Q = Q statistic for statistical heterogeneity; τ^2 = estimate of the variance between RTE-tests; I^2 = percentage of the observed variance which is due to real differences in effect sizes; * p<.05. ** p<.01. ***p<.001.

Table II.3

Results of the publication bias tests in the RVC-configuration subset

r	*Egger's test*			Duval & Tweedie's trim-and-fill			
	Intercept	*95% CI*	*t*	*add k*	*g*	*95% CI*	*95% PI*
0.97	16.75	[6.55, 26.94]	3.22**	7	1.31***	[0.70, 1.91]	[-1.82, 4.44]
0.77	6.05	[2.37, 9.73]	3.22**	7	1.30***	[0.71, 1.90]	[-1.71, 4.32]
0.57	4.42	[1.73, 7.12]	3.22**	7	1.30***	[0.71, 1.90]	[-1.60, 4.21]

Note. r = correlation coefficient used to estimate the standard error of the effect size for each RTE-test; Egger's test for asymmetry due to publication bias; Intercept = intercept of asymmetry in the data; 95% CI = 95% confidence interval of the intercept; t = t-statistic of Egger's test; Duval & Tweedie's trim-and-fill = procedure to estimate the summary effect size without the publication bias; add k = number of added studies; g = estimate of summary effect size based on Hedge's g; 95% CI = 95% confidence interval of the summary effect size; 95% PI = 95% prediction interval of the summary effect size; * p<.05. ** p<.01. *** p<.001.

II.2.4. Review: The RTP as a test for RVCs

The results of the meta-analysis showed that the RTE, based on the design of RVC-tests, is a strong and significant effect in healthy participants. However, the meta-analysis does not provide information about the diagnostic quality of the RTP. The diagnostic quality is relevant because studies classified patients into RVC-positive or -negative depending on their RTP results (Leh et al., 2006; Striemer et al., 2009). Furthermore, researchers derived predictions about other RVCs from the RTP-results (Striemer et al., 2018). If the diagnostic quality of the RTP is low, the classification and the predictions would be imprecise. To estimate the diagnostic quality of the RTP, we reviewed results in patient studies. Initially, we investigated how many patients with HVFD showed RVCs in the RTP. As measures for the diagnostic quality, we estimated the sensitivity and reliability. Regarding sensitivity, we evaluated how good the RTP detects the presence of visual functions. Mathematically, the sensitivity is calculated by dividing the number of true positives by the sum of true positives and true negatives (Lalkhen & McCluskey, 2008). Hence, we need to know if participants are true positives or negatives, meaning visual functions are present or absent. Therefore, we reviewed results of the RTP measured in healthy participants as well as in the sighted visual field of patients. In both cases, visual functions are truly present. Consequently, the sensitivity should be ideally close to 100% in these tests.

Next, we estimated the reliability by comparing results in patients that were tested in multiple occasions. If a patient has true RVCs and the RTE has a high reliability, the effect should be found in every test.

Knowing sensitivity and reliability, we can estimate how good the RTP classifies patients. However, it is still unclear if predictions based on the RTP-results about the performance in other RVC-tasks are valid. The prediction implies that the RTP measures visual functions within the blind field required for the other RVC-task. If this were true for all other types of RVCs, the RTP would indicate the minimal configuration criterion (MCC) of RVCs. Having a MCC-test would be helpful in recruiting patients for RVC-studies or in planning rehabilitation strategies. To test whether the RTP is a MCC-test, we can make the following hypothesis: (1) If the RTE is significant, the patient might also show RVCs in other tasks. (2) If the RTE is not significant, the patient must not show RVCs in other tasks. If the second assumption is violated, the claim that the RTP indicates the MCC must be withdrawn.

As our conclusions about sensitivity, reliability, and the MCC-test are drawn from studies varying in sample and in experimental characteristics, it is also necessary to take methodological issues into account when discussing the relevance of given set of findings.

II.2.4.1. RVCs measured by the RTP

Fifteen studies using the RTP reported on a sample of patients with HVFD (Table II.4). Thereof, two studies compared their HVFD-sample with other clinical groups: HVFD-patients with comorbid neglect (Müller-Oehring et al., 2009) and patients with optic nerve lesions (Wüst et al., 2002). Moreover, five studies included a control group of healthy participants (Leh et al., 2006; Schärli et al., 1999; Tamietto et al., 2010; Tomaiuolo et al., 1997; Wüst et al., 2002).

To investigate the RTP as a test for RVCs, the comparison between double bilateral and single stimulation is crucial. RVC in the RTP is defined as faster reaction times for double bilateral targets compared to a single target. In the double bilateral condition, one target is presented within the sighted visual field and an identical target is simultaneously presented within the blind visual field. In total, 74 participants with HVFD (Table II.4) have been tested with these conditions. In five studies, a group analysis was performed. Thereof, one study showed a significant RTE for the double bilateral condition (Celeghin, Savazzi, et al., 2015). Group analysis in none of the other studies yielded significant results (Marzi et al., 1986; Müller-Oehring et al., 2009; Ross et al., 2018; Tomaiuolo et al., 1997). Hence, we checked whether there were special features in the study of Celeghin, Savazzi, et al. (2015) that could explain their positive results and that might be used to improve the RTP in the future. Interestingly, the RTP in Celeghin, Savazzi, et al. (2015) differed from the other studies in the number of targets presented within the hemifields. Authors presented single or quadruple targets. If the target number increased within the blind visual field, reaction times decreased significantly on the group level. Yet, this was only true if the quadruple target followed the gestalt-laws. Importantly, this was the only study with a significant group effect in the RVC-condition leading to the assumption that an increased number of related targets in the blind visual field might enhance RVC-performance. The advantage of gestalt-like configurations was later replicated by Georgy et al. (2016). To summarize, 12.77% (6 of 47) participants showed a RTE in the RVC-condition in group analysis (Figure II.4).

Fourteen studies presented findings from single-case analysis (the exception is Celeghin, Savazzi, et al., 2015). However, four patients (DR, SE, JB, GY) were tested and reported multiple times in different studies (see Table II.4). Accordingly, evidence from these repeated examinations of the same patients should not be treated as independent cases of empirical support. Thus, when computing the sum of all patients reported to having shown RTE, these patients were counted only once.

Table II.4

Overview of studies investigating RVCs with the RTE

Study	N	Etiology	RVC-positive
Marzi et al. (1986)	20	PCL	4 (GD, SC, EC, MF)
Corbetta et al. (1990)	4 (Case 1-4)	PCL	2 (Case 2, Case 3)
Tomaiuolo et al. (1997)	4 (DR, SE, IG, JB)	H	2 (DR, SE)
Schärli et al. (1999)	9	PCL	0
de Gelder et al. (2001)	1 (GY)	PCL	1 (GY)
Wüst et al. (2002)	8 (Post 1-8)	PCL	2 (Post6, Post7)
Leh et al. (2006)	5 (DR, SE, LF, FD, JB)	H	3 (DR, LF, SE)
Marzi et al. (2009)	1 (CA)	PCL	1 (CA)
Müller-Oehring et al. (2009)	11	PCL	0
Striemer et al. (2009)	1 (CB)	PCL	1 (CB)
Tamietto et al. (2010)	1 (GY)	PCL	1 (GY)
Whitwell et al. (2011)	1 (SY)	PCL	0
Celeghin, Savazzi, et al. (2015)	6 (P1-P6)	PCL	6 (P1-P6; only group analysis)
Georgy et al. (2016)	2 (DR, SE)	H	2 (DR, SE)
Ross et al. (2018)	6 (P1-P6)	PCL	1 (P4)
Sum	**74**		**21**

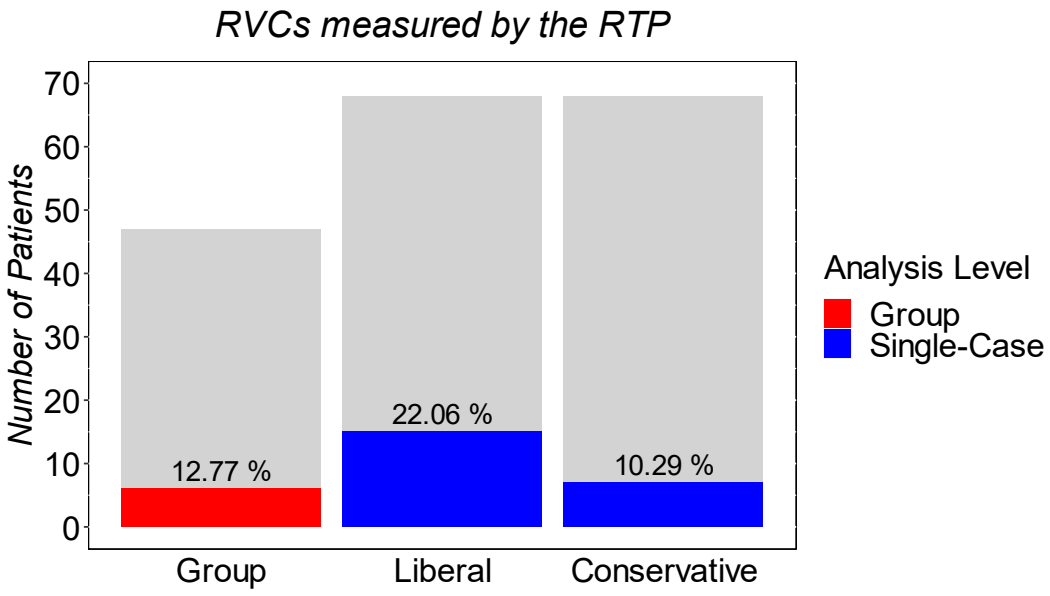
Note. N = number of patients with homonymous visual field defects. Patient codes are written in brackets. Underlined patient codes indicate that this patient has been tested in multiple studies. Patients that have been tested multiple times are counted only once for the overall number of patients. Etiology = cause of visual field defect; PCL = post chiasmal lesion; H = hemispherectomized; RVC-positive = patients with at least one significant RTE in at least one occasion; Studies with grey background investigated also the double unilateral condition with targets only in the sighted visual field.

To estimate the prevalence of RVCs in RTPs, we initially applied the most liberal criterion for RVCs: Patients need one significant RTE in single-case analysis of at least one occasion (for instance in one session or for one target location) irrespective of other results. With this most liberal criterion, 22.06% of patients (15 out of 68) were RVC-positive (Figure II.4). Secondly, we applied the most conservative criterion for RVCs: Patients need a significant RTE in all tested occasions. With this most conservative criterion only 10.29% of patients (7 out of 68) were categorized to be RVC-positive (Figure II.4). It is worth noting that only one of the patients tested in multiple sessions within one study showed consistent positive results (patient CA in Marzi et al., 2009). Furthermore, most patients fulfilling the conservative criterion were recruited on the basis of their RVCs in previous experiments (patients DR, SE, GY, LF, and CB; Table II.5). As RVCs are remnants of visual functions, we rather applied the liberal criterion for the remainder of this article to avoid underestimating the performance.

In summary, the RTP was analyzed on group level and on single-case level. Overall, 12.77% (group analysis) - 22.05% (single-case analysis) of patients had a significant RTE in the RVC-condition (Figure II.4). Before we can use these values as an estimate of the prevalence of RVCs, it is necessary to determine how sensitive the RTP measures the presence of vision.

Figure II.4

Number of patients defined as RVC*-positive on the basis of a significant RTE*



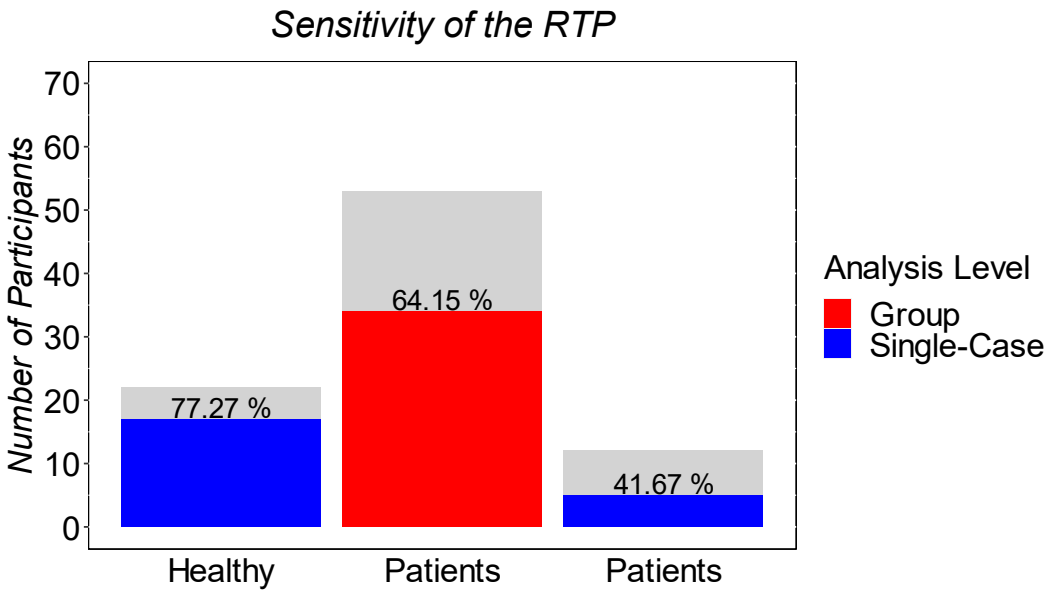
Note. Summary of results presented in the literature. The grey bar graphs show the number of patients investigated with the RTP. The red (group level) or blue (single-case level) areas show the number of patients with a significant RTE indicating RVCs. The numbers within bars show the percentage of patients with a significant RTE indicating RVCs.

II.2.4.2. How good is the sensitivity of the RTP?

The sensitivity of the RTP is calculated by dividing the number of participants with a significant RTE by the number of participants with vision. Hence, it is essential to know whether vision is truly present or not. For this purpose, we reviewed the RTE tested within the sighted visual field of patients and in healthy participants. Furthermore, results are most precise if the RTE is analyzed per participant in a single-case analysis. In the selection of studies from our systematic literature review, only one study calculated a single-case analysis with healthy participants. The analysis of Schärli et al. (1999) showed that 17 out of 22 healthy participants (77.27%) had a significant RTE (Figure II.5). Regarding patients with HVFD, four studies showed a significant RTE on group level within the sighted field (Celeghin, Savazzi, et al., 2015; Corbetta et al., 1990; Marzi et al., 1986; Tomaiuolo et al., 1997). In contrast, this difference was not significant in group analysis of Wüst et al. (2002) and Müller-Oehring et al. (2009). Single-case analysis were significant in three of four patients in Tomaiuolo et al. (1997) and in two of eight patients in Wüst et al. (2002). In summary, the RTE has been tested in the sighted visual field of 53 HVFD-patients. Group effects have been significant for a total of 34 patients (64.15%). A single-case analysis was calculated for 12 participants, whereby 5 had a significant RTE (41.67%; Figure II.5).

Figure II.5

Sensitivity of the RTP measured in healthy participants and in the sighted field of patients



Note. Summary of results presented in the literature. The grey bar graphs show the number of participants investigated with the RTP. The red (group level) or blue (single-case level) areas show the number of participants with a significant RTE. The numbers within bars show the percentage of patients with a significant RTE indicating RVCs.

To conclude, the RTP detected the presence of visual functions within the sighted visual field in 41.67%-77.27% of participants (Figure II.5). This is considerably below the expected value of 100%. In all studies reported in this section, the RTE was tested only once in the sighted field of patients or in healthy participants. Following this, it is still unclear whether the RTP detects the presence of visual functions reliably.

II.2.4.3. How good is the reliability of the RTP?

The reliability is estimated by comparing results across multiple sessions. As an outcome, the RTE is either present or absent. The reliability is high if the RTP has the same outcome in the same participant in multiple sessions. As the RTP was tested only once in the sighted field of patients or in healthy participants, we evaluated results within the blind field of patients. With our liberal criterion, 15 patients were identified as RVC-positive by having a significant RTE in the single-case analysis in at least one occasion (Table II.5).

Twelve of these participants were tested in multiple sessions. Thereof, eight (66.67%) patients showed a significant RTE only in certain sessions or for certain target locations (Figure II.6). Two participants (SC and MF in Marzi et al., 1986) even showed significant reaction time differences in the opposite direction in other sessions. Four patients (DS, SE, and LF in Leh et al., 2006; CA in Marzi et al., 2009) showed an RTE depending on certain color conditions that should specifically test the contribution of the superior colliculi (SC). As this specificity for the SC has been questioned (Hall & Colby, 2014), the lack of a significant RTE in these conditions is possibly a sign of the unreliability of the effects. As this issue has not been clarified yet, we do not include these inconsistencies to our estimate of reliability. In Wüst et al. (2002) the two RVC-positive patients (Post6, Post7) showed the RTE only for one set of target locations. It could be that RVCs are only present at certain parts of the visual field. For instance, studies showed that training RVCs is highly location specific in chronic HVFDs (Huxlin et al., 2009; Saionz et al., 2020). In Wüst et al. (2002), the specificity would be confirmed if these patients showed other types of RVCs also only for these locations. However, only patient Post6 showed RVCs in another task. In the RTP, Post6 had significant results for positions 4 and 6 (position numbers 1-9 from figure 4 in Wüst et al., 2002), In the manual localization task, Post6 showed above chance performance for positions 2, 3, 4, 6. Hence, only positions 4 and 6 have corresponding RVC-results. Therefore, we still categorize Post6 and Post7 to have inconsistent results in the RTP.

Table II.5

Results of all RTE-results of patients with at least one significant RTE

Study	Patient	RTE results
Marzi et al. (1986)	GD	1 sign. RTE in 2 sessions
	SC	1 sign. RTE & 1 RTE in opposite direction in 6 sessions;
	EC	2 sign. RTEs in 9 sessions
	MF	2 sign. RTEs & 1 RTE in opposite direction in 4 sessions;
Corbetta et al. (1990)	Case 2	2 sign. RTEs in 7 sessions; sign. RTE across all sessions;
	Case 3	1 sign. RTE in 5 sessions
Tomaiuolo et al. (1997)	DR	1 sign. RTE in 1 session
Leh et al. (2006)		1 sign. RT only for certain colors;
Georgy et al. (2016)		1 sign. RTE in 1 session
Tomaiuolo et al. (1997)	SE	1 sign. RTE in 1 session
Leh et al. (2006)		1 sign. RTE only for certain colors;
Georgy et al. (2016)		1 sign. RTE in 1 session
de Gelder et al. (2001)	GY	1 sign. RTE in 1 session
Tamietto et al. (2010)		1 sign. RTE in 1 session
Wüst et al. (2002)	Post 6	1 sign. RTE in 3 sets of locations
	Post 7	1 sign. RTE in 3 sets of locations
Leh et al. (2006)	LF	1 sign. RTE only for certain colors;
Marzi et al. (2009)	CA	2 sign. RTEs in 2 sessions; only for certain colors
Striemer et al. (2009)	CB	1 sign. RTE in 1 session
Ross et al. (2018)	P4	1 sign. RTE in 1 session

Note. Patients with unreliable results are underlined and highlighted with grey background. RTE = redundant target effect; sign. = significant at an α-level of 0.05.

To summarize, only 33.33% of patients that were tested multiple times showed consistent, positive results for the RVC-condition (Figure II.6). Importantly, it is unknown whether RVCs were stable across RTP-tests. Hence, the RTP might have correctly identified RVCs in the specific occasion(s) in which RVCs were present. Following this, results indicate a low correspondence of RTP-results but values should be only cautiously interpreted as estimate for the retest reliability of the RTP.

II.2.4.4. Is the RTP a MCC-test for RVCs?

To investigate whether the RTP indicates the MCC of RVCs, we compared the RTE-results to the results of other RVC-tests (Table II.6). Seven studies tested the RTP together with other RVC-tasks.

Table II.6

Overview of studies testing the RTE together with other RVC-tasks

Study	RTE positive	RVCs in other tasks
Corbetta et al. (1990)	Case 2 Case 3	Case 2: Manual localization task & temporal interaction Case 4: Manual localization task
Schärli et al. (1999)		PM: Temporal detection task
de Gelder et al. (2001)	GY	GY: E.g. congruency effect for emotional expressions of half and full faces
Wüst et al. (2002)	Post6 Post7	Post1: Manual localization task Post2: Manual localization task Post3: Manual localization task & target detection Post6: Manual localization task
Striemer et al. (2009)	CB	CB: Manual obstacle avoidance task
Whitwell et al. (2011)		SJ: Grasping task
Ross et al. (2018)	P4	P4: Manual localization task

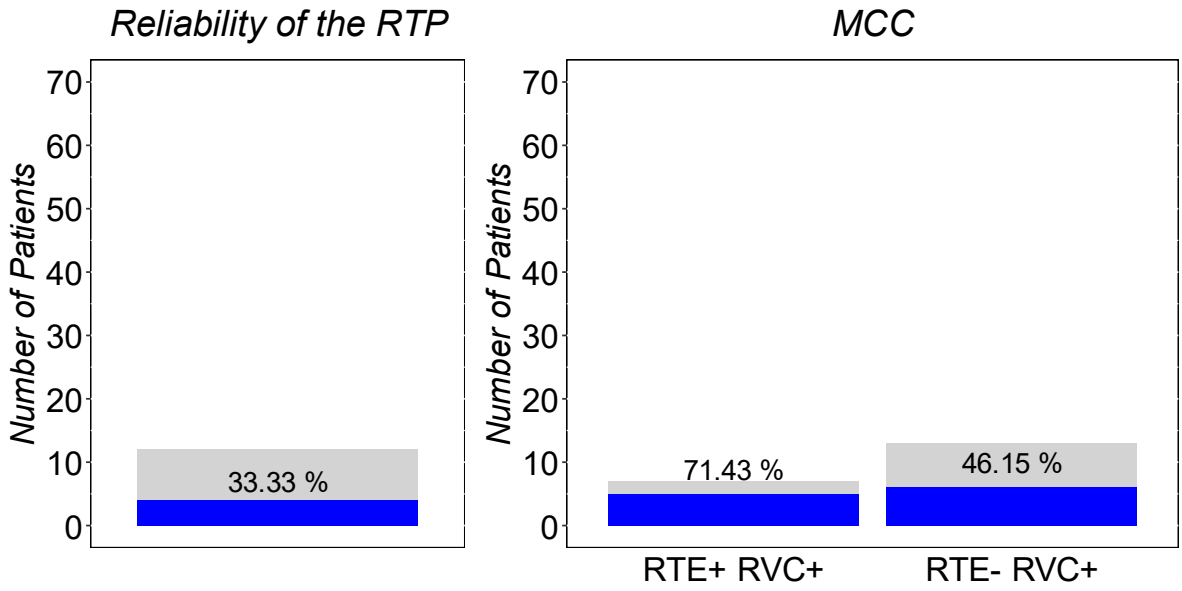
Note. Patient codes are underlined if they showed no RTE but RVCs in other tasks. RTE = redundant target effect.

Corbetta et al. (1990) showed a significant RTE for Case 2 and Case 3. Additionally, they tested the temporal interaction between hemifields by presenting two targets with a short delay. If healthy participants had to respond to the second target, their reaction times were prolonged. In patients with HVFD, the first target was presented within the blind visual field. If the reaction time to the second target within the sighted visual field increased, the behavior was an indicator for RVCs. This was true for Case 2. Furthermore Corbetta et al. (1990) also employed a pointing task with four LEDs in the blind visual field. Participants performed the manual localization after the LED flash. If participants had to fixate continuously, none of the patients showed RVCs. If participants were instructed to point and look to the possible location of the target, Case 2 and Case 4 showed pointing accuracies significantly above chance (switched-off LEDs were visible). To summarize, Case 3 showed RVCs only for the RTE whereas Case 2 showed RVCs across all tasks. Schärli et al. (1999) tested nine patients having no RTE in the RVC-condition. However, one patient (PM) showed RVCs in a temporal detection paradigm. Patient GY showed a significant RTE in two studies (de Gelder et al., 2001; Tamietto et al., 2010). In one of those studies, significant congruency effects for the emotional expression of half or full faces presented in the sighted and blind visual field were found (de Gelder et al., 2001). Moreover, this patient has been investigated in multiple other studies showing a broad spectrum of RVCs, for instance for color (Cowey & Stoerig, 2001) and motion (Morland et al., 1999) discrimination. Wüst et al. (2002) acquired data on the RTE as well as on target detection and localization. The RTP revealed positive results for patients Post6 and Post7. Patient Post3 had above-chance performance for target detection. Regarding target localization by pointing, four patients showed significant results (Post1, Post2, Post3, and Post6). Hence, one (Post6) out of two patients with RTE showed RVCs in another task. In turn, three patients (Post1, Post2, and Post3) showed no RTE but RVCs in other tasks. Patient CB showed a RTE and intact obstacle avoidance behavior within his blind visual field but only if obstacles were presented without time delay (Striemer et al., 2009). Whitwell et al. (2011) showed no RTE in patient SJ but a significant grip scaling to the size of objects presented within the blind visual field. In Ross et al. (2018), patient P4 showed RVCs in the RTP and also action blindsight (i.e. a significant and correct adaptation of pointing distance to target eccentricity in a localization task). Regarding the obstacle avoidance task, none of the patients showed a reliable adaptation of hand trajectories neither for one nor for two obstacles (Ross et al., 2018).

In summary, there were five out of seven cases confirming that patients with a RTE could also show RVCs in other tasks. In contrast, the critical assumption for MCC was violated by six patients showing no RTE but a significant RVC-result in other tasks (underlined in Table II.6, Figure II.6). To conclude, we cannot hold the claim that the RTP indicates whether the MCC of RVCs is fulfilled in the tested patient.

Figure II.6

Reliability of the RTP and the RTP as a test for the MCC of RVCs



Note. Summary of results presented in the literature. Analysis based on results of single-case analysis. Left plot: The grey bar graph shows the number of patients investigated with the RTP multiple times. The blue area shows the number of patients with consistent positive results. The number above within the bar shows the percentage of patients with consistent positive results. Right plot: The grey bar graphs show the number of patients investigated with the RTP and with other RVC-tasks. Patients are separated in having a significant (RTE+) or non-significant RTE (RTE-). The blue areas show the number of patients with positive results in other RVC-tasks (RVCs+). The numbers within or above bars show the percentages of patients with a significant RTE indicating RVCs.

II.2.4.5. Methodological issues of the RTP as a test for RVCs

In the literature, the RTE has been tested by varying experimental designs and analysis methods. The choice of stimuli, methods, and statistical tests is crucial for the diagnostic quality and outcome of the RTP. Following this, we review and discuss whether there are relevant methodological and statistical issues in studies testing the RTE in HVFD-patients.

Eye-tracking quality

First, it is possible that patients made eye movements bringing the target from the blind into the sighted visual field. This explanation can be ruled out with proper fixation control. Reviewing the literature, some studies applied multiple methods for fixation control. In this case, we report the method with higher precision. Marzi et al. (2009) instructed participants to fixate without further control of eye movements. In most studies, eye movements were monitored by an experimenter (Celeghin, Savazzi, et al., 2015; Corbetta et al., 1990; de Gelder et al., 2001; Marzi et al., 1986; Schärli et al., 1999; Striemer et al., 2009; Whitwell et al., 2011; Wüst et al., 2002). It is doubtful that this procedure is sufficient for RVC-research.

There are substantial differences in manual eye movement classification between researchers (Hooge et al., 2018, 2021). In particular, ratings varied in the number of fixations and the fixation duration. These differences could be ascribed to varying implicit thresholds of saccade velocity and minimum saccade amplitude. Furthermore, thresholds of raters were not stable but changed from start to end of the classification task. In this study, classification was done offline without time constraints with an interface showing x- and y-coordinate as well as velocity (Hooge et al., 2018, 2021). Hence, it is probable that online observation of eye movements might lead to even greater differences between raters. Regarding the RTP-literature, only two studies reported the quality of fixation control when fixation was monitored by an experimenter. Schärli et al. (1999) claimed to detect eye movements with amplitudes in excess of 1° when monitoring the eye-movements of healthy participants. Wüst et al. (2002) reported that they were able to detect eye movements with amplitudes larger than 2° with 100% reliability in a pilot test. Two studies used an eye tracker (Georgy et al., 2016; Ross et al., 2018). However, the eye-tracking image was not analyzed mathematically but only observed by an experimenter. This procedure is also subject to errors. Three studies used an eye-tracking system coupled with a quantitative analysis of the eye-recordings (Leh et al., 2006, Quick Glance 2SH, Eye Tech Digital Systems, Mesa, AZ, USA; Tamietto et al., 2010, iViewX SensoMotoric Instrument, 50 Hz; Tomaiuolo et al., 1997, ISCAN). Nonetheless, in two studies it is unclear at which temporal resolution the eye position was recorded. Additionally, only one study stated a criterion for fixation breaks (Leh et al., 2006, trials with eye movements > 3° away from fixation cross were excluded). Two studies used a secondary task at the fixation location to enforce compliance with the fixation requirement (Müller-Oehring et al., 2009; Wüst et al., 2002). These secondary tasks are also not without problems. A secondary task at the fixation spot can drain attentional capacities, and thereby potential interfere with performance in the experimental RVC-task (Smith et al., 2008). Moreover, unless the secondary task is specifically designed for central vision and adjusted to the specific visual acuity of each observer's central vision, use of such a task cannot rule out breaks of fixation (for an example see Ball et al., 2010).

To summarize, reliable fixation control requires the use of a high-resolution eye-tracking system with automated saccade detection. Only three out of fifteen studies used this type of control. Without reliable fixation control, it remains unclear whether "RVC"-performance results from stimulation of the blind field or the good field. Thus, in the absence of reliable fixation control, some above-chance performance with a RVC-task may not constitute evidence of residual vision in the blind field. Given that the majority of studies did not use highly reliable methods of fixation control, the incidence of RVCs might be exaggerated. To be fair, this problem is possible less of an issue for the type of bilateral stimulation typically used in RTP. In bilateral RTP, two targets are presented simultaneously to the two opposite

hemifields, meaning that eye-movements to the blind field might compromise detection in the sighted field and therefore not be in the best interest of the observer. Given that the second target in the blind field is not really necessary to solve the task and that observers never know whether a second target is in fact present in the blind field, there are few incentives for observes in the RTP to move their eyes into the blind field.

Light scatter

RVCs might be an artefact due to light scatter (Campion et al., 1983). Targets presented to the blind visual field elicit light that could spread also on retinal areas corresponding to the sighted visual field. Participants might then use this information to solve the task independent of RVCs within the blind visual field. In general, light scatter is strong with bright targets on a dark background. The reversed pattern, i.e. dark targets on a bright background, is less prone to light scatter (Campion et al., 1983; Danckert & Culham, 2010). There are various methods that have been used to test the potential impact of light scatter (Cowey, 2010). A thorough method is the presentation of targets within the natural blind spot which reflects the optic disc containing no retinal photoreceptors (Curcio et al., 1990). If targets still lead to above-chance performance, light must have reached photoreceptors surrounding the optic disc.

This procedure has been used by Schärli et al. (1999) who showed that the performance was at chance when a black flickering disc was presented on a light grey background within the natural blind spot. This confirms that black targets on a grey background are unproblematic regarding light scatter. Hence, the same conclusion can be drawn for other RTP-studies using this type of stimulation (for example Ross et al., 2018).

Three studies used other methods to avoid light scatter. Leh et al. (2006) used equiluminant target-background conditions. In Marzi et al. (2009) and in Tamietto et al. (2010) the target onset was masked by surrounding luminance changes. For one study with black and white checker-boards (de Gelder et al., 2001), authors do not address the problem of light scatter and we have no further information about this target type.

Four studies used stimulation with a high probability for light scatter (Corbetta et al., 1990; Marzi et al., 1986; Müller-Oehring et al., 2009; Tomaiuolo et al., 1997; Wüst et al., 2002), i.e. bright targets on a dark background. Fortunately, authors took precautions. Marzi et al. (1986) and Corbetta et al. (1990) tested the target within the blind spot proving that light scatter was not sufficient to detect it. Tomaiuolo et al. (1997) eliminated the influence of light scatter by flooding the entire visual field with a light intensity of 8 cd/m^2. This procedure was first used by Weiskrantz (1986). Wüst et al. (2002) used luminance values which were tested against the effect of light scatter in a previous study (Zihl & Werth, 1984). Müller-Oehring et al. (2009) claimed that their target-background luminance ratio (green circles with 96 cd/m^2

on grey background with 44 cd/m^2) minimizes light scatter but without giving evidence for the effectiveness of this procedure.

In conclusion, light scatter is presumably not responsible for positive RVC-results in RTP-studies. Nevertheless, evidence is sparse for some of the methods used to prove this (for instance Müller-Oehring et al., 2009).

Statistical analysis

In section II.2.4.2, we have seen that the sensitivity of the RTE is way below the perfect value of 100%. Arguably, the issue of sensitivity affects only negative findings, but should not impact the validity of positive findings. However, the interpretation of those positive findings is complicated by statistical issues.

Firstly, most of those studies used parametric tests (e.g. repeated-measures ANOVA, de Gelder et al., 2001; t-test, Tomaiuolo et al., 1997) that boast higher statistical power but are only appropriate when a normal distribution can be assumed which in the case of reaction-time data is highly unlikely (Bono et al., 2017).

Secondly, paired t-tests were used frequently in single-case analysis to compare reaction times between double and single stimulation conditions (for instance Marzi et al., 2009; Ross et al., 2018). Paired comparisons presume that trials of stimulation conditions can be paired on the basis of some common factor. It is unclear what this should be in single-case analysis. The frequent use of paired t-test appears problematic.

But by far the biggest problem is the lack of corrections for the well-known problem of α-error accumulation in the case of multiple testings. This is an obvious problem when a single patient is tested multiple times and an α-error of 5% is adopted for each individual test session. Similarly, the problem occurs when many patients are analyzed as a series of independent single-case studies. To illustrate this issue, we will look at a study that did both: Marzi et al. (1986) tested 20 patients in a maximum of 9 sessions. First, we need to define the α-level. As most studies did not specifically report the α-level, we deduced it from the reported results section (see Table II.B.1). In short, we can assume the conventional α-level of 5% for the vast majority of studies and analysis and hence use it also for our illustration. An alpha-level of 5% implies that we accept datasets as positive evidence for the RTE if the probability that such a dataset arises by chance is 5% or less (type-I-error rate). The stochastic model for the calculation of the α-error accumulation is a Bernoulli experiment with a binomial distribution (see appendix II.B for formulas and calculations).

To simulate the probability of false positive results, we assume that no patient has any visual function. Furthermore, Bernoulli experiments have the assumption that the random experiments run independently (Seber, 2013). If we would test a real patient with unknown visual functions in multiple sessions, the results for this patient are dependent. Following this,

Bernoulli experiments are a simplification of the experimental designs used to investigate the RTE.

Initially, we focus at the case in which one patient is tested in 9 sessions. The probability to get at least one significant RTE per chance is 37.0%. If 20 patients are tested in 9 sessions, the probability increases to >99.9%. In contrast to Marzi et al. (1986), most studies tested each participant in only one session. Regarding this, if 20 patients are tested in one session, the probability to get at least one significant RTE per chance is 64.2%. Consequently, if we do not account for the α-error accumulation, it is highly likely to define patients as RVC-positive on the basis of chance findings.

To reduce the probability for chance findings again to 5%, we need to adjust the α-level per patient. For 20 patients, the α-level per patient has to be reduced to $\alpha = .00256$. If we test each patient 9 times, the α-level has to be reduced further to $\alpha = .00028$ per session. Applying such low α-levels might be too conservative to detect small effects caused by remnants of visual functions in RVC-patients. To get a more applicable procedure, we can approach the problem of α-error accumulation in another way. There are two possible events: Event A = the RTE occurs by chance; event B = the RTE occurs as a consequence of RVCs. The question that arises is: How many positive results are necessary to ensure that we can distinguish between those two events?

For a single patient, we can define the minimum number of sessions that have to be significant with $p \leq .05$ so that the probability to acquire the data-set by chance is below $\alpha = .05$. For 9 sessions, at least 3 sessions have to show a significant RTE. If a sample of 20 patients is tested in 9 sessions, it is necessary to use the corrected α-level per patient ($\alpha = .00256$). Thereby, a patient needs at least 4 significant RTEs to meet the type-I-error rate of 5% within the patient sample.

These calculations are however only valid if applied in a formal study with pre-specified sample size. Adjusting the α-level per patient ($\alpha = .00256$ for 9 sessions) or defining the minimum number of significant results (3 of 9 sessions), you can be reasonably sure that a patient fulfilling these criteria has some form of RVCs. Reasonably sure meaning, the probability that you might obtain the results by chance alone is below the accepted type-I-error rate of 5%. However, the situation is more complicated in studies where the number of patients to be assessed is not specified in advance. Hereby, many patients might be referred to an interested researcher, screened and only some who show interesting behavior might be further investigated and reported. Consequently, we do not know the full sample sizes and might underestimate the type-I-error probability (for 1 patient: 37.0%; for 20 patients: > 99.9%).

In summary, running single-case analysis of the RTE requires an unpaired non-parametric test. Furthermore, it is necessary to correct for the α-error accumulation in reference to a pre-specified number of patients.

II.2.5. Discussion

In our first study, we investigated the literature on the RTP in healthy participants and in patients with HVFD. Initially, the meta-analysis showed that the RTE in healthy participants varies depending on certain experimental characteristic. RVCs are remnants of visual functions within the blind visual field. To increase the chances of finding RVCs, it is worthwhile to select the experimental features leading to the strongest RTE. Detection paradigms and analysis with the mean single reaction time led to the strongest effect. Furthermore, double unilateral and double bilateral stimulation led to similarly high effects. Fortunately, these characteristics are used in all RVC-studies. Selecting a subset of studies that measured the RTE similar to RVC-tests (detection paradigm, double bilateral stimulation, mean single reaction time) showed a robust and replicable effect in healthy participants but only if a potential publication bias was disregarded. Thus, future studies should always test the RTE on group level to reassure that the effect is present.

Reviewing the RVC-literature, 12.77% - 22.05% of patients with HVFD showed at least one significant RTE in the RVC-condition. Hence, the prevalence of RVCs as measured with the RTP seems to be low. Next, we estimated the sensitivity, meaning how good the RTP detects the presence of visual functions. The sensitivity of the RTP ranged between 41.67%-77.27%. Thereby, the sensitivity in healthy participants (77.27%) was higher than in the sighted field of HVFD patients (41.67%-64.15%). Importantly, visual functions were present in every case. Following this, we expected a sensitivity of 100%. However, results from the literature are far from this perfect value. This has considerable implications for RVC-research. If the sensitivity is low, there is a high chance for false-negative results. Hence, non-significant results for the blind visual field of a patient could mean that there are no RVCs or that the RTE was missing by chance.

Subsequently, we made an attempt to estimate the reliability of the RTP. Healthy participants as well as the sighted field of patients were tested only in one session. Thus, we could only rely on patients in which the RVC-condition was tested multiple times. Only 33.33% of those patients showed consistent positive results in the RVC-condition. As a prerequisite to estimate the retest reliability of the RTP, it is necessary that visual functions are stable across tests. However, there is no gold standard to measure RVCs and hence it is unclear whether RVCs were constant across test sessions or test locations. Following this, results from the RVC-condition indicate a low reliability but should be interpreted with caution.

Importantly, the methodology of these patient studies has several weaknesses. Most studies used a fixation control with low precision and unclear reliability. Hence, it is possible that patients made eye movements shifting the RVC-target to the sighted visual field. Statistical tests varied between studies and were in some cases unsuitable for single-case analysis. Noticeably, the α-level was not adjusted for multiple testing leading to high type-I-error rates. Consequently, the anyway low rate of RVCs, sensitivity, and reliability might still be an overestimation of positive results.

Lastly, we assumed that there might be a common neurological part that underlies all types of RVCs. This MCC would be the precondition for all RVCs. A test indicating the MCC would be highly useful in recruiting patients for RVC-studies and to evaluate the prevalence of RVCs. Furthermore, individual rehabilitation strategies could be adapted on the results of the MCC-test. For a MCC-test, we can make the following claim: Patients should only show RVCs if they have a positive result in an MCC test. As some authors used the RTP similar to a MCC-test (Leh et al., 2006; Striemer et al., 2009), it was worth considering the RTP as such. Reviewing the RVC-studies, we found six patients without RTE showing other types of RVCs. These six cases contradict the MCC-assumption. In conclusion, the RTP is no MCC-test.

In short, on the basis of the reviewed literature, the diagnostic quality of the RTP is low and the use of the RTE as a filter-condition for the inclusion of patients for further RVC-experiments (Striemer et al., 2018) is not warranted.

II.3. Study (2): The RTE in healthy participants

II.3.1. Introduction

In this section, we measured the redundant target effect (RTE) in two groups of healthy participants. The first sample has been tested to build a control group for patients with homonymous visual field defects (HVFDs). Hence, we designed the experiment to match the conditions in the clinical group. The second sample has been acquired as part of a previous study on light scatter (see first manuscript of dissertation). For our study on light-scatter, we presented visual targets with the observers' natural blind spot.

Initially, we focused on the control-group sample. Firstly, we tested whether we can replicate the RTE on the group level. Next, we addressed three of our main research questions: (1) How good is the sensitivity of the RTP? (2) How good is the reliability of the RTP? (3) How good is the specificity of the RTP?

(1) In our control group sample, every participant can see all targets in all conditions equally well. Hence, the RTP should detect the presence of visual functions in all participants. Consequently, we aim for a perfect sensitivity of 100%. This claim is justified keeping in mind

that RVC-tests should measure remnants of visual functions in HVFD-patients. Put differently, in RVC-investigations we are looking for the subtle effects of a very weak signal coming from the presumably blind field of a patient. A test that fails to pick up even the strong signal coming from a healthy person's sighted field is destined to disappoint as a RVC-test.

In previous studies, target-response (T-R) compatibility has been discussed to influence RTE-results (e.g. Grice et al., 1984; Grice & Gwynne, 1987; see section II.2.3.2). Hence, we tested whether T-R compatibility influenced our sensitivity estimates.

(2) To investigate the reliability of the RTP, we compared the results of the double unilateral and double bilateral conditions. With a good reliability, the redundancy gains between the two double conditions should have a high consistency.

Moreover, we examined whether it is possible to predict the redundancy gain in the double bilateral condition on the basis of findings from the double unilateral condition. Such a prediction model could prove very useful for application in a patient sample. In HVFD-patients, performance in the sighted field is usually used as a reference for RVCs in the blind field. In the RTP, the double unilateral condition measures the RTE within the sighted field. The double bilateral condition measures the RVCs within the blind field. However, the meta-analysis showed a higher summary effect size for double unilateral targets in comparison to double bilateral targets (see section II.2.3.2). Hence, we cannot simply use the redundancy gain in the double unilateral condition as an absolute reference. As a possible solution, a prediction model might consider the systematic bias between conditions thereby yielding a more valid reference for the RVC-condition.

(3) Specificity of the RTP was investigated using data of our previous light-scatter study. Thereby, we considered the double conditions in which one target is presented within the natural blind spot. As humans are physiologically blind at this spot of the visual field (Jonas et al., 1991), only one target can be visually processed. Thus, with perfect specificity, the test should reliably fail to find any evidence of a RTE coming from a redundant target presented to the blind spot (i.e. ideally the incidence of the RTE should be close to 0%).

II.3.2. Methods

II.3.2.1. Methods of sample 1: Control group

Apparatus

The task was programmed and run with Matlab (Version R2016b, MathWorks, Natick, MA) using the Psychophysics Toolbox (Version 3.0.13; 6. Juli 2016; Brainard, 1997; Kleiner et al., 2007). Targets were presented on a BenQ LCD-Screen with a frame rate of 144 Hz, a size of 532.3 x 298.8 mm and a resolution of 1920 x 1080 pixels. To keep a distance of 725 mm between the nasion and the center of the screen, the head was stabilized via a head- and

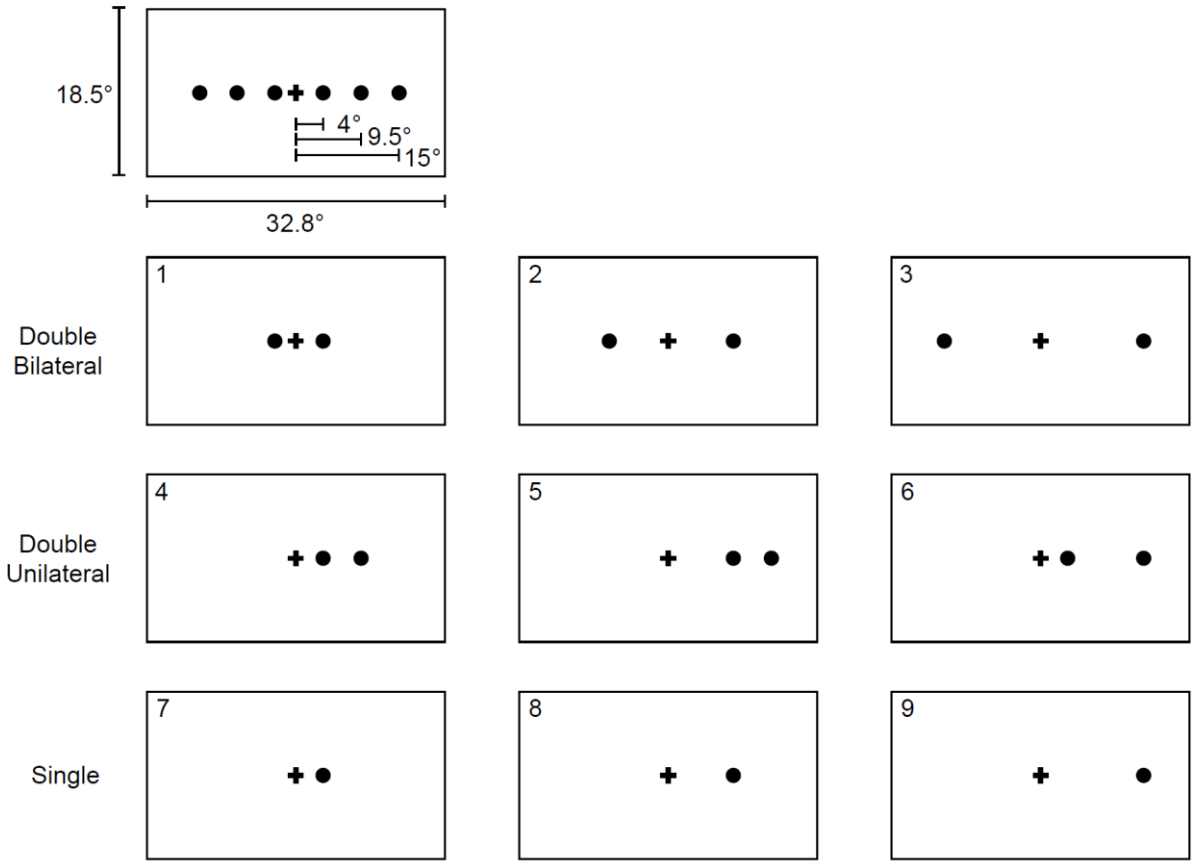
chinrest. Responses were made via a PST Serial Response Box. All sizes of the stimuli are given in degrees of visual angle (°) using the distance of the nasion to the center of the screen as a reference (1° = 45.67 pixel = 12.65 mm). This setting leads to a screen size of 32.8° x 18.5°. As the distance from the nasion to stimuli with a higher eccentricity increases, there is a small bias. Gaze position was tracked using an EyeLink 1000 Plus (SR Research). The eye-tracking settings were calibrated and validated with a 9-point pattern. If possible, eyes were tracked binocularly at 1000 Hz. If not, only the eye with better validation was tracked. Deviations of validation should be smaller than 1.5°. In some participants, there were deviations higher than 1.5° at the edge positions. Edge positions in the 9-point pattern were upper left, upper right, lower left, and lower right positions at an eccentricity of 17.4°. Importantly, validation was below 1° at the central position for all participants at all times ensuring high precision for the analysis of fixation behavior. Analysis of saccades, fixations, and blinks was done by the EyeLink parser. Saccade onset was determined by either a velocity of 30°/s or by an acceleration of 8000°/s^2 and an eye movement of at least 0.1°.

Stimuli

In the RTP, participants were instructed to press a button as fast as possible as soon as they saw one or two black circles (2° in diameter; 0 cd/m^2 luminance) on a uniform grey background (58 cd/m^2). Target positions were the same for all healthy participants lying at the horizontal midline with eccentricities of 4°, 9.5° and 15° on each hemifield (Figure II.7). Different eccentricity levels were chosen to cover the range of individually defined target positions in patients with HVFD. In HVFD-patients, double bilateral configurations should measure RVCs. Double unilateral configurations with targets only in the sighted field serve as the control condition. Furthermore, single targets are presented within the sighted field. Hence, we tested these target configurations in healthy participants in a similar way. In HVFD-patients, the side of the single and double unilateral targets is set by the HVFD. In the control group, the side of single and double unilateral targets was assigned in a counterbalanced order (see example for right condition in Figure II.7). All possible target configurations for double bilateral, double unilateral, and single conditions were tested equally often (each 20 trials; total of 180 trials). During the whole experiment (except for pauses) a black fixation symbol was presented at the center of the screen. The fixation symbol was a combination of a bull's eye with a cross hair (outer diameter: 1°; inner diameter and lines: 0.2°). This symbol was adapted from Thaler et al. (2013) as it showed the best fixation behavior compared to other types of fixation symbols.

Figure II.7

Target positions and configurations of the RTP for the control group



Note. Numbers at the upper left side refer to the numeration of target configurations and were not visible to the participants. The fixation symbol was the ABC symbol (Thaler et al., 2013). The fixation symbol is simplified in the figure for better visibility.

Procedure

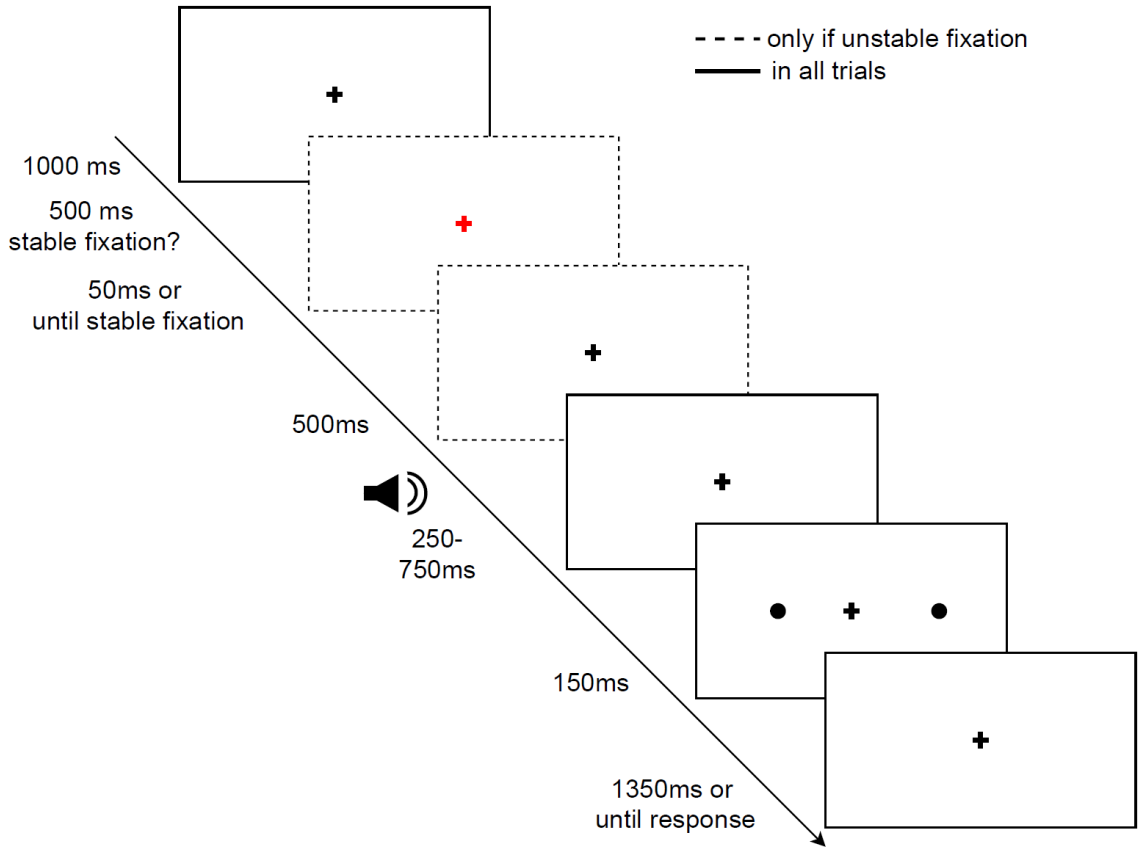
The RTP was part of an extensive test series of the control group. The study was approved by the ethics committee of the faculty 11 for psychology and educational sciences of the Ludwig-Maximilians-Universität in Munich. Initially, all participants read the study information and signed the consent sheet.

At the beginning of the RTP, there were 10 practice trials which could be repeated if necessary (accuracy and mean reaction time were displayed after each practice run). Target configurations in the practice trials were chosen randomly. Following this, experimental trials were presented. Every 44 trials, a break was provided. This break had to be terminated by the participant. At the beginning of a trial, the program checked whether the criteria for a stable fixation had been maintained for the last 500ms. Those criteria are described below. If fixation was not stable, the color of the fixation symbol changed to red for at least 50ms or until a continuous stable fixation for 500ms was registered. The fixation behavior was

analyzed in one eye only. If possible, the dominant eye was chosen. The criteria for a stable fixation were: Mean of gaze position within the fixation window (center of screen ± 3° to each side) and no single gaze data point more than 1.5° distant to the mean gaze position. When the color changed back to black, there was a short pause of 500ms before a beep (100ms, 800Hz carrier frequency) signaled the upcoming presentation of the targets. If the stable fixation was registered directly at the beginning, the beep occurred without delay. After the beep, there was a jittered time window of 250-750ms. Following this, one or two targets were presented for 151.8ms. Afterwards, participants had another 1350ms to respond. A trial terminated when a response was registered or the maximum duration (1350ms) was exceeded. If the button press happened before the target onset, a false positive response was defined and the trial was repeated at the end of the task. Between trials, there was a one second inter-trial interval. The trial procedure is illustrated in Figure II.8.

Figure II.8

Timing of one trial of the RTP in the control group



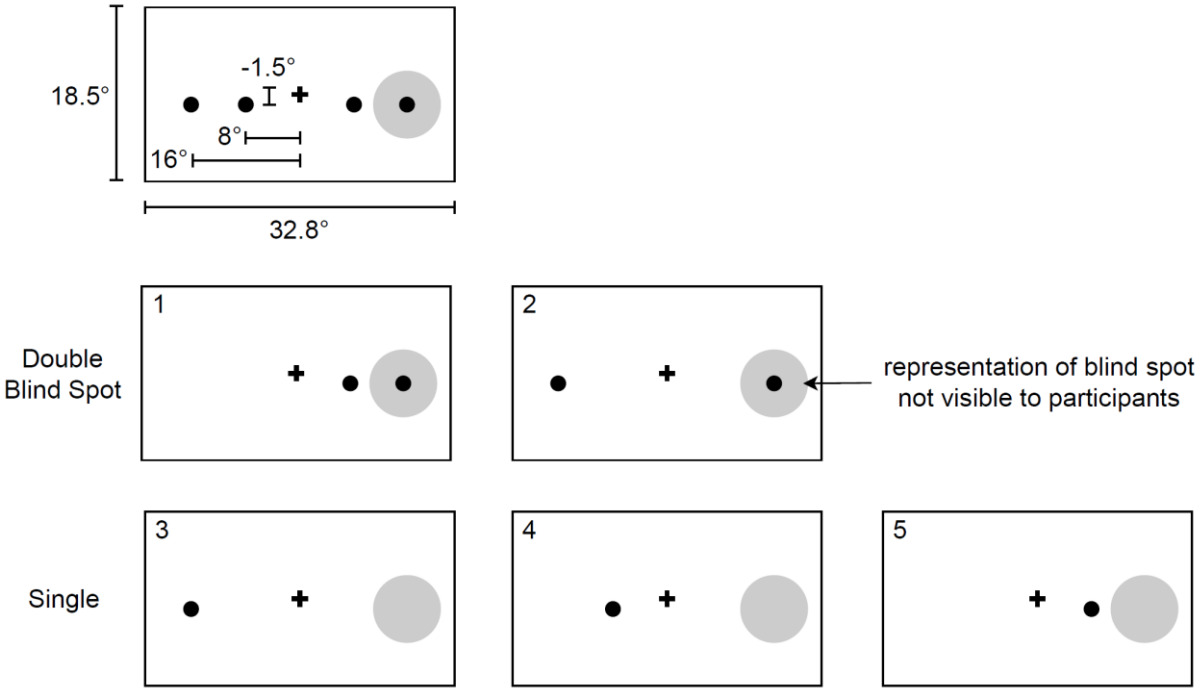
Note. The displays with dashed lines were only visible if there was no stable fixation for 500ms at the end of the inter-trial interval. The fixation symbol was the ABC symbol (Thaler et al., 2013). The fixation symbol is simplified in the figure for better visibility. ms = millisecond.

II.3.2.2. Methods of sample 2: Measuring specificity via blind-spot testing

The RTP was measured as part of the light scatter study (for details about the methods, see second manuscript of this dissertation). For the current research question, we considered the single condition and the blind-spot condition. Depending on the location of the blind spot, four target locations were defined individually (see an example in Figure II.9). In the single condition, one target was presented at one of the three locations in the sighted field (configurations 3-5 in Figure II.9; each 20 trials). In the blind-spot condition, one target was presented within the blind spot and one target in the sighted visual field leading to a unilateral (configuration 1 in Figure II.9; 30 trials) or bilateral configuration (configuration 2 in Figure II.9; 30 trials). A fixation break was defined if a gaze position during the time period 100ms before to 100ms after target presentation had a distance of more than 1° from the center of the fixation symbol. This was analyzed at the end of each trial. Trials with fixation breaks were repeated.

Figure II.9

Target positions and configurations of the RTP in the blind-spot experiment



Note. Numbers at the upper left side refer to the numeration of target configurations and were not visible to the participants. The fixation symbol was the ABC symbol (Thaler et al., 2013). The fixation symbol is simplified in the figure for better visibility.

II.3.2.3. Analysis

Preprocessing of data, for instance to extract information about fixation behavior, was done using Matlab (Version R2016b). Descriptive and inference statistics were calculated using R

(R version 3.6.1; 2019-07-05). For the analysis of reaction times, we used the following exclusion criteria. We excluded values that were either shorter than 100 ms (exclusion of anticipatory responses) or longer than the mean value plus 2.5 times the standard deviation per participant (exclusion of tardy responses). Subsequently, we calculated the arithmetic mean of reaction times for each target configuration. These values were then averaged to compute the target conditions. In the first sample of the control group the assignment was: configurations 1, 2, 3 = double bilateral stimulation; configurations 4, 5, 6 = double unilateral stimulation; configurations 7, 8, 9 = single stimulation (Figure II.7). In the second sample of the light-scatter study, the assignment was: configurations 1, 2 = double blind spot stimulation; configurations 3, 4, 5 = single stimulation (Figure II.9). Like this, we got one value for each target condition per participant. Following this, the redundancy gain was calculated by subtracting average reaction times of double conditions from the single target condition per participant.

Regarding the inference statistics, differences between two conditions on group level were tested with paired t-tests. For correlational analysis between two variables, we used the Pearson's product moment correlation coefficient. We applied a linear regression model to predict the redundancy gain of the double bilateral condition from the double unilateral condition. The assumption of normality distribution was tested with the Shapiro-Wilk test. Concerning group level, if assumptions for tests, e.g. assumption of normality distribution, were not fulfilled, we used non-parametric alternatives (unpaired t-test: Wilcoxon rank sum test; Pearson's product moment correlation coefficient: Spearman's rank correlation coefficient). For the single-case analysis, we used the individual reaction-time values (not the averages) as our input data. The distributions of such individual reaction-time values typically do not conform to a normal distribution. For this reason, we calculated unpaired exact Wilcoxon rank sum test per participant. The exact Wilcoxon rank sum test corrects for tied observations, if necessary (function 'wilcox.exact' in R package 'exactRankTest'; Hothorn & Hornik, 2015). Regarding effect sizes, we calculated Cohen's *d* for t-tests and the effect size estimate *r* for Wilcoxon tests (estimated by transforming the p-value into a z-value and then using the formula r = z/sqrt(N) with N = total sample size; Field et al., 2012, page 665). To keep our results comparable to previous studies, we applied a significance level of $\alpha \leq .05$. As we demonstrated in section II.2.4.5, this leads to an α-error accumulation. Hence, we applied an adjusted α-level additionally.

As a direct measure for the reliability, we calculated an intra-class correlation (ICC; Shrout & Fleiss, 1979) between double unilateral and double bilateral condition using the parameters recommended by Koo and Li (2016). Following this, we calculate a two-way mixed effects model for consistency with single raters (ICC (3,1) of Shrout & Fleiss, 1979). To interpret ICC-values, we applied the categorization of Koo and Li (2016) whereby the retest reliability

is poor for ICC < 0.5, moderate for 0.5 < ICC < 0.75, good for 0.75 < ICC < 0.9, and excellent for ICC > 0.9.

II.3.3. Results

II.3.3.1. Description of the samples

Sample 1

The following demographic information was self-declared via a questionnaire. In total, we tested 62 participants in the control group. We had to exclude five participants (*jj, pe, rn, yv, yy*) due to problems with calibration or compliance. Additionally, three participants (*em, ij, vy*) were excluded due to technical problems. One participant (*hq*) had to be excluded due to a very high amount of missed trials (44 trials, see below).

Following this, we had a sample of 53 participants with age ranging from 20-80 years (47.74±18.22; 27 males). 47 participants were right handed (4 left-handed, 1 two-handed, 1 unclear). Mother tongue was German in 47 participants. Other participants had enough knowledge in German to understand task instructions correctly. 18 participants had normal visual acuity and 24 participants needed a correction (glasses, contact lenses) to achieve acuity. In rare cases, testing was conducted without glasses due to issues with eye-tracking calibration but only if the participant declared to see the targets on the screen clearly. Older participants will often have multiple glasses (for daily life, reading, driving etc.). In these cases, we tried which glasses allowed best vision and best eye-tracking calibration. As targets were big (2°) and very salient, we did not expect an impact of slightly reduced visual acuity. The right eye was dominant in 35 participants.

Per default, all participants had 10 practice trials at the beginning of the experiment. In one participant (*oy*) the practice trials were repeated once. Missed trials (no key press despite stimulation) were not repeated and were usually very rare. Only one participant (*hq*) showed a very high amount of 44 missed trials. Following this, we excluded this participant from further analysis. The remaining sample had a maximum of 5 missed trials per participant (0.46±0.63%). False positive trials (key press before target onset, maximum 16 trials per participant, 1.43±1.62%) were repeated. Trials with reaction times below 100ms (maximum 8 trials per participant, 0.91±1.11%) and above mean + 2.5*SD per participant (maximum 10 trials per participant, 2.43±0.95%) were excluded.

With the remaining trials, we checked the stability of the fixation per trial. If there was a fixation (defined by the EyeLink parser) spanning the whole target period, we selected the gaze coordinates of the fixation for analysis. In other trials, we selected the raw gaze coordinates during the target period. A fixation break was defined as gaze coordinates located more than 1.5° away from the center of the fixation symbol. This criterion was stricter

than the online-check of fixation stability at the beginning of a trial (allowed distance: 3°; see section 110II.3.2.1). If the fixation break could be explained by blinks or a drift in gaze position, for instance due to slight head movements, the trial was kept in the analysis. We corrected for these cases manually. There was a maximum of 61 trials with breaks in fixation (in participant *zp*). However, there were fewer fixation breaks in general: No fixation breaks in 22 participants and fewer than 10 fixation breaks in another 23 participants (in total 3.03±6.19%). On average there were 167.70±11.66 (93.17±6.48%) of 180 trials left. As there were at least 10 trials per target configurations (20 trials planned), we kept all participants for statistical analysis. Reaction times per target condition per participant after pre-processing are plotted in Figure II.10 and Figure II.11.

Sample 2

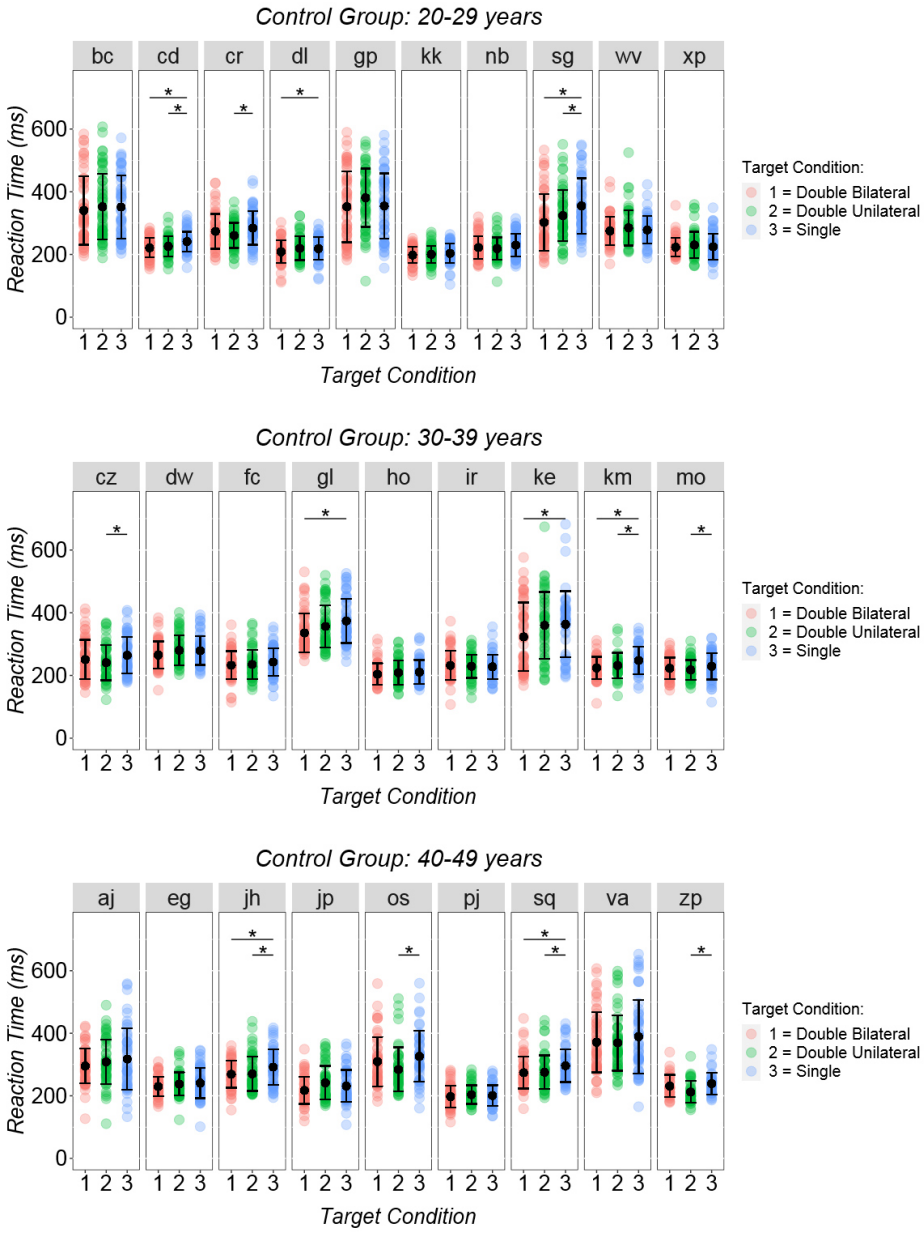
In the blind-spot experiment, 19 participants were included in the analysis of the RTP (age: 25.37±4.41 years). Per condition, there were 60 trials planned. Trials without responses (miss), trials with false positive responses, and trials with fixation breaks were excluded. Following this, there were on average 56.11 trials (SD = 3.14 trials, min = 47 trials) in the single and 56.58 trials (SD = 2.14 trials, min = 50 trials) in the blind-spot condition. Reaction times per target condition per participant after pre-processing are plotted in Figure II.14.

II.3.3.2. Replication of the RTE

Initially, we tested whether we can replicate the RTE in a group analysis of the healthy participants from the control group (sample 1). A RTE corresponds to a reduction in reaction times when two targets instead of just one target are presented. Therefore, we averaged mean reaction times for the target configurations with one target (7-9) and with two targets (1-6) per participant (Figure II.7). The condition with one target (276.81±46.80ms) had significantly longer reaction times than the condition with two targets (265.87±44.69ms, one-sided paired t-test: $t(52) = 7.80$, $p < .0001$, $d = 1.07$; $r_s = 0.97$, $p < .001$; Figure II.12). Results showed that we can replicate the RTE in our sample of normally sighted participants.

Figure II.10

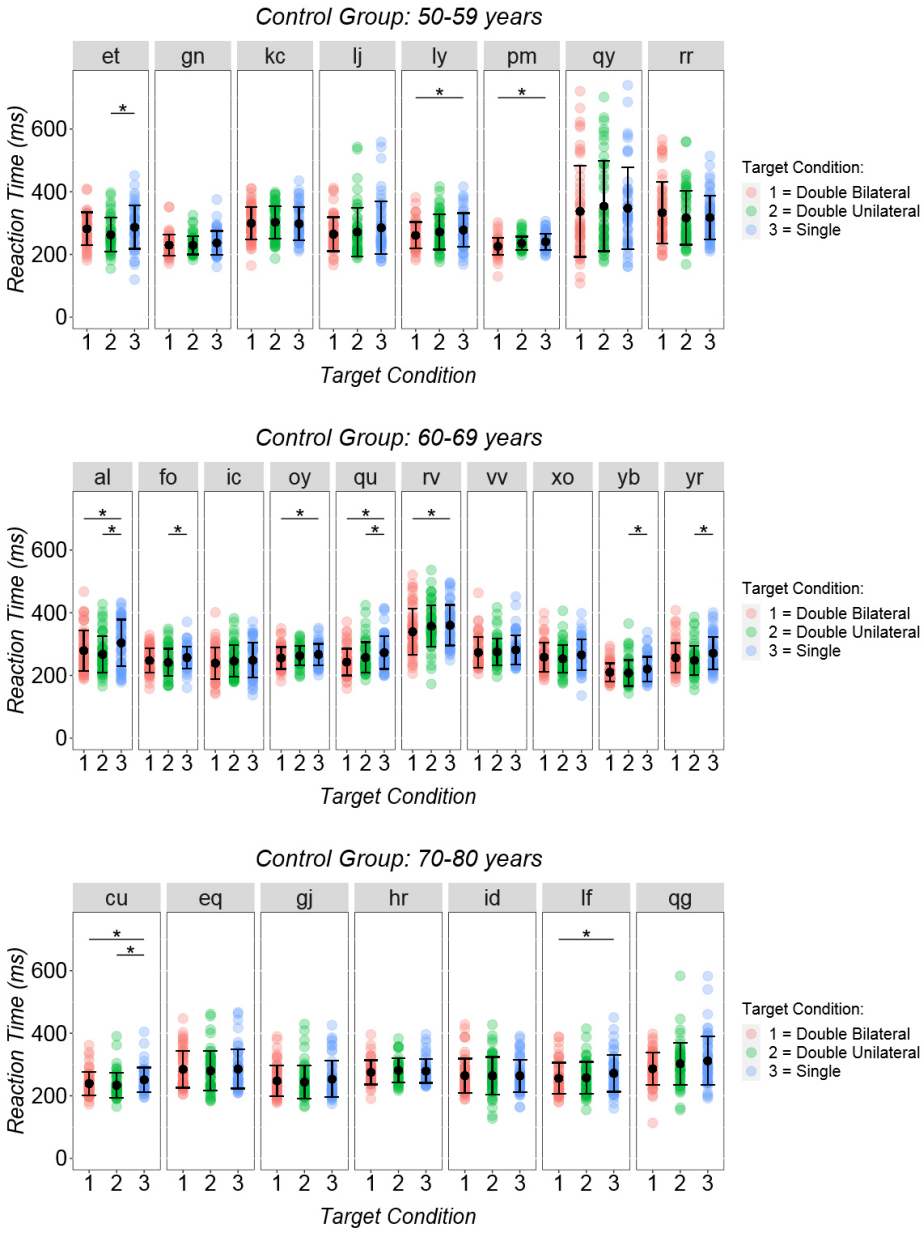
Control group: Reaction times per target condition per participant (20-49 years) after preprocessing



Note. Letters above the columns are the participant codes. Black points indicate mean reaction times. Error bars indicate standard deviation. Black stars and lines indicate a significant difference ($\alpha \leq .05$) between conditions in single-case analysis; ms = millisecond.

Figure II.11

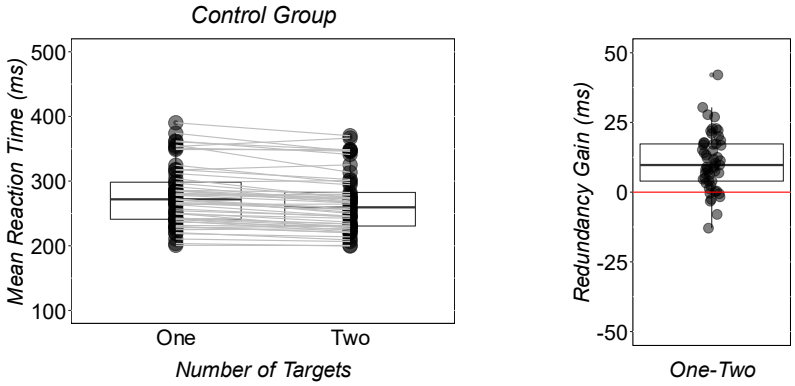
Control group: Reaction times per target condition per participant (50-80 years) after preprocessing



Note. Letters above the columns are the participant codes. Black points indicate mean reaction times. Error bars indicate standard deviation. Black stars and lines indicate a significant difference ($\alpha \leq .05$) between conditions in single-case analysis; ms = millisecond.

Figure II.12

Comparison of reaction times for one target and two target condition



Note. Left plot: Box plots of mean reaction times in response to one target (target configurations 7-9) or to two targets (target configurations 1-6). Grey lines connect values of one participant. Right plot: Box plots of redundancy gain per participant. Redundancy gain = difference in reaction times between one target and two targets. ms = millisecond.

II.3.3.3. Sensitivity of the RTP

One of our main research questions concerns the sensitivity of the RTP. To address this question, we examined the data from the control group (sample 1). Therefore, we calculated a single-case analysis. As it is common for patients, we analyzed double unilateral and double bilateral conditions separately. In the analysis, data points were reaction times per trial for each target condition. The average (±SD) number of trials per target condition was as follows: Double bilateral: 56.25±4.38, min = 34; double unilateral: 55.94±4.50, min = 39; single: 55.51±3.84, min = 40. As expected, data was not normally distributed in 41 participants in at least one target condition. Following this, we calculated a one-sided unpaired exact Wilcoxon rank sum test for all participants (Table II.7). Results showed that 17 (32.08%) healthy participant had a significant RTE for the double unilateral condition. For the double bilateral condition, 16 (30.19%) healthy participants showed a significant effect. Following this, the RTP detected the presence of visual function in 47.17% of participants in at least one double condition[1]. In contrast, 100% of participants were fully sighted.

[1] When the α-level was adjusted for N = 53 and 2 sessions per participant (α ≤ .00048; see section II.2.4.5 and appendix II.B), the RTE was significant for 3 participants (5.66%) in the double bilateral condition and 1 participant (1.89%) in the double unilateral condition. 49 participants (92.46%) had no significant RTE in either condition.

Table II.7

Control group: Results of the single-case analysis

Control Group	Single vs. Double Unilateral is significant	Single vs. Double Unilateral is not significant	Sum
Single vs. Double Bilateral is significant	**8** **15.09%** **(al, cd, cu, jh, km, qu, sg, sq)**	8 15.09% (dl, gl, ke, lf, ly, oy, pm, rv)	16 30.19%
Single vs. Double Bilateral is not significant	9 16.98% (cr, cz, et, fo, mo, os, yb, yr, zp)	28 52.83%	37 69.81%
Sum	17 32.08%	36 67.92%	53 100%

Note. Numbers indicate the absolute and relative frequency of results in each cell. Participant codes are displayed in brackets. $\alpha \leq .05$.

In the literature, some studies indicated that a target-response (T-R) incompatibility reduces the redundancy gain (see section II.2.3.2). Following this, it could be that the low rate of significant results in our sample is due to T-R incompatibility. In patients, the side of the double unilateral and single target condition is defined by the visual field defect and the choice for the response hand might be restricted due to hemiparesis. To keep results of our healthy participants comparable to patient studies, we assigned the side of the double unilateral and single target condition to be left or right in a counterbalanced order. The response hand was always the dominant hand. Hence, in approximately half of the right handers, single and double unilateral stimulation is on the incompatible left hemifield. Thereby, we can distinguish between the following combinations: (1) single compatible vs. double unilateral compatible; (2) single compatible vs. double bilateral; (3) single incompatible vs. double unilateral incompatible; (4) single incompatible vs. double bilateral. We argue that if both conditions, single and double unilateral stimulation, are incompatible, reaction times are affected similarly and hence the redundancy gain should be as high as for the compatible condition. Concerning double bilateral stimulation, there might be a differential effect. On the one hand, single incompatible stimulation might prolong reaction times. Hence, the bilateral gain should be increased. On the other hand, single compatible stimulation accelerates reaction times and consequently should decrease the redundancy gain.

As there were only few left-handers, we selected only the right-handers and split the results of the single-case analysis depending on the compatibility (compatible: right target side; incompatible: left target side; see Table II.C.1 and Table II.C.2. Overall, results were similar

showing 56.52% of participants without a significant RTE in either condition. Hence, there is no advantage for T-R-compatible stimulation. Regarding the bilateral vs. single incompatible stimulation, 8 participants (33.33%) showed a significant RTE. For bilateral vs. single compatible stimulation, 6 participants (26.09%) had a significant RTE. Hence, the T-R compatibility cannot explain the overall low rate of significant RTE in the entire sample.

II.3.3.4. Reliability of the RTP

To estimate the reliability of the RTP, we analyzed data of the control group (sample 1). Initially, we compared results between double conditions on group level. A two-sided paired t-test showed that the redundancy gain for the double bilateral condition (12.73±11.49ms) is significantly higher than for the double unilateral condition (9.14±12.31ms; $t(52) = 2.13$, $p = .038$, $d = 0.29$; Figure II.13). Even though the redundancy gain differed significantly between the double target conditions, the difference could still be correlated across conditions. Therefore, we calculated a Spearman correlation coefficient between redundancy gain values of the double target conditions. The test revealed a significant correlation of $r_s = .52$, $p < .001$ (Figure II.13).

Furthermore, we made an attempt to predict the redundancy gain in the double bilateral condition from the redundancy gain in the double unilateral condition. The prediction model might be useful in HVFD-patients. Given the systematic bias in the redundancy gains between double conditions, the double unilateral condition, i.e. the control condition in HVFD-patients, is no valid reference for the double bilateral condition, i.e. the RVC-condition in HVFD-patients. The predicted bilateral gain considers the systematic bias between double conditions and might hence be a more valid reference to evaluate RVCs. For this purpose, we calculated a linear regression (Figure II.13). The model was significant ($F(1,51) = 14.57$, $p < .001$, $R^2 = 0.222$). The unilateral gain was a significant predictor for the bilateral gain ($\beta = 0.44$, $t = 3.82$, $p < .001$) with the following formula:

$$bilateral\ gain = 8.71 + 0.44 * unilateral\ gain \quad \text{(II.1)}$$

As the linear regression explains only 22.2% of the variance in the data, it seems to be unsuitable for the application in HVFD-patients.

As a direct measure for the reliability, we calculated an ICC (Shrout & Fleiss, 1979). Results show an ICC of 0.47 with $F(52,52) = 2.8$, $p < .001$, CI = [0.27, 0.63] indicating a poor reliability (Koo & Li, 2016).

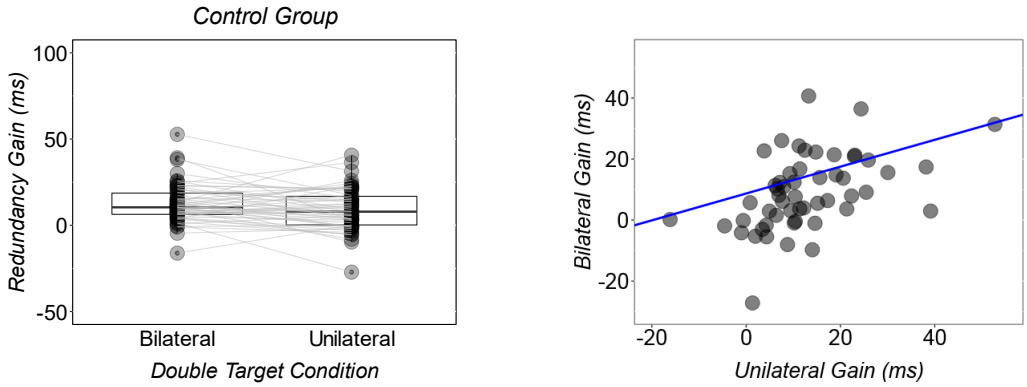
Furthermore, we addressed the question of reliability looking at the results of the single-case analysis (Table II.7). Of all participants, 28 (52.83%) showed a consistent negative and 8 (15.09%) a consistent positive RTE. 17 (32.08%) participants had an inconsistent results

pattern. Following this, even though the visual functions did not vary, the RTP showed inconsistent results in about one third of the sample indicating a low reliability.

To summarize, on group level the bilateral gain was significantly higher than the unilateral gain. Nevertheless, the redundancy gain values correlated significantly. However, a simple linear regression, trying to predict the bilateral gain on the basis of the unilateral gain, explained only 22% of the variance. Furthermore, the ICC between double conditions was poor. Regarding the single-case analysis, 32.08% of healthy participants showed inconsistent results. Taken together, our findings suggest that the reliability of findings in the RTP is fairly low.

Figure II.13

Comparison and correlation between the redundancy gain for the double bilateral and double unilateral target conditions



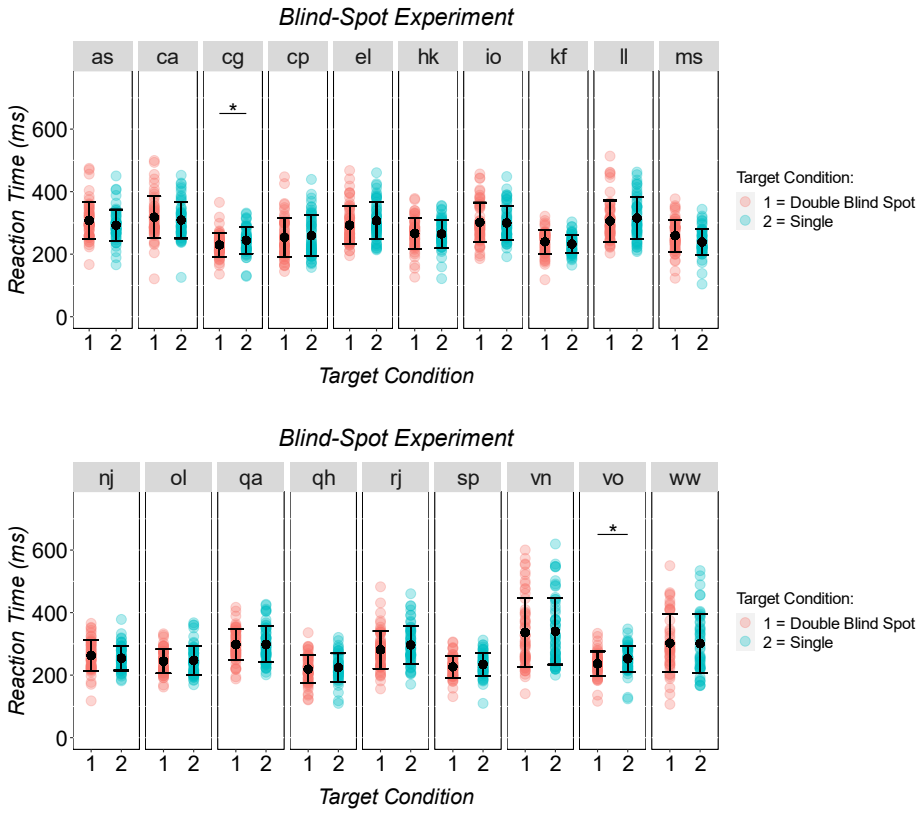
Note. Left plot: Box plots of redundancy gain per double target condition. Grey lines connect values of one participant. Right plot: The blue line shows the linear regression with the unilateral gain as the predictor for the bilateral gain. Redundancy gain = difference in reaction times between single and double target condition; bilateral gain = redundancy gain for double bilateral condition; unilateral gain = redundancy gain for double unilateral condition; ms = milliseconds.

II.3.3.5. Specificity of the RTP

To estimate the specificity of the RTP, we use the second sample of healthy participants from our previous blind-spot experiment. To estimate the specificity of the RTP, we applied a single-case analysis to the blind-spot condition. We calculated the single-case analysis for each participant with the same statistical procedure as for the control group (sample 1). Only in four participants, reaction time data of all target conditions was normally distributed. Following this, we calculated one-sided unpaired exact Wilcoxon rank sum tests for all participants.

Figure II.14

Blind-spot experiment: Reaction times per target condition per participant after preprocessing



Note. Letters above the columns are the participant codes. Black points indicate mean reaction times. Error bars indicate standard deviation. Black stars and lines indicate a significant difference (α ≤ .05) between conditions in single-case analysis; ms = millisecond.

Table II.8

Blind-spot experiment: Results of the single-case analysis

Condition	Significant	Not Significant	Sum
Double Blind Spot	2 10.53% (*cg, vo*)	17 89.47%	19 100%

Note. Numbers indicate the absolute and relative frequency of results in each cell. Participant codes are displayed in brackets. α =.05.

Results showed a significant RTE for two participants (*cg*, *vo;* Table II.8; Figure II.14) leading to a specificity of 89.47%[2]. We did not find a reason that could explain the RTE in the blind-spot condition in these two participants: Targets were properly located in the center of the blind spot, they did not show extreme reaction times, and trials with fixation breaks were generally repeated. It seems most likely that those findings are due to random fluctuations in reaction time data. The fact that such fluctuations occur and can mimic a RTE shows that specificity is high but not perfect.

II.3.4. Discussion

In study (2), we tested a RTP in two samples of healthy participants. In our first sample, we replicated the RTE on group level. Regarding our research questions, we first estimated the sensitivity. As all participants were normally sighted, the RTP should have yielded positive effects in 100% of participants. In the single-case analysis, 47.17% of participants showed a significant RTE in at least one double condition. Hence, the sensitivity to detect the presence of visual functions is very low.

The reliability was estimated by comparing the double unilateral and the double bilateral condition. Results of the group analysis showed that the double bilateral stimulation leads to a significantly higher redundancy gain. Thereby, redundancy gains for double bilateral and double unilateral conditions were highly correlated. Still, the ICC between double conditions revealed a poor reliability. Regarding the single-case analysis, results were inconsistent in 32.08% of participants. Only 15.09% of participants showed a consistent positive result. The RTP aims to detect the ability to process a visual target in the visual field. Given that this underlying visual function is the same in both double conditions, the poor consistency across conditions demonstrated the poor reliability of RTP as a measure of preserved visual processing.

Concerning the specificity, we presented data from our second sample of healthy participants. In this experiment, we tested the RTE with a redundant target within the natural blind spot. As the target within the natural blind spot cannot be visually processed, no participant should have a significant RTE. Results showed a high but not perfect specificity of 89.47%.

[2] When the α-level was adjusted for N=19 ($\alpha < .0027$; see section II.2.4.5 and appendix II.B), no participant showed a significant RTE.

II.4. Study (3): The RTE in patients with homonymous visual field defects

II.4.1. Introduction

In study (3), we present data of a redundant target paradigm (RTP) tested in patients with homonymous visual field defects (HVFDs). This patient sample was tested in the context of a training study. In the intervention, patients trained to discriminate movement direction within the blind visual field. Thereby, patients were tested extensively before and after the training period of approximately two months.

With the patient data, we investigated two of our main research questions: (1) How good is the sensitivity of the RTP? (2) How good is the reliability of the RTP?

(1) Regarding the sensitivity, we calculated a single-case analysis for the double target conditions separately. Patients with HVFD have visual functions within their sighted field. In the RTP, the sighted visual field is tested with the double unilateral condition. Hence, the RTP should detect the presence of visual functions for this condition in patients with a sensitivity of 100%.

In the course of the single-case analysis, we analyzed also the double bilateral condition as a measure for RVCs. In the double bilateral condition, one target is presented in the sighted visual field and a second, redundant target is simultaneously presented in the blind visual field. It is a sign for RVCs if reaction times are significantly reduced in the double bilateral condition compared to a single visible target.

(2) As we tested the patients at two points in time, we can estimate the retest reliability. For this, we correlated the redundancy gain values between points in time on group level and calculated an intra-class correlation (ICC). Furthermore, we compared results of the single-case analysis between points in time. If the reliability of the RTP is high, the ICC should be > 0.75 (Koo & Li, 2016) and results on individual level should show a high correspondence.

II.4.2. Methods

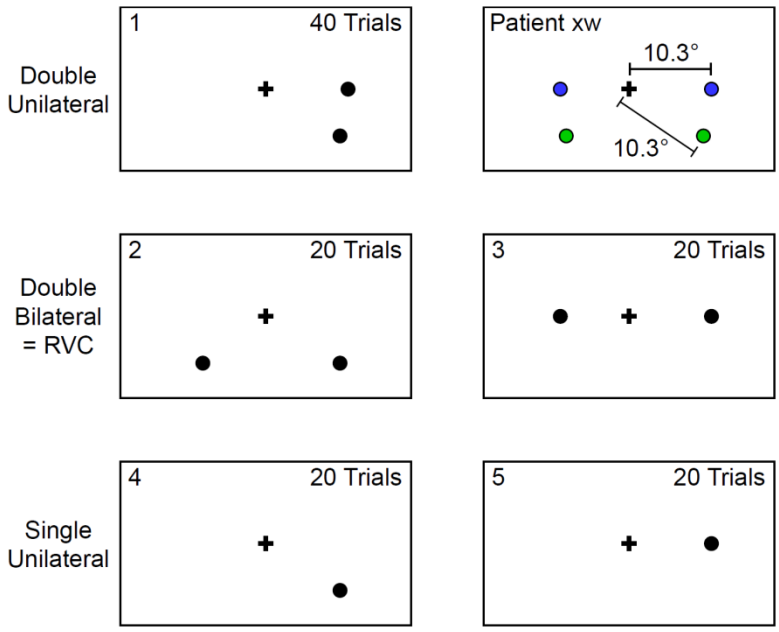
Patients were recruited via hospitals and outpatient clinics in the greater area of Munich. Inclusion criteria were an acquired, post-chiasmatic brain lesion as stated by medical reports and a HVFD determined by Octopus perimetry. Exclusion criteria were any eye disease with the exception of a successfully and fully healed cataract surgery. Furthermore, we excluded visuospatial neglect by testing line-bisection, copying of line drawings, and cancellation tests (NET, neglect-test, Fels & Geissner, 1997; SNT, sensitive neglect test, Reinhard et al., 2016). In addition to examining lateralized attentional deficit in the visual domain, we checked extinction in the auditory and tactile domain with a custom-made protocol.

Moreover, we measured general attentional (Perception and Attention Functions, WAF, Vienna Test System, Sturm, 2006) and memory functions (Logical Memory, Wechsler, 2009) to make sure that patients were capable to comply with task instructions.

The apparatus and basic methods of the RTP for the patient group were the same as for the control group. Therefore, we will only describe the differences. Three target positions were defined individually within the blind visual field based on the results of a custom-made perimetry paradigm. Target positions had approximately the same eccentricity and had about the same distance to the visual field border (Figure II.15, Table II.9). The target positions within the blind visual field were then mirrored to the sighted field. Two of the homologous target pairs were trained, the remaining served as a control condition. For the RTP, one of the trained target pairs and the control targets were used. The choice for the training target pair was counterbalanced for patients with hemianopia. For patients with quadrantanopia, the target pair matching the eccentricity of the control targets was chosen. Target conditions for the RTP were as follows (Figure II.15): Double unilateral condition with two targets in the sighted visual field (configuration 1), double bilateral condition with one target in the sighted and one target in the blind visual field (configurations 2 and 3), and single condition with one target in the sighted visual field (configurations 4 and 5). Target configurations of the double bilateral and single condition were tested with 20 trials each. The double unilateral target configuration was presented twice as often (40 trials). This summed up to a total of 120 trials. For the statistical analysis, we used the same procedure as for the datasets with healthy participants (see section II.3.2.3).

Figure II.15

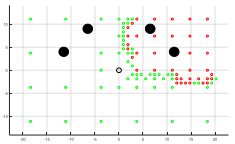
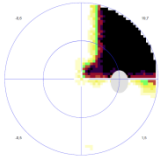
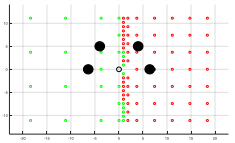
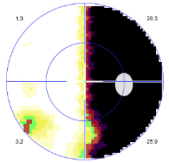
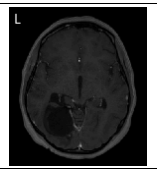
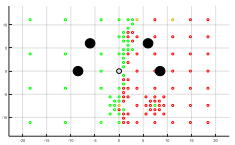
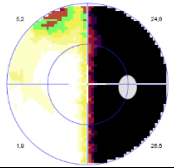
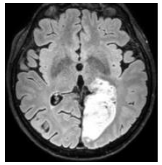
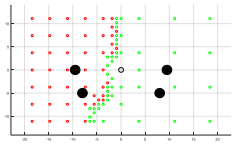
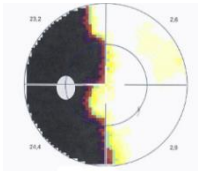
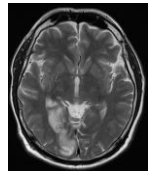
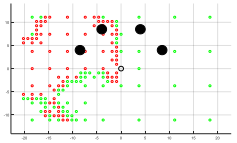
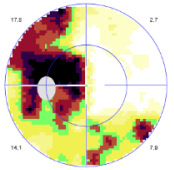
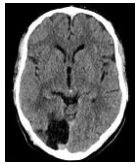
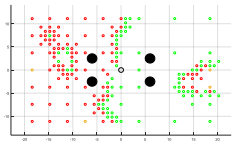
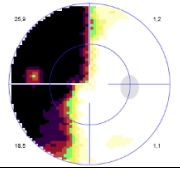
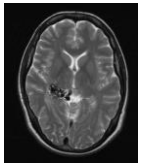
Example for target configurations in the patient sample (patient xw)

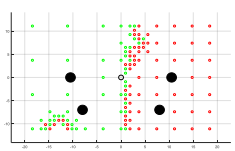
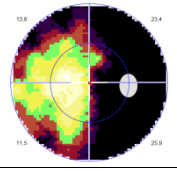
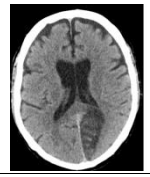
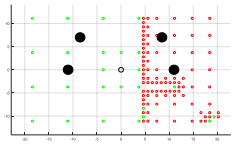
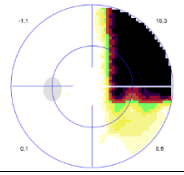
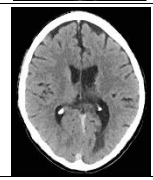
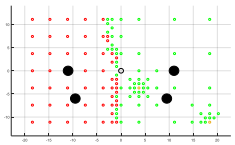
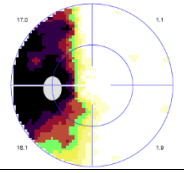
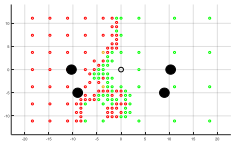
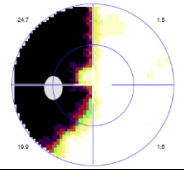
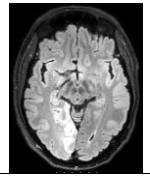
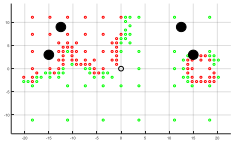
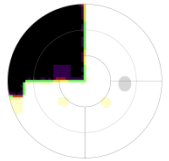
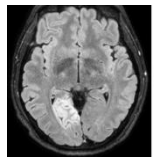


Note. Numbers in the upper left corners refer to the target configurations. Numbers in the upper right corners indicate the number of trials. Blue circles = control positions; green circles = training positions; The annotations were not visible to the patients. The fixation symbol was the ABC symbol (Thaler et al., 2013). The fixation symbol is simplified in the figure for better visibility. RVC = residual visual capacity.

Table II.9

Demographic and clinical information of the patient sample

Patient	Sex	Age (years)	TSO (days)	TB (days)	Etiology	Targets within visual field	Octopus perimetry	Clinical neuroimaging
bm	m	67	178	125	Partial ischemic infarction of left arteria cerebri posterior	*R* 		
bw	f	45	541	118	Surgical removal of a left parieto-occipital meningeom (WHO stage I)	*R* 		
hw	f	69	349	118	Ischemic infarction of basilar artery	*R* 		
la	m	52	286	113	Ischemic infarction of right arteria cerebri posterior	*L* 		
od	m	64	955	88	Hemorrhagic infarction of right arteria cerebri posterior (P2); Ischemic infarction of right internal capsule; Old ischemic lesions of right caput nuclei caudate, right putamen, and pons	*L* 		
sr	f	42	1842	106	Right thalamus bleeding due to arteriovenous malformation	*R* 		

ti	m	77	617		Ischemic infarction of left arteria cerebri posterior	*R*			
wa	m	57	481	70	Ischemic infarction of left arteria cerebri posterior	*L*			
wu	m	50	382	147	Intracerebral bleeding right temporal/ temporoparietal	*L*			
xw	m	46	185	206	Ischemic infarction of right arteria cerebri posterior	*L*			
zo	m	34	108	133	Ischemic infarction of right arteria cerebri posterior	*R*			

Note. Age and gender were self-declared via a demographic questionnaire; Etiology as stated in the medical report; TSO in days is calculated from the date of the lesion as stated in the medical report to the date of the first RTP-session; Targets within visual field: Location of the RTP-targets printed on the visual field of the dominant eye; the visual field was tested in a custom-made lab perimetry; green circles: seen test points; red circles: missed test points; orange circles: test point once seen, once missed; black circles: targets of the RTP; the dominant eye is indicated by the upper left letter. Octopus perimetry of the dominant eye with 30° radius. For patient *wu*, the visual field of the non-dominant left eye is shown because the perimetry in the dominant right eye stopped prematurely due to a technical error. TSO = time since lesion onset; TB = time between RTP-sessions; RTP = redundant target paradigm; m = male; f = female; R = right; L = left.

II.4.3. Results

II.4.3.1. Sample

We included eleven patients in the analysis of the RTE (*bm, bw, hw, la, od, sr, ti, wa, wu, xw, zo,* Table II.9). Patient *ti* dropped out after the pre-test but before the start of the training period due to a non-neurological disease. Hence, there were only ten patients in the dataset of the post-test.

The following demographic information was self-declared via a questionnaire. The patient group had a mean age of 54.82±13.17 years (range: 34-77 years). Three patients were female (*bm, hw, sr*) and two were left-handed (*la, od*). In four patients, the dominant eye was the left eye (*la, od, wa, xw*). All patients had German as their native language. Ten patients needed a correction (glasses or contact lenses) for full acuity. See Table II.9 for further information about patients and the etiology of the HVFD.

II.4.3.2. Pre-processing

Pre-test

All patients needed ten practice trials, except patient *ti,* who needed 20 practice trials. Four patients *(la, od, sr, ti*) had one miss trial in which there was no response although a target was present. The other patients had no miss trials. On average 0.98±1.43% of trials were false positives, i.e. trials in which patients responded before target onset. Next, we excluded trials due to anticipatory or delayed responses. Over all patients, there were 9 trials with reaction times below 100ms (0.68±0.50%). In addition, we excluded trials with reaction times longer than mean + 2.5*SD per patient. On average, there were 2.58±0.79% delayed responses per patient. Next, we excluded 5.30±5.02% trials due to fixation breaks per patient (same criterion and procedure as for the control group sample; see section II.3.3.1). For the double unilateral configuration (40 trials planned), the minimum remaining number of trials was 33 (90.91±6.35%). For the double bilateral configurations (each 20 trials planned) the minimum number of trials left was 16 (92.73±5.72%). For the single configurations (each 20 trials planned), the minimum number of trials left was 15 (89.77±6.98%). The reaction times of the trials after preprocessing are plotted in Figure II.16 per patient per target condition.

Post-test

All patients needed ten practice trials, except patient *sr,* who needed 20 practice trials. Before analyzing, we scanned the data and excluded all trials with missed responses, i.e. patients did not respond even though a target was present. Additionally, trials with false positive responses, i.e. responses prior to target onset, were excluded. Two patients had one miss trial (*bw, sr*). All other patients had no miss trials. On average, there were 1±1.17% false positive trials per patient. Following this, we excluded trials due to anticipatory or

delayed responses. Across all patients, there were 14 trials with reaction times below 100ms (1.17±1.93%). Furthermore, we excluded reaction times that were above mean + 2.5*SD per patient. Delayed responses accounted for an average of 1.75±0.73% trials per patient. Subsequently, we excluded trials due to fixation breaks (same criterion and procedure as for the control group sample; see section II.3.3.1). On average 16.33±25.50% of trials were excluded due to fixation breaks. Importantly, there were two patients with a very high number of fixation breaks: *bm* with 68 and *wa* with 85 trials with fixation breaks. Other patients had a maximum of 14 trials with fixation breaks (4.48±4.34%). Noteworthy, two patients, *bm* (49 = 40.83%) and *wa* (27 trials = 22.5%), had a very low number of remaining trials. Other patients had at least 101 trials left (92.81±5.25%). Following this, we excluded patients *wa* and *bm* from further analysis of the post-test. In conclusion, the sample of the post-test consisted of eight patients (*bw, hw, la, od, sr, wu, xw*, and *zo*). For the remaining patients, there were at least 34 trials (93.13±5.79%) for the double unilateral configuration (40 trials planned). For the double bilateral configurations (each 20 trials planned), there were a minimum of 15 trials (91.56±7.90%). For the single configurations (each 20 trials planned), there were a minimum of 15 trials (93.75±6.71%). The resulting reaction times for each target condition are plotted for individual patients in Figure II.16.

II.4.3.3. How good is the sensitivity of the RTP?

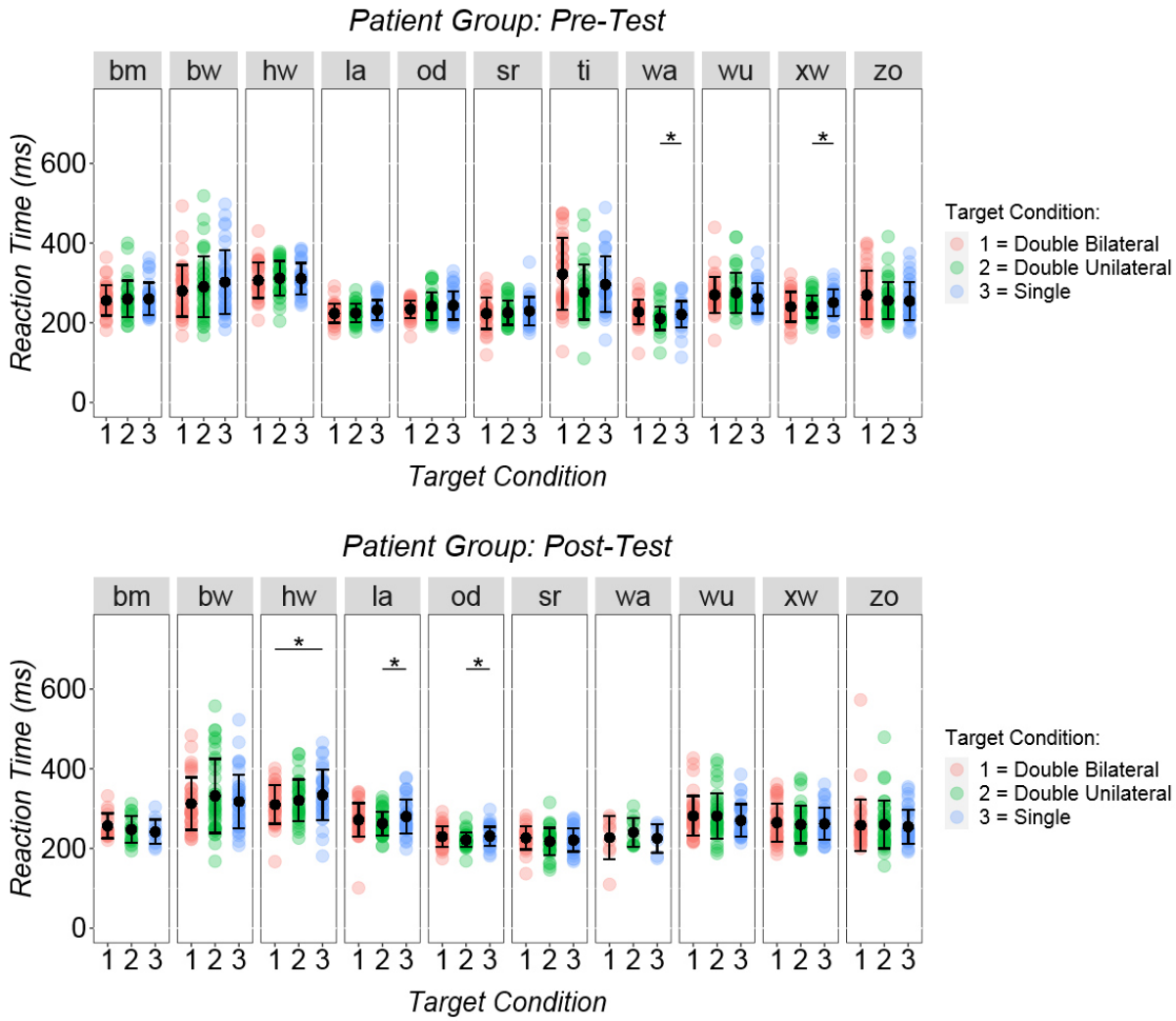
To estimate the sensitivity of the RTE in the patient group, we ran a single case analysis for the double unilateral stimulation within the sighted visual field for the two points in time independently.

In the double unilateral condition, two targets are presented simultaneously within the sighted visual field. As all targets can be seen correctly within the sighted visual field, we expect a perfect sensitivity, meaning 100% of patients should show a RTE. In the pre-test, data was normally distributed in all three target conditions only for two patients (*hw, xw*). Results showed that two patients (*wa, xw; 18.18%*) had a significant RTE for the double unilateral condition (Figure II.16, Table II.10)[3]. In the post-test, in three (*hw, la, sr*) out of eight patients data was normally distributed in all three target conditions. Two patients (*la, od; 25%*) showed a significant RTE between single and double unilateral condition (Figure II.16, Table II.10)[6].

[3] When the α-level was adjusted for N = 8 patients included in the analysis of both points in time and 4 sessions (2 points in time with 2 conditions each; $\alpha \leq .0016$; see section II.2.4.5 and appendix II.B), no patient had a significant RTE in the pre-test nor in the post-test for either double condition.

Figure II.16

Patients: Reaction times per target condition per participant after preprocessing



Note. Letters above the columns are the patient codes. Black points indicate mean reaction times. Error bars indicate standard deviation. Colored points indicate single reaction time values. Lower plot: Patients *bm* and *wa* were excluded from post-test analysis due to a high number of excluded trials. Black stars indicate a significant difference ($\alpha \leq .05$) between conditions in single-case analysis. ms = millisecond.

Table II.10

Patients: Results of the single-case analysis

Pre-test

HVFD patients	Single vs. Double Unilateral is significant	Single vs. Double Unilateral is not significant	Sum
Single vs. Double Bilateral is significant	0 0%	0 0%	0 0%
Single vs. Double Bilateral is not significant	2 18.18% (*wa, xw*)	9 81.82% (*bm, bw, hw, la, od, sr, ti, wu, zo*)	11 100%
Sum	2 18.18%	9 81.82%	N = 11 100%

Post-test

HVFD patients	Single vs. Double Unilateral is significant	Single vs. Double Unilateral is not significant	Sum
Single vs. Double Bilateral is significant	0 0%	**1** **12.5%** **(hw)**	1 12.5%
Single vs. Double Bilateral is not significant	2 25% (la, od)	5 62.5% (bw, sr, wu, xw, zo)	7 87.5%
Sum	2 25%	6 75%	N = 8 100%

Note. Numbers indicate the absolute and relative frequency of results in each cell. Patient codes are displayed in brackets. $\alpha \leq .05$.

In addition to the sensitivity, we analyzed RVCs in the blind field of patients (Figure II.16, Table II.10)[6]. RVC is defined as a significant RTE obtained by comparing single and double bilateral condition in a single-case analysis. Regarding the pre-test, no patient had a RTE for the double bilateral condition. In the post-test, one patient (*hw)* showed a significant RTE for the double bilateral condition. In summary, one patient showed a RVC-positive result at one point in time. Importantly, there is no gold standard to measure RVCs leaving the true RVCs of patients unknown. Hence, results of the double bilateral condition are interesting for themselves but cannot be used to estimate the RTP-sensitivity.

To summarize, the sensitivity of the RTP in the sighted field of patients was only 18.18% - 25%.

II.4.3.4. How good is the reliability of the RTP?

To estimate the reliability of the RTP in the patient sample, we compared results of the sighted visual field between points in time. The correspondence between test results should be high as we presume stable visual functions within the sighted visual field. To measure the RTE in the sighted visual field, we calculated the unilateral redundancy gain, i.e. the difference in reaction times between single and double unilateral conditions.

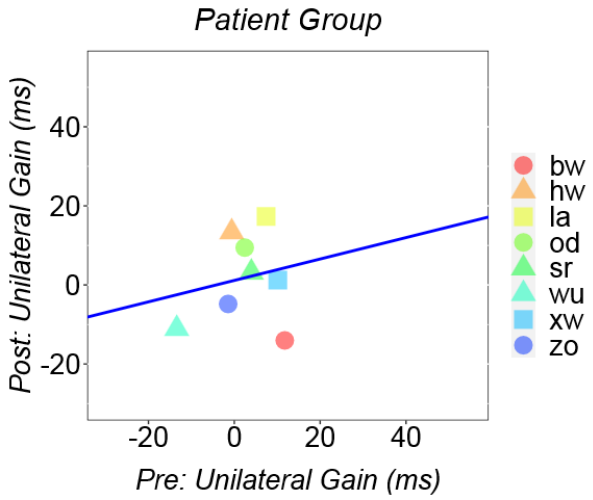
Initially, we analyzed data on group level by correlating the unilateral redundancy gain between points in time. The Pearson correlation was not significant ($r(6) = .19$, $p = .649$; Figure II.17). A linear regression showed that the unilateral redundancy gain in the pre-test was no significant coefficient ($\beta = 0.27$, $p = 0.65$) for the unilateral redundancy gain in the post-test. The regression model was not significant (adjusted $R^2 = -0.12$, $F(1,6) = 0.229$, $p = .649$; Figure II.17).

Next, we calculated an ICC of the unilateral redundancy gain between points in time. The ICC was 0.24 with $F(7, 7) = 1.6$, $p = .26$, CI = [-0.40, 0.72] which indicates poor reliability (Koo & Li, 2016).

Regarding the single-case analysis, we compared results of the double unilateral condition between points in time (Table II.10). Thereof, five of eight patients (62.5%) showed consistent negative results. None of these patients had a significant RTE in the double unilateral condition at either point in time. All three patients with one positive RTE showed inconsistent results (*wa* is not counted despite the positive RTE in the pre-test because he was excluded for the post-test). It is worth noting that visual functions were present in the sighted visual field at both points in time. Hence, the lacking correspondence of positive results in the sighted visual field indicates a low retest reliability.

Figure II.17

Correlation of the redundancy gain for the double unilateral condition between pre- and post-test



Note. The blue line indicates the linear regression line. Unilateral gain = difference in reaction times between single and double unilateral condition. ms = millisecond;

II.4.4. Discussion

In our patient sample, the sensitivity of the RTP measured in the sighted visual field was 18.18% - 25%. As we aimed for 100%, the result indicates a poor sensitivity. Regarding the retest reliability of the RTP within the sighted visual field, the ICC was poor between points in time. In the single-case analysis, patients with a significant RTE (37.5%) showed the positive result only at one point in time. Hence, there was no consistency for positive results showing a low retest reliability in the sighted field of patients.

Importantly, the patient sample was small (N = 11), especially in the post-test (N = 8) limiting the generalizability of results. Furthermore, we included patients in the ICC-analysis even though single-case analysis showed no significant RTE for the double unilateral condition. Hence, estimates about sensitivity and reliability should be interpreted with caution.

With respect to RVCs, one patient had a significant RTE in the double bilateral condition indicating RVCs. Prior to the experiment we had no knowledge about RVCs in the blind field of patients. As there is no gold standard to measure RVCs, we cannot verify whether the RTP missed patients with true RVCs or whether the RTP correctly identified the only patient (*hw*) truly showing RVCs at one point in time. Consequently, results of the RVC-condition cannot be taken into account for the estimate of sensitivity or reliability.

II.5. General Discussion

In three studies, we investigated the diagnostic quality of the redundant target paradigm (RTP) as a measure for residual visual capacities (RVCs) in the blind field of patients. The RTP is based on the redundant target effect (RTE) which describes reduced reaction times in response to two simultaneously presented targets compared to reaction times in response to a single target. In our meta-analysis, we found a significant positive summary effect size on group level in healthy participants. The summary effect size varied depending on experimental features. As effects were low for two-choice paradigms and vertical target configurations, future experiments should avoid these features. To estimate the summary effect size of the RTP as used to measure RVCs, we selected a subgroup of studies using a detection paradigm and a double bilateral target configuration as well as analyzing mean reaction times per condition. It is worth noting that these studies measured the RTE in healthy participants but used the experimental features similar to RVC-studies. Results for this subgroup predict a range of true effects above zero for similar studies. This means that there should be a significant RTE in subsequent studies applying these experimental features in healthy participants. Importantly, the publication bias might have led to an overestimation of the summary effect sizes in the meta-analysis. Hence, researchers should conduct preregistered studies about the RTE to get a more valid estimate of its true effect size.

In agreement with the results of the meta-analysis, we replicated the RTE in our sample of healthy participants. Interestingly, the unilateral redundancy gain was smaller than the bilateral redundancy gain. This finding is in contrast to the higher summary effect size for unilateral target configurations in the meta-analysis.

Previous studies also showed differences in the redundancy gain between double unilateral and double bilateral conditions. In Tomaiuolo et al. (1997) reaction times between double conditions did not differ significantly. Qualitatively, the unilateral redundancy gain was bigger by 1 millisecond (Tomaiuolo et al., 1997). In Murray et al. (2001) reaction times in response to unilateral double stimulation were faster than to bilateral double stimulation in the upper visual field but not in the lower visual field. Furthermore, Murray et al. (2001) suggested that the interhemispheric transmission time necessary for bilateral targets might have reduced the redundancy gain. However, a study using a matching task showed reaction time facilitation for bilateral target pairs in contrast to unilateral or vertical target pairs (Ludwig et al., 1993).

Taken together, results were inconsistent about the direction of redundancy gain differences. One reason for this might be that so far only few studies investigated the unilateral gain in contrast to over 20 studies testing the bilateral gain.

Importantly, the difference in redundancy gains between double conditions is relevant for the interpretation of results in HVFD-patients. In studies on RVCs in HVFD-patients, the double unilateral condition is typically used as reference for the to-be-expected redundancy gain with double bilateral targets. Put simply, it is often assumed that the redundancy gain in the double unilateral and the double bilateral condition are the same. It is then tempting to interpret differences in redundancy gains in the two conditions as a measure of the difference in strength of the signals coming from the blind versus the sighted field. However, the findings from us and others show that such differences in redundancy gains are also found in healthy participants with two sighted hemifields. This suggests that unilateral-vs-bilateral differences in HVFD-patients cannot be used as a measure for assessing the relative strengths of the visual signals coming from the two visual hemifields.

Following this, it is worth further investigating the redundancy gain difference between double unilateral and double bilateral condition. It might be possible to predict the redundancy gain in the double bilateral condition from the double unilateral condition while considering the systematic difference. The predicted value could then be used as a more valid reference for RVC-results. Our endeavor to predict the bilateral gain from the unilateral gain in healthy participants via a simple linear regression was unfortunately unsuccessful. Future studies might develop other prediction models including more variables potentially relevant for the RTE.

In the meta-analysis, we focused on the RTE on group level. However, in RVC-research, it is necessary to draw conclusions on single-case level, meaning to determine the presence or absence of RVCs for each individual patient. In this regard, the diagnostic quality of the RTP is decisive. Hence, we made an attempt to estimate the diagnostic quality of the RTP. In particular, we were interested in four main research questions: (1) How good is the sensitivity of the RTP? (2) How good is the specificity of the RTP? (3) How good is the reliability of the RTP? (4) Does the RTP indicate whether the minimal configuration criterion (MCC) for RVCs is fulfilled in a given patient?

II.5.1. How good is the sensitivity of the RTP?

In RVC-studies, we want to measure remnants of visual functions. Hence it is necessary that the RTP detects the presence of visual functions with a high sensitivity. In the best case, the RTP detects with 100% accuracy any visual signal still available in a given part of the visual field. Applied to healthy observers or the sighted visual field of HVFD-patients, i.e. in cases were visual functions are available, it is expected that the RTP yields a significant RTE in every single case.

Reviewing the literature, there were six studies that investigated the RTE within the sighted visual field of HVFD-patients. Testing the sighted visual field, double unilateral and single target conditions were compared. In summary, 41.67%-64.15% of patients had a significant RTE. In our sample of patients with HVFD, 18.18%-25% showed a significant RTE for targets within the sighted visual field. In general, the sensitivity values for patients were lower than for healthy participants. Some of this reduced RTE-prevalence found in the sighted field of HVFD-patients can probably be attributed to '*sight-blindness*', i.e. the phenomenon that patients with HVFD also have reduced visual capacities in the remaining visual field (for a review see Chokron et al., 2016). Sight-blindness is manifested for example as a reduced contrast sensitivity (Chokron et al., 2016). However, targets for the RTP are high in contrast, very salient, and patients can detect them easily. Additionally, perimetry results prove that visual function is present within the tested visual area. As the RTP should detect the presence of visual functions, the maximum value of 64.15% is far from the aspired level.

Regarding healthy participants, only one study in the literature provided single-case analysis. The results showed that 77.27% of participants had a significant RTE (Schärli et al., 1999). Schärli et al. (1999) compared a double unilateral and a single target condition. In comparison, results from our sample yielded only a sensitivity of 32.08% for this double condition. Hence, our study resulted in a considerably lower estimate of the sensitivity. There are two possible reasons for this difference. First, in Schärli et al. (1999) each condition was tested with 120 trials, whereas we only used 60 trials. In RVC-studies, a wide range of 20 (Ross et al., 2018) to 160 (de Gelder et al., 2001) trials per target conditions has been used. Qualitatively, there was no clear relationship between the number of trials and the presence of the RTE. For group analysis, it is possible to calculate the statistical power depending on the sample size and on the number of trials (Baker et al., 2019). However, to our knowledge, there is no possibility to calculate the power for a single-case design with a non-parametric test. Hence, we cannot evaluate the influence of the statistical power quantitatively so far.

Second, in contrast to our static black circular target, the black disk of Schärli et al. (1999) was flickering. Therefore, the higher sensitivity value of Schärli et al. (1999) could be explained by a stronger salience of the flickering target. As studies in the meta-analysis used a variety of target types with different colors and diverse geometric forms or letters, it was not possible to analyze the effect of certain target features on redundancy gain. Results in RVC-studies showed that colors might play a role (Leh et al., 2006; Marzi et al., 2009) and that targets following the gestalt-laws have an advantage (Celeghin, Savazzi, et al., 2015; Georgy et al., 2016). Following this, future studies should test which target features lead to the greatest RTE first in healthy participants and then apply it in patient samples.

Schärli et al. (1999) tested 22 healthy participants without giving details about the age range. Authors only stated that healthy participants were not age-matched to HVFD-patients (Schärli et al., 1999). In contrast, we measured the RTP in a sample more than twice the size, namely 53 healthy participants (sample 1). Furthermore, we covered an age range from 20 to 80 years distributed approximately equal across age decades (see Figure II.10 and Figure II.11). Following this, our sensitivity estimate is based on a bigger sample size covering a broad age range. Still, it is worth investigating whether a higher trial number and a flickering target might improve the diagnostic quality of the RTE.

To our knowledge, there is no former study that investigated the sensitivity for bilateral redundant targets in healthy participants. The double bilateral condition consists of one target in the left and one target in the right hemifield. In our sample, 30.19% of participants had a significant RTE. Taken together, 47.17% of participants showed a significant RTE in at least one redundant target condition.

In summary, we get estimates of sensitivity ranging between 18.18% - 77.27% even if 100% of the investigated participants had visual functions at the target positions. We argue that this sensitivity is insufficient. If the probability for a RTE is low even though the presence of visual function is confirmed, it can be expected that the ability of the RTP to pick up much weaker signals from the blind visual field of HVFD-patients will be even worse.

Comparing the sensitivity value of 47.17% in our control group with medical diagnostic tests, the meaning of this criterion gets even clearer. Test kits analyzing the human immunodeficiency virus (HIV) have a sensitivity of ≥ 99% meaning that at least 99 of 100 HIV-positive patients are detected by the screening test (Abrahim et al., 2019). If a HIV test kit would have a sensitivity of 47%, 53 out of 100 patients would go undetected, deprived of medication, and maybe even spread the HIV-infection.

In RVC-research, the consequences are not life-threatening. Still the frequency of RVCs will be underestimated leading to reduced prevalence estimates and biased implications for vision theories. In RVC-research, it is common to group patients in RVC-positive or RVC-negative depending on behavioral results. The neuronal correlate of RVCs is then defined by searching for neurological structures that are preserved in the RVC-positive group and destroyed in the RVC-negative group. This procedure has been used for example to define the LGN-V5 pathway responsible for the Riddoch phenomenon (e.g. Ajina & Bridge, 2018; Ajina et al., 2015). Similar approaches have been applied to RVC-results based on the RTP. For instance, the absence of the RTE has been attributed to an extensive lesion affecting the basal ganglia (patient IG in Tomaiuolo et al., 1997). Furthermore, Wüst et al. (2002) proposed the hypothesis about spared islands in V1 and argued that patients without RTE might not have enough functional neurons left within the lesioned area to show the

RTE. In addition, they assumed that the location specificity of RVC-behavior, as shown with the RTP, could be related to the pattern of preserved neurons (Wüst et al., 2002). However, the RTP could be absent in these patients or in certain locations of the visual field just because of its low sensitivity and completely independent of any preserved or lesioned neuronal structures. This means that negative findings based on the RTP have to be treated with caution and the validity of models based on such findings is therefore questionable.

It follows that the sensitivity of RVC-tests has to be measured always before using those tests to label patients as RVC-positive or RVC-negative. A positive example of how this might be done is provided by Ajina et al.'s (2015) study on the Riddoch phenomenon. Regarding the RVC-test for the Riddoch phenomenon, results of healthy participants and of the sighted field in HVFD-patients showed an accuracy of 100% even at the lowest level of contrast (Ajina et al., 2015). Hence, the sensitivity has been 100% and conclusions about underlying neuronal structures are valid.

II.5.2. How good is the specificity of the RTP?

In our literature review, we found no study that investigated the specificity of the RTP. We estimated the specificity on the basis of our blind-spot experiment. Hereby, the second redundant target is positioned within the natural blind spot. As participants are physiologically blind in this area of the visual field, we know that visual functions are absent (Curcio et al., 1990; Jonas et al., 1991). Results showed that 10.53% of participants had a significant RTE. Following this, the specificity of the RTP is 89.47%.

We can again use the analogy of medical tests to appreciate the relevance of specificity. Low specificity means a high number of false positives, i.e. a high number of patients who are falsely diagnosed with a certain disease. Such a false diagnosis will often entail the risk of unnecessary treatment. Mammography, for instance, leads to 20% false positive results in Europe probably leading to psychological burden, unnecessary biopsies, or lumpectomies (Løberg et al., 2015). Thereafter, it takes two years until all false positive cases are declared cancer-free (Løberg et al., 2015). In contrast, a RVC-positive result does not lead to invasive treatments. However, researchers might hold on to these patients for more extensive, time and cost consuming investigations and might also mistakenly use such findings to support or reject specific assumptions about the organization of the visual system in humans.

Given the specificity of 89.47%, we infer that testing RVCs with the RTP will lead only rarely to false positive results. Following this, we can state that if there is a significant RTE, visual function is in all likelihood present in the examined part of the visual field. However, research on RVCs is rarely done with large samples of patients. Not seldom, reports on RVCs contain just one patient. It is not clear how many other patients were also tested who may not have

been listed in the report because they did not show any signs of RVCs. Given this context, it is distinctly possible that some of those single-case reports on RVCs may in fact be based on a false positive finding.

It should also be mentioned that the finding on specificity is the result of a post-hoc single-case analysis of data from a previous study. The hypothesis in the original study did not concern the specificity of the RTP and we planned only group analysis. Consequently, future studies need to investigate this research question directly to replicate our result.

II.5.3. How good is the reliability of the RTP?

Next, we investigated the reliability of the RTP in two ways. Firstly, we investigated the consistency of results in repeated testing. Secondly, we investigated the correspondence of test results between unilateral and bilateral redundant target conditions. For both comparisons, we reviewed results from the literature and analyzed our own empirical data.

In patient studies of the literature, we checked whether RVC-positive results were consistent across multiple tests. RVCs were measured by presenting one target in the sighted and one target in the blind visual field. It is a sign for RVCs if reaction times in this double bilateral condition are significantly shorter than reaction times in response to a single target in the sighted field. In our review, twelve patients with HVFD were tested in multiple occasions and showed at least one significant RTE in the RVC-condition. Thereof, only 33.33% showed consistent positive results. In our sample, eight HVFD-patients were tested at two points in time. Thereof, only one patient showed a significant effect in the RVC-condition at one point in time.

Importantly, there is no gold standard in testing RVCs. Hence, the results of the RTP cannot be compared with true RVCs. In the literature, there are some patients, for instance patient GY (e.g. de Gelder et al., 2001; Tamietto et al., 2010), who show RVCs consistently across multiple tests reported in different studies making it likely that RVCs are truly present. However, as this was not the case for all HVFD-patients, neither in the literature nor in our clinical sample, the reliability of the RTP in the RVC-condition should be interpreted with caution.

Regarding the sighted visual field of patients, we expect stable visual functions. However, only three patients of our clinical sample showed a significant RTE for the double unilateral condition at one point in time. Hence, all positive results were inconsistent. On group level, the analysis showed a poor retest reliability within the sighted visual field in our patient sample. Following this, reports in the literature as well as our own data indicate poor reliability in multiple testing of the RTP.

Furthermore, we can estimate the reliability of the RTP by comparing results between double unilateral and double bilateral conditions. Initially, we reviewed the literature. Only seven of fourteen studies in the literature overview tested both double conditions in HVFD-patients. Importantly, true RVCs are unknown. Thus, we cannot expect a significant RTE in the RVC-condition, i.e. in the double bilateral condition. To account for this, we used the RVC-condition as the baseline selecting only those patients from the literature who showed at least one significant RTE in the double bilateral condition. Each of these patients (N = 16) had also a positive result in the double unilateral condition. The perfect correspondence indicates a high reliability between double conditions.

It is worth noting that this result might overestimate the true RTP-reliability because we applied a liberal criterion for the classification of the double unilateral condition. In particular, patients with a positive result either had a significant RTE on single-case level or were part of a sample showing a significant RTE on group-level. We have seen in healthy participants that not all participants included in a sample with a significant group effect also have the effect on single-case level. Hence, this liberal criterion likely overestimates the correspondence between double unilateral RTE and double bilateral RTE in the patients of the literature overview.

Next, we analyzed data from our sample of healthy participants. On group level, the reliability between double unilateral and double bilateral condition was poor. Comparing conditions in the single-case analysis of healthy participants, only 15.09% showed a significant RTE in both double conditions.

To summarize, comparisons between multiple tests and between double conditions revealed a low reliability. This was true even for healthy participants and for the sighted field of patients. In both cases, visual functions in the tested field are assumed to be undiminished. The lack of agreement in positive findings in those cases therefore demonstrates the poor reliability of the RTP.

To further illustrate the importance of high reliability in diagnostic tests, we can look at measurements of intra-ocular pressure (IOP) in open angle glaucoma patients. Realini et al. (2011) tested the IOP seven times with two-hour intervals at each of two visits with a Goldmann tonometer. This device is the clinical gold standard. The retest reliability between visits (e.g. 8:00 o'clock at visit 1 versus 8:00 o'clock at visit 2) was poor to moderate (our classification of ICCs based on Koo & Li, 2016). This result shows that the common clinical practice of testing IOP once per day does not take into account intra-individual variability. ICCs for changes between two consecutive times (e.g. change from 8:00-10:00 o'clock at visit 1 versus change from 8:00-10:00 o'clock at visit 2) were once again lower, some even around zero (Realini et al., 2011). This is especially problematic for clinical trials investigating

the outcome of glaucoma therapies by testing one time before and one time after intervention at one visit. The same holds true for the adaptation of individual medication dosage. As a consequence, the efficacy measures of glaucoma therapies might be biased and the individual patient might not get the optimal medication dosage.

The same issues appear for the RTP in RVC-research. As the RTP has a poor reliability, it is hardly possible to distinguish between changes due to a treatment or due to a random error.

II.5.4. Is the RTP a MCC-test for RVCs?

Using the RTP, RVCs are tested with the double bilateral condition (Marzi et al., 1986). In the literature, 15 studies used a RTP to measure RVCs with varying experimental designs. As it was common in these studies, we defined a patient as RVC-positive if there was a significant RTE in at least one occasion. With this liberal criterion 12.77%-22.06% of patients with HVFDs showed RVCs. Concerning our sample of eleven patients, only one patient showed a significant RTE in the RVC-condition at one point in time. In general, patients are often selected for studies if it is already known that they show some type of RVCs. In our study, we included all recruited participants without previous knowledge about RVCs. Taken together, the RVC-prevalence measured by the RTP ranged from 9.09%-22.06%.

Measuring the prevalence of RVCs is a tough task given the various types of RVCs ranging from simple detection of targets to the discrimination of emotional faces (Danckert et al., 2019). Given the time and cost constraints in research and in the clinic, it is not feasible to measure all RVC-types. One solution could be a test that determines whether a patient shows the necessary, but not sufficient, neuronal and behavioral conditions, i.e. the minimal configuration criterion (MCC), underlying all types of RVCs. With a MCC-test at hand, it would be possible to define how many HVFD-patients fulfill the preconditions for RVCs.

A MCC-test would furthermore be helpful to plan rehabilitation strategies for a single patient. If a patient fulfills the MCC of RVCs, restorative treatments aiming to improve RVCs would more likely be effective.

Similarly, a MCC-test would allow recruiting suitable patients for RVC-studies. Researchers often aim to draw conclusions from RVCs to the neuronal correlates of visual functions and of visual consciousness. However, if patients do not fulfill the MCC, the conclusions would be invalid.

Authors of previous studies interpreted the RTP as a MCC-test. For instance, Striemer et al. (2009) reported the presence of obstacle avoidance in a HVFD-patient without awareness for the obstacles. However, this finding could not be replicated in a subsequent study testing six HVFD-patients (Ross et al., 2018). Striemer et al. (2018) dismissed the results as contradicting evidence because only one of the six HVFD-patients in Ross et al. (2018) had a

significant RTE. In this sense, a significant RTE was taken as a necessary precondition for other types of RVCs.

Following this, it was worthwhile to investigate whether the RTP is a MCC-test. To investigate whether a test indicates the MCC of RVCs, we can check whether the test confirms the following assumption: Patients having any type of RVCs must also show a positive result in the MCC-test. Or put differently: Patients having a negative result in the MCC-test must not show any other type of RVCs. To test this assumption for the RTP, we reviewed the literature. Thereby, seven studies investigated the RTE as well as other types of RVCs. Results showed that six patients had no significant RTE in the RVC-condition but positive results in other RVC-tasks. These six cases reported in the literature contradicted the assumption of a MCC-test. In conclusion, the RTP does not indicate whether a given patient fulfills the MCC of RVCs. Consequently, the absence of a RTE does not allow conclusions about the absence or presence of other RVC-types.

Knowing the poor sensitivity of the RTP, this finding is not surprising. A poor sensitivity means a high rate of false negative results, i.e. RVCs are present in a patient but not detected by the RTP. In such a case, it is to be expected that other RVC-tests yield positive results. If follows that a MCC-test needs a high sensitivity. In this respect, the low diagnostic quality of the RTP makes it an unsuitable test to determine whether patients fulfill the preconditions for RVC-research.

The demand to show a significant RTE in patients before interpreting other types of RVCs can therefore not be maintained. Consequently, the findings of Ross et al. (2018) have to be considered for theories about obstacle avoidance in HVFD-patients.

Does this mean that we have to give up on the idea of a MCC-test?

In the literature, various types of RVCs have been described, for instance the Riddoch phenomenon (Riddoch, 1917), action blindsight (Danckert & Rossetti, 2005), or affective blindsight (Celeghin, de Gelder, et al., 2015). Studies investigating the neuronal correlates of RVCs presented evidence for specific pathways. In action blindsight, visual information might be processed via the pulvinar to dorso-parietal areas (Danckert & Rossetti, 2005). In contrast, affective blindsight is thought to rely on connections between SC and the amygdala (Ajina et al., 2020). Following this, a common neurological MCC must be located before the system splits up into more specialized pathways, for example within the optic tract or at the retinal level. The RTP requires neither motion or face perception nor a target-oriented guidance of movements. Moreover, the RTP has various other advantages like an easy experimental implementation and the lack of response criteria. Hence, it was a good but unsuccessful attempt for a MCC-test. In the future, it might be worth investigating possibilities

to improve the diagnostic quality of the RTP and subsequently re-evaluate its potential to be a MCC-test.

Besides, there could be other ways to indicate the MCC.

One promising approach is the use of parametric designs. If behavioral performance or neuronal activity can be modulated by certain target characteristics, like contrast (Ajina et al., 2015) or speed (Ajina & Bridge, 2018) it provides compelling evidence for RVCs. It might be promising to develop these tests further to achieve a MCC-test.

Further approaches concern the early stages of the visual system. After a lesion in V1, the preceding neuronal structures are affected by trans-synaptic retrograde degeneration (TRD; e.g. Cowey et al., 2011). It is possible that the extent of the TRD determines whether a patient may still possess some RVCs or not. If too many neurons degenerate in the optic tract, the transmission of visual information to midbrain or higher visual areas is inhibited. Consequently, the visual information might not reach still intact modules in the visual system preventing RVCs. On the basis of these considerations, the MCC could be the preservation versus degeneration of early visual pathways. The extent of the TRD can be measured at the retinal level using optical coherence tomography (e.g. Yamashita et al., 2016). Hence, we propose the hypothesis that if the retina is affected by TRD, the patient is unlikely to show any form of RVCs. However, it is also possible that the TRD does not provide a dichotomous categorization but a continuous scale. Thereby, RVCs might be increasingly less likely or weaker with higher levels of TRD. It is a task for future research to test these hypotheses.

To summarize, the MCC determines the neuronal and behavioral preconditions necessary for any type of RVCs. Our findings show that the RTP is no MCC-test. Future research might investigate whether other RVC-measurements indicate the MCC. Having a MCC-test would be helpful to estimate the prevalence of RVCs, to plan rehabilitation strategies for patients, and to recruit suitable patients for RVC-research.

II.5.5. Conclusion

In three studies, we investigated the RTP and its use as a measure for RVCs, e.g. blindsight, in HVFD-patients. The RTP is based on the RTE which describes reduced reaction times in response to two redundant targets in comparison to reaction times in response to a single target.

In the meta-analysis, the RTE showed a positive summary effect size on group-level in healthy participants. This means that we can expect to find a RTE in subsequent studies using a design similar to RVC-studies (detection task, bilateral redundant targets, and mean reaction times per target condition). However, the publication bias might have led to an overestimation of the summary effect size. To counteract the publication bias and thus get a

more valid estimate of the true effect size, scientists should conduct pre-registered RTP-studies in the future.

In HVFD-patients, the RTP should detect RVCs on single-case level. With respect to this application, we estimated the diagnostic quality of the RTP.

In the literature, 12.77%-22.05% of HVFD-patients were classified as RVC-positive by the RTP. In our clinical sample, this was true for one patient (9.09%). To estimate the diagnostic quality, results from the test of interest should ideally be compared to results from a gold-standard test. However, there is no gold standard to measure RVCs. Hence, the RVC-condition cannot be used to estimate the diagnostic quality of the RTP.

Consequently, we relied on cases in which visual functions are reliably present, namely healthy participants and the sighted field of HVFD-patients.

In the context of the RTP, the sensitivity indicates how good the RTP detects the presence of visual functions. Sensitivity was low with values ranging between 18.18% - 77.27%. This means that the RTP might lead to a high number of false negative results. Consequently, the absence of a RTE in a patient does not imply the absence of RVCs.

Our findings on specificity indicate how good the RTP detects the absence of visual functions. Specificity was 89.47%, meaning that the RTP might lead only rarely to false positive results. Consequently, the presence of a RTE in a patient likely indicates the presence of RVCs.

The reliability was estimated as the correspondence between multiple RTP-results in the same participant for whom stable visual functions can be assumed. Intra-class correlations between redundant conditions in healthy participants as well as between test sessions in patients indicated a low reliability on group level. This finding was supported by low correspondence of RTE-results in single-case analysis. Following this, the RTP has a poor reliability.

Additionally, we evaluated whether the RTE indicates the existence of the neuronal and behavioral precondition, i.e. the MCC, for other types of RVCs. This analysis was motivated by previous studies considering the RTE to be a necessary requirement for the validity of other RVC-measurements. If this were true, RVCs should only be present if a patient also had a significant RTE. Contrary to this assumption, there were six patients reported in the literature having no RTE but RVCs in other tasks. Following this, the RTP is not a valid MCC test implying that it is unreasonable to demand a significant RTE as a precondition for not dismissing findings from RVC-studies.

Importantly, some values about the diagnostic quality were based on previous reports in the literature having varying RTP-designs and analysis methods. This means that the flaws of

the studies used in our literature research will also contaminate and undermine to some extent our conclusions on the diagnostic quality of the RTP. In addition, the patient sample tested in our study was small, thereby limiting the generalizability of results. Therefore, subsequent studies should re-evaluate the diagnostic quality by testing the RTP in the sighted visual field of a greater number of HVFD-patients in multiple sessions separated by short time intervals.

It is worth noting that a significant RTE was, in almost all cases, defined by applying a significance level of $\alpha = 5\%$. This seems reasonable as long as we test only one single patient in only one single test session. In this case the conventional significance level means that we accept that false positive results (type-I-error) will occur with a probability of 5%. However, scientists or clinicians often test a number of HVFD-patients and employ multiple testing sessions. In such a situation, the risk of finding a false-positive result is not equal to 5% but much higher. Following this, we recommend to adjust the α-level when looking for RVC-cases in a group of patients.

However, we do not claim that RVCs itself are a statistical artefact. There are a number of reported patients who consistently show RVCs in a variety of tasks, including the RTP, in different labs and over numerous years, for instance patient GY (e.g. de Gelder et al., 2001; Tamietto et al., 2010) or the hemispherectomized patient DR (Georgy et al., 2016; Leh et al., 2006).

Still, the low diagnostic quality indicates that the RTP does not measure RVCs precisely. Hence, previous and subsequent RTP-results should be evaluated in light of a poor sensitivity and a poor reliability.

II.6. References

Abrahim, S. A., Girma, M., Habteselassie, A., Gezahegn, N., Feleke, A., Berheto, T. M., Demissie, M., Belete, W., & Deressa, T. (2019). Diagnostic accuracy of HIV test kits, Genscreen Ultra and Bioelisa. *HIV/AIDS (Auckland, NZ)*, *11*, 17. https://doi.org/10.2147/HIV.S184603

Ajina, S., & Bridge, H. (2016). Blindsight and Unconscious Vision: What They Teach Us about the Human Visual System. *Neuroscientist*. https://doi.org/10.1177/1073858416673817

Ajina, S., & Bridge, H. (2018). Blindsight relies on a functional connection between hMT+ and the lateral geniculate nucleus, not the pulvinar. *PLOS Biology*, *16*(7), e2005769. https://doi.org/10.1371/journal.pbio.2005769

Ajina, S., Pestilli, F., Rokem, A., Kennard, C., & Bridge, H. (2015). Human blindsight is mediated by an intact geniculo-extrastriate pathway. *Elife*, *4*. https://doi.org/10.7554/eLife.08935

Ajina, S., Pollard, M., & Bridge, H. (2020). The Superior Colliculus and Amygdala Support Evaluation of Face Trait in Blindsight. *Frontiers in neurology*, *11*, 769. https://doi.org/10.3389/fneur.2020.00769

Azzopardi, P., & Cowey, A. (1998). Blindsight and visual awareness. *Consciousness and Cognition*, *7*(3), 292-311. https://doi.org/10.1006/ccog.1998.0358

Baker, D. H., Vilidaite, G., Lygo, F. A., Smith, A. K., Flack, T. R., Gouws, A. D., & Andrews, T. J. (2019). Power contours: Optimising sample size and precision in experimental psychology and human neuroscience. *Psychological Methods*. https://doi.org/http://dx.doi.org/10.1037/met0000337

Ball, K., Smith, D., Ellison, A., & Schenk, T. J. E. b. r. (2010). A body-centred frame of reference drives spatial priming in visual search. *204*(4), 585-594. https://doi.org/https://doi.org/10.1007/s00221-010-2327-y

Barbur, J., Ruddock, K., & Waterfield, V. A. (1980). Human visual responses in the absence of the geniculo-calcarine projection. *Brain: a journal of neurology*, *103*(4), 905-928. https://doi.org/10.1093/brain/103.4.905

Baujat, B., Mahé, C., Pignon, J. P., & Hill, C. (2002). A graphical method for exploring heterogeneity in meta-analyses: application to a meta-analysis of 65 trials. *Statistics in Medicine*, *21*(18), 2641-2652. https://doi.org/https://doi.org/10.1002/sim.1221

Ben-David, B. M., Eidels, A., & Donkin, C. (2014). Effects of aging and distractors on detection of redundant visual targets and capacity: do older adults integrate visual targets differently than younger adults? *PLoS One*, *9*(12), e113551. https://doi.org/10.1371/journal.pone.0113551

Bono, R., Blanca, M. J., Arnau, J., & Gómez-Benito, J. (2017). Non-normal distributions commonly used in health, education, and social sciences: a systematic review. *Frontiers in psychology*, *8*, 1602. https://doi.org/https://doi.org/10.3389/fpsyg.2017.01602

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2009). *Introduction to meta-analysis*. Wiley.

Brainard, D. (1997). The Psychophysics Toolbox. *Spatial Vision*, *10*(4), 433-436.

Campion, J., Latto, R., & Smith, Y. (1983). Is blindsight an effect of scattered light, spared cortex, and near-threshold vision? *Behavioral and Brain Sciences*, *6*(3), 423-448. https://doi.org/10.1017/S0140525X00016861

Cavanaugh, M. R., & Huxlin, K. R. (2017). Visual discrimination training improves Humphrey perimetry in chronic cortically induced blindness. *Neurology*, *88*(19), 1856-1864. https://doi.org/10.1212/wnl.0000000000003921

Celeghin, A., de Gelder, B., & Tamietto, M. (2015). From affective blindsight to emotional consciousness. *Consciousness and Cognition*, *36*, 414-425. https://doi.org/10.1016/j.concog.2015.05.007

Celeghin, A., Savazzi, S., Barabas, M., Bendini, M., & Marzi, C. A. (2015). Blindsight is sensitive to stimulus numerosity and configuration: evidence from the redundant signal effect. *Experimental brain research*, *233*(5), 1617-1623. https://doi.org/10.1007/s00221-015-4236-6

Chokron, S., Perez, C., & Peyrin, C. (2016). Behavioral Consequences and Cortical Reorganization in Homonymous Hemianopia. *Frontiers in systems neuroscience*, *10*, 57. https://doi.org/10.3389/fnsys.2016.00057

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. Routledge Academic.

Cooper, H. M., Hedges, L. V., & Valentine, J., C. (2009). *Handbook of Research Synthesis and Meta-Analysis* (2 ed.). Russel Sage Foundation.

Corballis, M. C. (2002). Hemispheric interactions in simple reaction time. *Neuropsychologia*, *40*(4), 423-434. https://doi.org/https://doi.org/10.1016/S0028-3932(01)00097-5

Corbetta, M., Marzi, C. A., Tassinari, G., & Aglioti, S. (1990). Effectiveness of different task paradigms in revealing blindsight. *Brain*, *113*, 603-616. https://www.ncbi.nlm.nih.gov/pubmed/2364262

Cowey, A. (2010). The blindsight saga. *Experimental brain research*, *200*(1), 3-24. https://doi.org/10.1007/s00221-009-1914-2

Cowey, A., Alexander, I., & Stoerig, P. (2011). Transneuronal retrograde degeneration of retinal ganglion cells and optic tract in hemianopic monkeys and humans. *Brain*, *134*, 2149-2157. https://doi.org/10.1093/brain/awr125

Cowey, A., & Stoerig, P. (2001). Detection and discrimination of chromatic targets in hemianopic macaque monkeys and humans. *European Journal of Neuroscience*, *14*(8), 1320-1330. https://doi.org/https://doi.org/10.1046/j.0953-816x.2001.01761.x

Cowey, A., & Weiskrantz, L. (1963). A perimetric study of visual field defects in monkeys. *Quarterly Journal of Experimental Psychology*, *15*(2), 91-115. https://doi.org/https://doi.org/10.1080/17470216308416561

Curcio, C. A., Sloan, K. R., Kalina, R. E., & Hendrickson, A. E. (1990). Human photoreceptor topography. *Journal of Comparative Neurology*, *292*(4), 497-523. https://doi.org/ https://doi.org/10.1002/cne.902920402

Danckert, J., & Culham, J. C. (2010). Reflections on blindsight: Neuroimaging and behavioural explorations clarify a case of reversed localisation in the blind field of a patient with hemianopia. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale*, *64*(2), 86. https://doi.org/https://doi.org/10.1037/a0017426

Danckert, J., & Rossetti, Y. (2005). Blindsight in action: what can the different sub-types of blindsight tell us about the control of visually guided actions? *Neuroscience & Biobehavioral Reviews*, *29*(7), 1035-1046. https://doi.org/10.1016/j.neubiorev.2005.02.001

Danckert, J., Tamietto, M., & Rossetti, Y. (2019). Definition: Blindsight. *Cortex*, *119*, 569-570. https://doi.org/10.1016/j.cortex.2019.01.027

de Gelder, B., Pourtois, G., van Raamsdonk, M., Vroomen, J., & Weiskrantz, L. (2001). Unseen stimuli modulate conscious visual experience: evidence from inter-hemispheric summation. *Neuroreport*, *12*(2), 385-391.

Donkin, C., Little, D. R., & Houpt, J. W. (2014). Assessing the speed--accuracy trade-off effect on the capacity of information processing. *Journal of Experimental Psychology: Human Perception and Performance*, *40*(3), 1183-1202. https://doi.org/10.1037/a0035947

Duval, S., & Tweedie, R. (2000). Trim and Fill: A Simple Funnel-Plot–Based Method of Testing and Adjusting for Publication Bias in Meta-Analysis. *Biometrics*, *56*(2), 455-463. https://doi.org/https://doi.org/10.1111/j.0006-341X.2000.00455.x

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, *315*(7109), 629-634. https://doi.org/10.1136/bmj.315.7109.629 %J BMJ

Fels, M., & Geissner, E. (1997). *Neglect Test. Ein Verfahren zur Erfassung visueller Neglectphänomene. Deutsche überarbeitete Adaption des Behavioural Inattention Test (Wilson, Cockburn & Halligan, 1987)* (2nd corrected edition ed.). Hogrefe-Verlag für Psychologie.

Field, A., Miles, J., & Field, Z. (2012). *Discovering statistics using R*. Sage publications.

Fischer, R., & Miller, J. (2008). Differential redundancy gain in onset detection versus offset detection. *Perception & Psychophysics*, *70*(3), 431-436. https://doi.org/10.3758/pp.70.3.431

Florio, V., Marzi, C. A., Girelli, A., & Savazzi, S. (2008). Enhanced redundancy gain in schizophrenics: a correlate of callosal dysfunction? *Neuropsychologia*, *46*(11), 2808-2815. https://doi.org/10.1016/j.neuropsychologia.2008.05.007

Fox, D. M., Goodale, M. A., & Bourne, J. A. (2020). The Age-Dependent Neural Substrates of Blindsight. *Trends in neurosciences*, *43*(4), 242-252. https://doi.org/10.1016/j.tins.2020.01.007

Garric, C., Sebaa, A., Caetta, F., Perez, C., Savatovsky, J., Sergent, C., & Chokron, S. (2019). Dissociation between objective and subjective perceptual experiences in a population of hemianopic patients: A new form of blindsight? *Cortex*, *117*, 299-310. https://doi.org/10.1016/j.cortex.2019.05.006

Georgy, L., Celeghin, A., Marzi, C. A., Tamietto, M., & Ptito, A. (2016). The superior colliculus is sensitive to gestalt-like stimulus configuration in hemispherectomy patients. *Cortex*, *81*, 151-161. https://doi.org/https://doi.org/10.1016/j.cortex.2016.04.018

Grasso, P. A., Pietrelli, M., Zanon, M., Ladavas, E., & Bertini, C. (2020). Alpha oscillations reveal implicit visual processing of motion in hemianopia. *Cortex*, *122*, 81-96. https://doi.org/10.1016/j.cortex.2018.08.009

Grice, G. R., & Canham, L. (1990). Redundancy phenomena are affected by response requirements. *Perception & Psychophysics*, *48*(3), 209-213.

Grice, G. R., Canham, L., & Gwynne, J. W. (1984). Absence of a redundant-signals effect in a reaction time task with divided attention. *Perception & Psychophysics*, *36*(6), 565-570. https://doi.org/https://doi.org/10.3758/BF03207517

Grice, G. R., & Gwynne, J. W. (1987). Dependence of target redundancy effects on noise conditions and number of targets. *Perception & Psychophysics*, *42*(1), 29-36. https://doi.org/https://doi.org/10.3758/BF03211511

Hall, N., & Colby, C. (2014). S-cone visual stimuli activate superior colliculus neurons in old world monkeys: implications for understanding blindsight. *Journal of Cognitive Neuroscience*, *26*(6), 1234-1256. https://doi.org/10.1162/jocn_a_00555

Harrer, M., Cuijpers, P., Furukawa, T., & Ebert, D. D. (2019a). *dmetar: Companion R Package For The Guide 'Doing Meta-Analysis in R'*. In (Version R package version 0.0.9000.) http://dmetar.protectlab.org/

Harrer, M., Cuijpers, P., Furukawa, T., & Ebert, D. D. (2019b). *Doing Meta-Analysis in R: A Hands-on Guide*. Retrieved 03.30 from https://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/

Hesse, C., Billino, J., & Schenk, T. (2018). On the role of V1 in avoiding obstacles. *Cortex*, *98*, 276-282. https://doi.org/10.1016/j.cortex.2017.11.004

Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *BMJ*, *327*(7414), 557-560. https://doi.org/https://doi.org/10.1136/bmj.327.7414.557

Holmes, G. (1918). Disturbances of Vision by Cerebral Lesions. *British Journal of Ophthalmology*, *2*(7), 353-384. https://www.ncbi.nlm.nih.gov/pubmed/18167806

Hooge, I. T., Niehorster, D. C., Nyström, M., Andersson, R., & Hessels, R. S. (2018). Is human classification by experienced untrained observers a gold standard in fixation detection? *Behavior Research Methods*, *50*(5), 1864-1881. https://doi.org/https://doi.org/10.3758/s13428-017-0955-x

Hooge, I. T., Niehorster, D. C., Nyström, M., Andersson, R., & Hessels, R. S. (2021). Correction to:“Is human classification by experienced untrained observers a gold standard in fixation detection?”. *Behavior Research Methods*, 1-2. https://doi.org/https://doi.org/10.3758/s13428-017-0955-x

Hothorn, T., & Hornik, K. (2015, 2015-02-20). *Exact Distribution for Rank and Permutation Tests*. http://ftp.uni-bayreuth.de/math/statlib/R/CRAN/doc/packages/exactRankTests.pdf

Huxlin, K. R., Martin, T., Kelly, K., Riley, M., Friedman, D. I., Burgin, W. S., & Hayhoe, M. (2009). Perceptual relearning of complex visual motion after V1 damage in humans. *Journal of Neuroscience*, *29*(13), 3981-3991. https://doi.org/10.1523/JNEUROSCI.4882-08.2009

IntHout, J., Ioannidis, J. P., Rovers, M. M., & Goeman, J. J. (2016). Plea for routinely presenting prediction intervals in meta-analysis. *BMJ Open*, *6*(7). https://doi.org/10.1136/bmjopen-2015-010247

Jonas, J. B., Gusek, G. C., & Fernández, M. C. (1991). Correlation of the blind spot size to the area of the optic disk and parapapillary atrophy. *American journal of ophthalmology*, *111*(5), 559-565. https://doi.org/https://doi.org/10.1016/S0002-9394(14)73698-0

Kasten, E., Wüst, S., Behrens-Baumann, W., & Sabel, B. A. (1998). Computer-based training for the treatment of partial blindness. *Nature medicine*, *4*(9), 1083-1087. https://doi.org/10.1038/2079

Kleiner, M., Brainard, D., & Pelli, D. (2007). What's new in Psychtoolbox-3? Perception 36 ECVP Abstract Supplement. In.

Kolominsky-Rabas, P. L., Heuschmann, P. U., Marschall, D., Emmert, M., Baltzer, N., Neundorfer, B., Schoffski, O., & Krobot, K. J. (2006). Lifetime cost of ischemic stroke in Germany: results and national projections from a population-based stroke registry: the Erlangen Stroke Project. *Stroke*, *37*(5), 1179-1183. https://doi.org/10.1161/01.STR.0000217450.21310.90

Kolominsky-Rabas, P. L., Wiedmann, S., Weingartner, M., Liman, T. G., Endres, M., Schwab, S., Buchfelder, M., & Heuschmann, P. U. (2015). Time trends in incidence of pathological and etiological stroke subtypes during 16 years: the Erlangen Stroke Project. *Neuroepidemiology*, *44*(1), 24-29. https://doi.org/10.1159/000371353

Koo, T. K., & Li, M. Y. (2016). A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *Journal of chiropractic medicine*, *15*(2), 155-163. https://doi.org/https://doi.org/10.1016/j.jcm.2016.02.012

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Frontiers in psychology*, *4*, 863. https://doi.org/10.3389/fpsyg.2013.00863

Lalkhen, A. G., & McCluskey, A. (2008). Clinical tests: sensitivity and specificity. *Continuing Education in Anaesthesia Critical Care & Pain*, *8*(6), 221-223. https://doi.org/https://doi.org/10.1093/bjaceaccp/mkn041

Lawrence, E. S., Coshall, C., Dundas, R., Stewart, J., Rudd, A. G., Howard, R., & Wolfe, C. D. (2001). Estimates of the prevalence of acute stroke impairments and disability in a multiethnic population. *Stroke*, *32*(6), 1279-1284. https://doi.org/https://doi.org/10.1161/01.STR.32.6.1279

Leh, S. E., Mullen, K. T., & Ptito, A. (2006). Absence of S-cone input in human blindsight following hemispherectomy. *European Journal of Neuroscience*, *24*(10), 2954-2960. https://doi.org/ https://doi.org/10.1111/j.1460-9568.2006.05178.x

Løberg, M., Lousdal, M. L., Bretthauer, M., & Kalager, M. (2015). Benefits and harms of mammography screening. *Breast Cancer Research*, *17*(1), 1-12. https://doi.org/https://doi.org/10.1186/s13058-015-0525-z

Ludwig, T., Jeeves, M. A., Norman, W., & DeWitt, R. (1993). The bilateral field advantage on a letter-matching task. *Cortex*, *29*(4), 691-713. https://doi.org/https://doi.org/10.1016/S0010-9452(13)80291-2

Marzi, C. A., Mancini, F., Metitieri, T., & Savazzi, S. (2009). Blindsight following visual cortex deafferentation disappears with purple and red stimuli: A case study. *Neuropsychologia*, *47*(5), 1382-1385. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2009.01.023

Marzi, C. A., Tassinari, G., Aglioti, S., & Lutzemberger, L. (1986). Spatial summation across the vertical meridian in hemianopics: a test of blindsight. *Neuropsychologia*, *24*(6), 749-758. https://www.ncbi.nlm.nih.gov/pubmed/3808284

Mazzi, C., Bagattini, C., & Savazzi, S. (2016). Blind-Sight vs. Degraded-Sight: Different Measures Tell a Different Story. *Frontiers in psychology*, *7*, 901. https://doi.org/10.3389/fpsyg.2016.00901

Miller, J. (2007). Contralateral and ipsilateral motor activation in visual simple reaction time: A test of the hemispheric coactivation model. *Experimental brain research*, *176*(4), 539-558. https://doi.org/https://doi.org/10.1007/s00221-006-0641-1

Miller, J., & Adam, J. J. (2006). Redundancy gain with static versus moving hands: A test of the hemispheric coactivation model. *Acta psychologica*, *122*(1), 1-10. https://doi.org/https://doi.org/10.1016/j.actpsy.2005.08.003

Miller, J., & Van Nes, F. (2007). Effects of response task and accessory stimuli on redundancy gain: Tests of the hemispheric coactivation model. *Journal of Experimental Psychology: Human Perception and Performance*, *33*(4), 829. https://doi.org/https://doi.org/10.1037/0096-1523.33.4.829

Millington, R. S., Yasuda, C. L., Jindahra, P., Jenkinson, M., Barbur, J., Kennard, C., Cendes, F., Plant, G. T., & Bridge, H. (2014). Quantifying the pattern of optic tract degeneration in human hemianopia. *Journal of Neurology, Neurosurgery & Psychiatry*, *85*(4), 379-386. https://doi.org/10.1136/jnnp-2013-306577

Milner, A., & Goodale, M. (1995). *The visual brain in action*. Oxford University Press New York.

Milner, A., & Goodale, M. (2008). Two visual systems re-viewed. *Neuropsychologia*, *46*(3), 774-785. https://doi.org/10.1016/j.neuropsychologia.2007.10.005

Miniussi, C., Girelli, M., & Marzi, C. A. (1998). Neural site of the redundant target effect: Electrophysiological evidence. *Journal of Cognitive Neuroscience*, *10*(2), 216-230. https://doi.org/10.1162/089892998562663

Mooshagian, E., Kaplan, J., Zaidel, E., & Iacoboni, M. (2008). Fast visuomotor processing of redundant targets: the role of the right temporo-parietal junction. *PLoS One*, *3*(6), e2348. https://doi.org/10.1371/journal.pone.0002348

Mordkoff, J. T., Miller, J., & Roch, A.-C. (1996). Absence of coactivation in the motor component: Evidence from psychophysiological measures of target detection. *Journal of Experimental Psychology: Human Perception and Performance*, *22*(1), 25. https://doi.org/https://doi.org/10.1037/0096-1523.22.1.25

Morland, A. B., Jones, S. R., Finlay, A. L., Deyzac, E., Lê, S., & Kemp, S. (1999). Visual perception of motion, luminance and colour in a human hemianope. *Brain*, *122*(6), 1183-1198. https://doi.org/https://doi.org/10.1093/brain/122.6.1183

Müller-Oehring, E. M., Schulte, T., Kasten, E., Poggel, D. A., Müller, I., Wüstenberg, T., & Sabel, B. A. (2009). Parallel interhemispheric processing in hemineglect: Relation to visual field defects. *Neuropsychologia*, *47*(12), 2397-2408. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2009.04.014

Murray, M. M., Foxe, J. J., Higgins, B. A., Javitt, D. C., & Schroeder, C. E. (2001). Visuo-spatial neural response interactions in early cortical processing during a simple reaction time task: a high-density electrical mapping study. *Neuropsychologia*, *39*(8), 828-844. https://doi.org/https://doi.org/10.1016/S0028-3932(01)00004-5

Ogourtsova, T., Korner-Bitensky, N., Leh, S. E., Eskes, G., & Ptito, A. (2011). Superior colliculi involvement in poststroke unilateral spatial neglect: A pilot study. *Topics in stroke rehabilitation*, *18*(6), 770-785. https://doi.org/https://doi.org/10.1310/tsr1806-770

Omura, K., Tsukamoto, T., Kotani, Y., Ohgami, Y., Minami, M., & Inoue, Y. (2004). Different mechanisms involved in interhemispheric transfer of visuomotor information. *Neuroreport*, *15*(18), 2707-2711.

Overgaard, M. (2011). Visual experience and blindsight: a methodological review. *Experimental brain research*, *209*(4), 473-479. https://doi.org/10.1007/s00221-011-2578-2

Pasik, T., & Pasik, P. (1971). The visual world of monkeys deprived of striate cortex: effective stimulus parameters and the importance of the accessory optic system. *Vision research*, *11*, 419-IN455. https://doi.org/https://doi.org/10.1016/0042-6989(71)90055-1

Phillips, I. (2020). Making sense of blindsense: A commentary on Garric et al., 2019. *Cortex*, *127*, 388-392. https://doi.org/10.1016/j.cortex.2019.11.016

Pöppel, E., Held, R., & Frost, D. (1973). Residual visual function after brain wounds involving the central visual pathways in man. *Nature*, *243*(5405), 295-296. https://doi.org/https://doi.org/10.1038/243295a0

Ptito, A., & Leh, S. E. (2007). Neural substrates of blindsight after hemispherectomy. *Neuroscientist*, *13*(5), 506-518. https://doi.org/10.1177/1073858407300598

Raab, D. H. (1962). Statistical facilitation of simple reaction times. *Transactions of the New York Academy of Sciences*, *24*, 574-590.

Railo, H., Andersson, E., Kaasinen, V., Laine, T., & Koivisto, M. (2014). Unlike in clinical blindsight patients, unconscious processing of chromatic information depends on early visual cortex in healthy humans. *Brain stimulation*, *7*(3), 415-420.

Realini, T., Weinreb, N., & Wisniewski, S. (2011). Short-term repeatability of diurnal intraocular pressure patterns in glaucomatous individuals. *Ophthalmology*, *118*(1), 47-51. https://doi.org/https://doi.org/10.1016/j.ophtha.2010.04.027

Reinhard, J., Schreiber, A., Schiefer, U., Kasten, E., Sabel, B. A., Kenkel, S., Vonthein, R., & Trauzettel-Klosinski, S. (2005). Does visual restitution training change absolute homonymous visual field defects? A fundus controlled study. *British Journal of Ophthalmology*, *89*(1), 30-35. https://doi.org/10.1136/bjo.2003.040543

Reinhard, S., Leonhard, E., & Kerkhoff, G. (2016). *Sensitiver Neglect Test (SNT) single and dual task*. Clinical Neuropsychology Group.

Richards, W. (1973). Visual processing in scotomata. *Experimental brain research*, *17*(4), 333-347. https://doi.org/https://doi.org/10.1007/BF00234098

Riddoch, G. (1917). DISSOCIATION OF VISUAL PERCEPTIONS DUE TO OCCIPITAL INJURIES WITH ESPECIALL REFERENCE TO APPRECIATION OF MOVEMENT. *Brain*, *40*(1), 15-57. https://doi.org/https://doi.org/10.1093/brain/40.1.15

Ridgway, N., Milders, M., & Sahraie, A. (2008). Redundant target effect and the processing of colour and luminance. *Experimental brain research*, *187*(1), 153-160. https://doi.org/10.1007/s00221-008-1293-0

Rosenthal, R. (1993). *Meta-Analytic Procedures For Social Research* (Revised Edition ed., Vol. 6). Sage Publications.

Roser, M., & Corballis, M. C. (2002). Interhemispheric neural summation in the split brain with symmetrical and asymmetrical displays. *Neuropsychologia*, *40*(8), 1300-1312. https://doi.org/https://doi.org/10.1016/S0028-3932(01)00219-6

Ross, A. I., Schenk, T., Billino, J., Macleod, M. J., & Hesse, C. (2018). Avoiding unseen obstacles: Subcortical vision is not sufficient to maintain normal obstacle avoidance behaviour during reaching. *Cortex*, *98*, 177-193. https://doi.org/https://doi.org/10.1016/j.cortex.2016.09.010

Rucker, V., Heuschmann, P. U., O'Flaherty, M., Weingartner, M., Hess, M., Sedlak, C., Schwab, S., & Kolominsky-Rabas, P. L. (2020). Twenty-Year Time Trends in Long-Term Case-Fatality and Recurrence Rates After Ischemic Stroke Stratified by Etiology. *Stroke*, *51*(9), 2778-2785. https://doi.org/10.1161/STROKEAHA.120.029972

Saionz, E. L., Tadin, D., Melnick, M. D., & Huxlin, K. R. (2020). Functional preservation and enhanced capacity for visual restoration in subacute occipital stroke. *Brain*, *143*(6), 1857-1872. https://doi.org/10.1093/brain/awaa128

Savazzi, S., & Marzi, C. A. (2004). The superior colliculus subserves interhemispheric neural summation in both normals and patients with a total section or agenesis of the corpus callosum. *Neuropsychologia*, *42*(12), 1608-1618. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2004.04.011

Savazzi, S., & Marzi, C. A. (2008). Does the redundant signal effect occur at an early visual stage? *Experimental brain research*, *184*(2), 275-281. https://doi.org/10.1007/s00221-007-1182-y

Schärli, H., Harman, A. M., & Hogben, J. H. (1999). Blindsight in subjects with homonymous visual field defects. *Journal of Cognitive Neuroscience*, *11*(1), 52-66. https://doi.org/https://doi.org/10.1162/089892999563247

Schindler, I., Rice, N. J., McIntosh, R. D., Rossetti, Y., Vighetto, A., & Milner, A. D. (2004). Automatic avoidance of obstacles is a dorsal stream function: evidence from optic ataxia. *Nature neuroscience*, *7*(7), 779-784. https://doi.org/10.1038/nn1273

Schröter, H., Fiedler, A., Miller, J., & Ulrich, R. (2011). Fusion prevents the redundant signals effect: Evidence from stereoscopically presented stimuli. *Journal of Experimental Psychology: Human Perception and Performance*, *37*(5), 1361-1368. https://doi.org/10.1037/a0024280

Schwarzer, G., Carpenter, J. R., & Rücker, G. (2015). *Meta-analysis with R* (Vol. 4784). Springer.

Seber, G. A. F. (2013). *Statistical models for proportions and probabilities*. Springer. https://doi.org/10.1007/978-3-642-39041-8

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: uses in assessing rater reliability. *Psychological bulletin*, *86*(2), 420. https://doi.org/https://doi.org/10.1037/0033-2909.86.2.420

Smith, D. T., Lane, A. R., & Schenk, T. (2008). Arm position does not attenuate visual loss in patients with homonymous field deficits. *Neuropsychologia*, *46*(9), 2320-2325. https://doi.org/10.1016/j.neuropsychologia.2008.03.010

Stoerig, P., Hübner, M., & Pöppel, E. (1985). Signal detection analysis of residual vision in a field defect due to a post-geniculate lesion. *Neuropsychologia*, *23*(5), 589-599. https://doi.org/https://doi.org/10.1016/0028-3932(85)90061-2

Striemer, C. L., Chapman, C. S., & Goodale, M. A. (2009). "Real-time" obstacle avoidance in the absence of primary visual cortex. *Proceedings of the National Academy of Sciences*, *106*(37), 15996-16001. https://doi.org/10.1073/pnas.0905549106

Striemer, C. L., Chapman, C. S., & Goodale, M. A. (2018). The role of non-conscious visual processing in obstacle avoidance: A commentary on Ross et al. (2016). *Cortex*, *98*, 269-275. https://doi.org/10.1016/j.cortex.2017.03.024

Sturm, W. (2006). *Wahrnehmungs- und Aufmerksamkeitsfunktionen. Manual*. Schuhfried.

Tamietto, M., Cauda, F., Corazzini, L. L., Savazzi, S., Marzi, C. A., Goebel, R., Weiskrantz, L., & de Gelder, B. (2010). Collicular vision guides nonconscious behavior. *Journal of Cognitive Neuroscience*, *22*(5), 888-902. https://doi.org/https://doi.org/10.1162/jocn.2009.21225

Thaler, L., Schütz, A. C., Goodale, M. A., & Gegenfurtner, K. R. (2013). What is the best fixation target? The effect of target shape on stability of fixational eye movements. *Vision research*, *76*, 31-42. https://doi.org/10.1016/j.visres.2012.10.012

Tomaiuolo, F., Ptito, M., Marzi, C. A., Paus, T., & Ptito, A. (1997). Blindsight in hemispherectomized patients as revealed by spatial summation across the vertical meridian. *Brain*, *120*(5), 795-803. https://doi.org/https://doi.org/10.1093/brain/120.5.795

Turatto, M., Mazza, V., Savazzi, S., & Marzi, C. A. (2004). The role of the magnocellular and parvocellular systems in the redundant target effect. *Experimental brain research*, *158*(2), 141-150. https://doi.org/10.1007/s00221-004-1884-3

Van der Heijden, A., Schreuder, R., Maris, L., & Neerincx, M. (1984). Some evidence for correlated separate activation in a simple letter-detection task. *Perception & Psychophysics*, *36*(6), 577-585.

van Koningsbruggen, M., Koller, K., & Rafal, R. D. (2017). Deafferentation of the superior colliculus abolishes spatial summation of redundant visual signals. *Frontiers in systems neuroscience*, *11*, 9.

Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, *36*(3), 1-48. https://doi.org/10.18637/jss.v036.i03

Viechtbauer, W., & Cheung, M. W. L. (2010). Outlier and influence diagnostics for meta-analysis. *Research synthesis methods*, *1*(2), 112-125. https://doi.org/https://doi.org/10.1002/jrsm.11

Wechsler, D. (2009). *Wechsel Memory Scales - Forth Edition (WMS-IV): Technical and interpretive manual*. Pearson Clinical Assessment.

Weiskrantz, L. (1986). *Blindsight: A case study and implications*. Clarendon Press.

Weiskrantz, L. (1999). *Consciousness lost and found: A neuropsychological exploration*. OUP Oxford.

Weiskrantz, L., Barbur, J., & Sahraie, A. (1995). Parameters affecting conscious versus unconscious visual discrimination with damage to the visual cortex (V1). *Proceedings of the National Academy of Sciences*, *92*(13), 6122-6126. https://www.ncbi.nlm.nih.gov/pubmed/7597090

Weiskrantz, L., Warrington, E. K., Sanders, M. D., & Marshall, J. (1974). Visual capacity in the hemianopic field following a restricted occipital ablation. *Brain*, *97*(4), 709-728. https://www.ncbi.nlm.nih.gov/pubmed/4434190

Whitwell, R. L., Striemer, C. L., Nicolle, D. A., & Goodale, M. A. (2011). Grasping the non-conscious: preserved grip scaling to unseen objects for immediate but not delayed grasping following a unilateral lesion to primary visual cortex. *Vision research*, *51*(8), 908-924. https://doi.org/10.1016/j.visres.2011.02.005

Wüst, S., Kasten, E., & Sabel, B. A. (2002). Blindsight after optic nerve injury indicates functionality of spared fibers. *Journal of Cognitive Neuroscience*, *14*(2), 243-253. https://doi.org/https://doi.org/10.1162/089892902317236876

Yamashita, T., Miki, A., Goto, K., Araki, S., Takizawa, G., Ieki, Y., Kiryu, J., Tabuchi, A., Iguchi, Y., Kimura, K., & Yagita, Y. (2016). Retinal Ganglion Cell Atrophy in Homonymous Hemianopia due to Acquired Occipital Lesions Observed Using Cirrus High-Definition-OCT. *Journal of Ophthalmology*, *2016*, 2394957. https://doi.org/10.1155/2016/2394957

Yu, J.-C., Chang, T.-Y., & Yang, C.-T. (2014). Individual differences in working memory capacity and workload capacity. *Frontiers in psychology*, *5*, 1465.

Zhang, X., Kedar, S., Lynn, M. J., Newman, N. J., & Biousse, V. (2006). Homonymous hemianopia in stroke. *Journal of Neuro-Ophthalmology*, *26*(3), 180-183. https://doi.org/10.1097/01.wno.0000235587.41040.39

Zihl, J., & von Cramon, D. (1980). Registration of light stimuli in the cortically blind hemifield and its effect on localization. *Behavioural brain research*, *1*(4), 287-298. https://doi.org/https://doi.org/10.1016/0166-4328(80)90022-4

Zihl, J., & von Cramon, D. (1985). Visual field recovery from scotoma in patients with postgeniculate damage. A review of 55 cases. *Brain*, *108 (Pt 2)*, 335-365. https://www.ncbi.nlm.nih.gov/pubmed/4005527

Zihl, J., & Werth, R. (1984). Contributions to the study of "blindsight"—I. Can stray light account for saccadic localization in patients with postgeniculate field defects? *Neuropsychologia*, *22*(1), 1-11. https://doi.org/https://doi.org/10.1016/0028-3932(84)90002-2

Appendix II. A Meta-analysis of the RTE in healthy participants

Methods

If Cohen's d was not reported for the RTE-tests, we estimated Cohen's d based on the reported test statistic using formula (A.1)-(A.3) (Rosenthal, 1993).

$$\text{Cohen's } d_z = \frac{2\times r}{\sqrt{1-r^2}} \text{ with } r = \frac{Z}{\sqrt{n}} \quad \text{(A.1)}$$

$$\text{Cohen's } d_z = \frac{t}{\sqrt{n}} \quad \text{(A.2)}$$

$$\text{Cohen's } d_z = \sqrt{\frac{F}{n}} \quad \text{(A.3)}$$

Where Z is a normalized test statistic, *t* is the test statistic of a paired t-Test, *F* is the F-statistic of a repeated measures ANOVA with 1 degree of freedom (df) and *n* is the sample size. These formulas are based on the following relation between t- and F-values with df = 1 (Rosenthal, 1993):

$$F = t^2 \quad \text{(A.4)}$$

Cohen's d_z is also referred to as the standardized mean difference (Lakens, 2013). To transform the standardized mean difference (d_z) to the more familiar Cohens' *d*, we applied the following formula (Cohen, 1988):

$$Cohen's\ d = d_z \times \sqrt{2} \quad \text{(A.5)}$$

The resulting estimates of Cohen's *d* were then corrected for the population bias by using Hedges' *g* correction (Cooper et al., 2009):

$$\text{Hedges'} g = \text{Cohen's } d \times \left(1 - \frac{3}{4(n-1)-1}\right) \quad \text{(A.6)}$$

Next, we calculated the variance of the effect size v_d (Cooper et al., 2009):

$$v_g = \left(\frac{1}{n} + \frac{g^2}{2n}\right) 2(1-r) \quad \text{(A.7)}$$

As the correlation in reaction times between single and double stimulus condition was never reported, we applied a best-guess procedure. Thereby, we used the data of our control group sample (see M2 3.) to calculate the correlation coefficient. The result showed a significant spearman correlation of $r_s = 0.97$, $p < .001$. As we cannot expect such a high correlation in all studies included in the meta-analysis, we repeated the analysis for r = 0.97, r = 0.77, and r = 0.57. Like this, we get a range of plausible results.

Derived, from this, we calculated the standard error (SE) of the effect size (Cooper et al., 2009).

$$SE_g = \sqrt{v_g} \quad \text{(A.8)}$$

The estimated values of Hedge's g and SE were then input to the meta-analysis functions of the R packages *meta* (Schwarzer et al., 2015) and *metafor* (Viechtbauer, 2010).

Results

Table II.A.1

Results of meta-analysis across all included RTE-tests

r	*k*	*g*	*95% CI*	95% PI	*Q*	τ^2	I^2
0.97	32	1.85***	[1.35, 2.35]	[-1.14, 4.84]	6523.6***	2.08	99.5
0.77	32	1.74***	[1.29, 2.19]	[-0.85, 4.34]	850.9***	1.56	96.4
0.57	32	1.67***	[1.23, 2.10]	[-0.75, 4.09]	455.1***	1.36	93.2

Note. r = correlation coefficient used to estimate the standard error of the effect size for each experiment; k = number of included effects; g = estimate of summary effect size based on Hedge's g; 95% CI = 95% confidence interval of the summary effect size; 95% PI = the 95% prediction interval of the summary effect size; Q = Q statistic for statistical heterogeneity; τ^2 = estimate of the between-study variance; I^2 = percentage of the observed variance which is due to real differences in effect sizes; * p<.05. ** p<.01. ***p<.001.

Table II.A.2

Results of subgroup analysis for random effects model with r = 0.77 and r = 0.57

r = 0.77

model	*k*	*g*	*95% CI*	95% PI	*Q*	τ^2	I^2	*Q-G*
faster	8	0.79	[-0.04, 1.62]	[-2.27, 3.85]	*280.2*	*1.39*	*97.5*	6.8**
mean	25	2.06***	[1.59, 2.53]	[-0.30, 4.41]	530.6	1.23	95.7	
bilateral	21	2.03***	[1.50, 2.56]	[-0.51, 4.57]	473.0	1.40	95.8	
unilateral	3	2.98***	[2.50, 3.47]	[-0.16, 6.12]	0.35	0	0.0	43.4***
vertical	8	0.59*	[0.07, 1.12]	[-1.32, 2.51]	154.5	0.54	96.6	
detection	22	2.25***	[1.79, 2.72]	[0.03, 4.47]	377.0	1.07	94.4	
go/ no-go	5	1.20***	[0.86, 1.54]	[0.03, 2.37]	14.9	0.10	73.1	24.37***
two-choice	5	0.06	[-0.76, 0.88]	[-3.18, 3.30]	172.4	0.86	97.7	

r = 0.57

model	*k*	*g*	*95% CI*	95% PI	*Q*	τ^2	I^2	*Q-G*
faster	8	0.78	[-0.05, 1.60]	[-2.23, 3.78]	*149.9*	*1.33*	*95.3*	*6.2**
mean	24	1.97***	[1.52, 2.42]	[-0.19, 4.13]	283.8	1.04	91.9	
bilateral	21	1.95***	[1.44, 2.46]	[-0.39, 4.30]	253.0	1.19	92.1	
unilateral	3	2.98***	[2.32, 3.64]	[-1.32, 7.28]	0.19	0	0.0	33.3***
vertical	8	0.59*	[0.07, 1.20]	[-1.27, 2.44]	82.6	0.51	91.5	
detection	22	2.17***	[1.71, 2.62]	[0.12, 4.21]	201.7	0.91	89.6	
go/ no-go	5	1.17***	[0.82, 1.52]	[0.11, 2.22]	8.0	0.08	49.7	22.9***
two-choice	5	0.06	[-0.76, 0.88]	[-3.15, 3.27]	92.2	0.84	95.7	

Note. Model = Model of subgroup analysis: Faster single RT vs. mean single RT; k = number of included effects; g = estimate of summary effect size based on Hedge's g; 95% CI = 95% confidence interval of the summary effect size; 95% PI = the 95% prediction interval of the summary effect size; Q = Q statistic for statistical heterogeneity; τ^2 = estimate of the between-study variance; I^2 = percentage of the observed variance which is due to real differences in effect sizes; Q Groups= Q statistic for subgroup differences; * p<.05. ** p<.01. ***p<.001.

Table II.A.3

Studies defined as outliers based on the influence analysis within the RVC-configuration subset

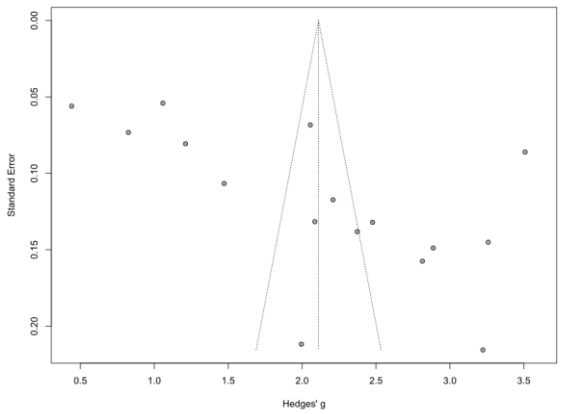
r	*Influence Analysis*	*DIFFITS*	*Cook's distance*	*Covariance Ratio*	Baujat plot	Outside 95%-CI of pooled effect
	Savazzi, 2004, Exp. 1	Savazzi, 2004, Exp. 1*	Savazzi, 2004, Exp. 1*	Savazzi, 2004, Exp. 1*		above
0.97					Omura et al., 2004	below
					Corballis, 2002	above
		Savazzi, 2004, Exp. 1	Savazzi, 2004, Exp. 1	Savazzi, 2004, Exp. 1		above
0.77					Omura et al., 2004	below
					Corballis, 2002	above
				Savazzi, 2004, Exp. 1		above
0,57				Omura et al., 2004	Omura et al., 2004	below
		Corballis, 2002	Corballis, 2002		Corballis, 2002	above

Note. r = correlation coefficient used to estimate the standard error of the effect size for each experiment; Influence Analysis = Study marked as outlier by *InfluenceAnalysis* function (Harrer et al., 2019a). DIFFITS = How much the predicted pooled effect changes after excluding the study in standard deviations. Cook's distance = Distance between the fitted values of all *k* studies by including versus excluding the study. Covariance Ratio = Ratio of the variance-covariance matrix of parameter estimates with excluded versus included study. Baujat plot = Plot shows the contribution of each study to the heterogeneity in the meta-analysis. Outside 95%-CI of pooled effect = Indicates if the outliers defined by the previous measures are above or below the 95% confidence interval of the pooled effect. * outside the cutoff suggested by Viechtbauer and Cheung (2010).

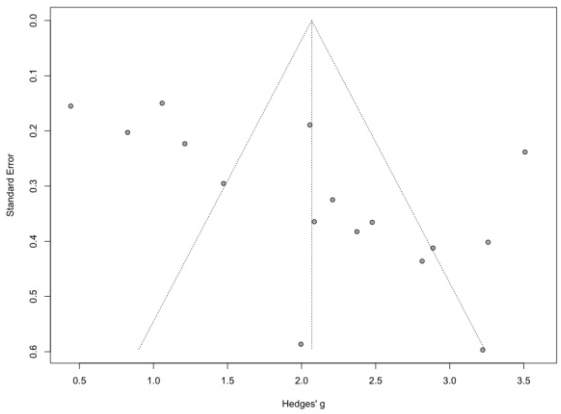
Figure II.A.1

Funnel plots for the random effects model with outlier correction of the RVC-configuration subset

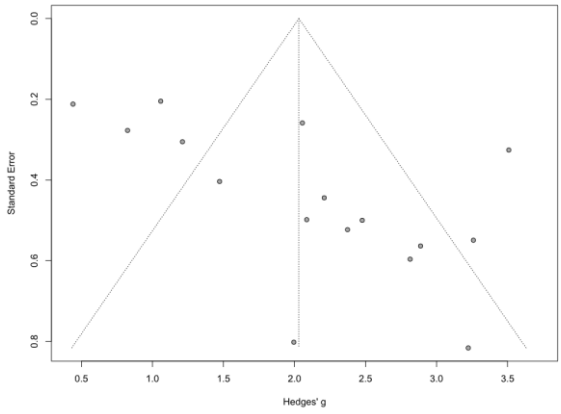
r = 0.57



r = 0.77



r = 0.97



Note. The funnel plots show the standard error on the inverted y-axis and Hedge's g on the x-asix. Each dot represents one study. The inverted funnel is centered on the random-effects meta-analysis estimate of the RTE. The RVC-configuration subset are all effects using the mean single RT of a detection paradigm with a bilateral double stimulation.

Appendix II. B Alpha-error accumulation in single-case analysis

Table II.B.1

Alpha levels used in the RVC-literature

Study	*Information*
Marzi et al. (1986)	p-value of .01-.05 for group analysis
Corbetta et al. (1990)	p-value of .01-.05 defined as significant
Tomaiuolo et al. (1997)	p-value of .01-.05 defined as significant
Schärli et al. (1999)	$\alpha \leq .05$
de Gelder et al. (2001)	p-value of .01-.05 defined as significant
Wüst et al. (2002)	p-value of .01-.05 defined as significant; α-level was Bonferroni corrected if more than one binomial test
Leh et al. (2006)	p-value of .01-.05 defined as significant
Marzi et al. (2009)	p-value of .01-.05 defined as significant; ANOVA with Bonferroni corrected post-hoc tests
Müller-Oehring et al. (2009)	tendency between $p \geq .05$ and $p \leq .1$
Striemer et al. (2009)	p-value of .01-.05 defined as significant; ANOVA with Bonferroni corrected post-hoc tests
Tamietto et al. (2010)	p-value of .01-.05 defined as significant; ANOVA with Bonferroni corrected post-hoc tests
Whitwell et al. (2011)	$\alpha \leq .05$
Celeghin, Savazzi, et al. (2015)	p-value of .01-.05 defined as significant
Georgy et al. (2016)	all significant results of the single case analysis were $p \leq .002$; ANOVA with Bonferroni corrected post-hoc tests
Ross et al. (2018)	$\alpha \leq .05$

The stochastic model is a Bernoulli experiment with a binomial distribution (Seber, 2013):

$$P(A = k) = B(n, p, k) = \binom{n}{k} \times p^k \times (1-p)^{n-k} \quad \text{(B.1)}$$

Where *n* is the number of repetitions of the experiment, *k* is the number of occurrences of the event *A* and *p* is the probability of the event *A*. For our example, *n* is the number of patients, *k* is the number times a significant RTE was obtained and the probability *p* for a significant RTE is 5%.

1. Question: 'How high is the probability that we will get at least one significant RTE per chance in 9 sessions?'

   To get this probability, we calculate the counter-probability for zero occurrences of the event:

   $$P_p^n(k \geq 1) = 1 - P_p^n(k = 0) = 1 - \binom{n}{k} \times p^k \times (1-p)^{n-k} \quad \text{(B.2)}$$

   This formula can be rearranged to a calculation that is easier to handle:

   $$\mathrm{P}_p^{\mathrm{n}}(\mathrm{k} \geq 1) = 1\text{- }(1\text{-p})^{\mathrm{n}} \quad \text{(B.3)}$$

   Inserting p = .05 and n = 9 sessions, the resulting probability is 37.0%.

2. Question: 'How high is the probability that we get at least one significant RTE per chance for 20 patients if we test each patient in 9 sessions'

   On the basis of our first result, we use the formula (B.3) and input p = .370 for the probability per participant and n = 20 for the number of repetitions.

   The result is a probability of >99.9%.

3. Question: 'How high is the probability that we get at least one significant RTE per chance for 20 patients if we test each patient in one session?'

   To answer this question, we input n = 20 and p = .05 in formula (B.3). As a result, the probability is 64.2%.

4. Question: 'What is the α-level per patient if the type-I-error rate should be 5% for a sample of 20 patients?'

   For the calculation, we know that $\mathrm{P}_p^{\mathrm{n}}(\mathrm{k} \geq 1) = .05$ and n = 20. Therefore, we need to rearrange formula (B.3) to calculate p:

   $$p = 1 - (1 - \mathrm{P}_p^{\mathrm{n}}(\mathrm{k} \geq 1))^{\frac{1}{n}} \quad \text{(B.4)}$$

   The calculation shows that the α-level has to be p ≤ .00256 for each patient to get a type-I-error rate of 5% for a sample of 20 patients.

5. Question: 'What is the α-level per session if the type-I-error rate should be 5% for a sample of 20 patients each tested in 9 sessions?'

   Again, we can use formula (B.4), whereby $P_p^n(k \geq 1) = .00256$ and n = 9. The resulting value is p = .00028. Consequently, to get a type-I-error rate of 5% for the group of patients, the α-value per session must be p ≤ .00028.

6. Question: 'In how many sessions per patient do we need a significant RTE with p ≤ .05, so that the probability to acquire this result by chance is below 5%?'

   For this calculation, we know that n = 9 sessions, p ≤ .05, and $P_{0.05}^9(A \leq k) \leq .05$. We computed the answer numerically (Table II.B.2). It turns out that the correct answer is 3, meaning that if the number of sessions where an RTE is obtained is 3 or more, the probability to observe such an event by chance slips below 5% and thus below the threshold required to ensure that type-I-error rate for the 9 sessions does not exceed the acceptable level of 5%.

   Table II.B.2

   Results of formula (B.1) with n = 9, p ≤ .05, and k ≤ 1 to k ≤ 9

k	$P_{0.05}^9(A \leq k)$	below .05	below .00256
1	0.36975	0	0
2	0.07121	0	0
3	**0.00836**	**1**	0
4	**0.00064**	1	**1**
5	0.00003	1	1
6	0.00000	1	1
7	0.00000	1	1
8	0.00000	1	1
9	0.00000	1	1

7. Question: 'In how many sessions per patient do we need a significant RTE with p ≤ .05, so that the probability to acquire this result by chance is below 0.256%?'

   For this calculation, we know that n = 9 sessions, p ≤ .05, and $P_{0.05}^9(A \leq k) \leq .00256$. We computed the answer numerically (Table II.B.2). It turns out that the correct answer is 4, meaning that if the number of sessions where an RTE is obtained is 4 or more, the probability to observe such an event by chance slips below 0.256% and thus below the threshold required to ensure that type-I-error rate for the entire study with 20 patients does not exceed the acceptable level of 5%.

We corrected the alpha-level for our empirical data with the following calculations.

Control group:

8. Question: 'What is the alpha-level per participant if the type-I-error rate should be 5% for a sample of 53 participants?'

   Inserting $P_p^n(k \geq 1) = .05$ and n = 53 in formula (B.4) we see that the α-level has to be p ≤ .00097 for each participant to get a type-I-error rate of 5% for a sample of 53 patients.

9. Question: 'What is the alpha-level per session if the type-I-error rate should be 5% for a sample of 53 participants each tested in 2 sessions (double bilateral condition; double unilateral condition)?'

   Using formula (B.4), with $P_p^n(k \geq 1) = .00097$ and n = 2, the resulting value is p = .00048. Consequently, to get a type-I-error rate of 5% for the group of patients, the α-value per session must be p ≤ .00048.

Blind spot experiment:

10. Question: 'What is the alpha-level per participant if the type-I-error rate should be 5% for a sample of 19 participants?'

    Inserting $P_p^n(k \geq 1) = .05$ and n = 19 in formula (B.4). we see that the α-level has to be p ≤ .0027 for each patient to get a type-I-error rate of 5% for a sample of 19 patients.

Patients:

11. Question: 'What is the alpha-level per patient if the type-I-error rate should be 5% for a sample of 8 patients?'

    Inserting $P_p^n(k \geq 1) = .05$ and n = 8 in formula (B.4) we see that the α-level has to be p ≤ .00639 for each patient to get a type-I-error rate of 5% for a sample of 53 patients.

12. Question: 'What is the alpha-level per session if the type-I-error rate should be 5% for a sample of 8 patients each tested in 4 sessions (2 points in time x 2 conditions)?'

    Using formula (B.4), with $P_p^n(k \geq 1) = .00639$ and n = 4, the resulting value is p = .0016. Consequently, to get a type-I-error rate of 5% for the group of patients, the α-value per session must be p ≤ .0016.

Appendix II.C Single-case analysis in healthy participants depending on target-response compatibility

Table II.C.1

Results of the single case analysis for right-handers and right stimulation

Control Group	Single vs. Double Unilateral is significant	Single vs. Double Unilateral is not significant	Sum
Single vs. Double Bilateral is significant	**3** **13.04%** **(cd, jh, qu)**	3 13.04% (gl, ly, oy)	6 26.08%
Single vs. Double Bilateral is not significant	4 17.39% (cz, fo, os, yr)	13 56.52%	17 73.92%
Sum	7 30.43%	16 69.57%	23 100%

Note. Numbers indicate the absolute and relative frequency of results in each cell. Participant codes are displayed in brackets. $\alpha \leq .05$

Table II.C.2

Results of the single case analysis for right-handers and left stimulation

Control Group	Single vs. Double Unilateral is significant	Single vs. Double Unilateral is not significant	Sum
Single vs. Double Bilateral is significant	**5** **21.74%** **(al, cu, km, sg, sq)**	3 13.04% (dl, lf, rv)	8 33.33%
Single vs. Double Bilateral is not significant	3 13.04% (cr, yb, zp)	13 56.52%	16 66.67%
Sum	8 33.33%	16 66.67%	24 100%

Note. Numbers indicate the absolute and relative frequency of results in each cell. Participant codes are displayed in brackets. $\alpha \leq .05$

III. Gaze-contingent stimulus removal leads to subsequent changes in overt attentional allocation

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Doris Schmid:	Methodology, Software, Investigation, Data curation, Writing - review & editing.
Thomas Schenk:	Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

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Gaze-contingent stimulus removal leads to subsequent changes in overt attentional allocation

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ABSTRACT

Spatial neglect is a debilitating neurological disorder marked by reduced exploration of contralesional space. We developed an intervention in which eye movements to and within one half of a search display were reduced over the course of several hundred trials. The aim of this study was to determine whether this intervention had an effect on the deployment of attention of healthy participants as a first step towards application in patients. The participants carried out a visual search task during which the stimuli in one half of the search display were removed whenever the participants made eye movements towards it. The stimuli in the other half were unaffected by eye movements. Indeed, this led to a steady relative decrease in fixations within the affected half over the course of the intervention. In five experiments, the performance in different spatial attention paradigms was measured before and after this intervention. In two visual search paradigms (feature and conjunction search), exploration of the affected half decreased compared to the unaffected half. In a Posner task with exogenous cues, a partial effect of the intervention was found. However, an attempt at replicating this effect was not successful. The fifth experiment showed that performance in a line bisection paradigm was not significantly influenced by the intervention. To conclude, the intervention showed the potential to influence the behavior of healthy participants in overt attentional exploration tasks.

1. Introduction

In this study we introduce an intervention which is ultimately aimed at application in neglect patients and describe its effects on visual exploration and attention in healthy participants. Spatial neglect is a frequent consequence of (right hemisphere) brain damage. Affected patients demonstrate decreased responses to contralesional stimuli in different domains (Kerkhoff, 2001). Most prominently, the exploration of visual space is markedly affected: Karnath et al. (1998) showed that the center of spontaneous exploratory behavior (eye and head movements) is shifted in an ipsilesional direction (right) in neglect patients (Karnath et al., 1998). In a study by Girotti et al. (1983), neglect patients needed more saccades to locate a flashed target in the left hemifield and failed to do so altogether in a quarter of the trials. Also, saccade latencies were higher in response to targets in the left hemifield. Similarly, Behrmann et al. (2001) reported leftward saccade planning (but not execution) deficits in neglect that were particularly pronounced for saccades to targets on the left. In free exploration tasks, Niemeier and Karnath (2000) found an explorational right bias but no differences in amplitude between leftward and rightward saccades. In neglect patients with frontal rather than parietal lesions, however, hypometric leftward saccades during exploration have been observed (Sprenger et al., 2002). The right bias can be observed during the exploration of natural images (Ptak et al., 2009) as well as during visual search (Sprenger et al., 2002) and is often increased by repeated fixations of targets on the right side during the latter (Husain et al., 2001; Sprenger et al., 2002). The ipsilesional exploration bias in neglect also seems to override the tendency of patients with homonymous hemianopia to compensate for their visual field defect by making more contra- than ipsilesional fixations (Ishiai et al., 1987). Walle and colleagues (2019) reported that neglect patients made more saccades to the right than to the left in a multiple object tracking task. They likewise demonstrated that the fixation distribution depended on neglect severity, with a stronger right bias in more severe cases of neglect. In milder cases of neglect, however, Walle and colleagues (2019) even found a left bias, interpreting it as a "compensational fixation strategy" (p. 17). This shows that an intervention aiming to bias neglect patients' fixations to the left side could be successful in reducing neglect severity.

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In the present study we introduce an intervention trying to implicitly correct the described exploration bias, since neglect patients often lack insight into their condition (Grattan et al., 2018). In the intervention, stimuli on the "preferred" (in neglect: ipsilesional) side are removed as soon as the gaze coordinates cross to this side of the search display while participants carry out a visual search task. Ideally, participants cease to explore that side and instead explore the side with constantly visible stimuli more actively. Thus, over the course of the intervention, a lateral imbalance in visual exploration behavior that goes against the existing bias – i.e. fewer fixations on the usually "preferred" (ipsilesional) side and more on the usually neglected side – is induced. "Left" and "right" in the intervention refer to the position on the screen and thus to positions relative to the trunk midline (i.a.), not relative to the current fixation position (i.e. retinal coordinates). The intervention thus operates in a trunk-based coordinate system, which is an important reference frame for describing the behavioral bias in neglect (Karnath et al., 1991).

The deficits in neglect have also been described in an attentional framework: patients have problems disengaging their attention from ipsilesional stimuli (Losier and Klein, 2001), which results in problems of relocating attention to contralesional stimuli, known as the 'disengage deficit'. According to the premotor theory of attention, there is a strong link between (eye) movement planning and covert attentional orienting (Craighero and Rizzolatti, 2005; Rizzolatti et al., 1987), which seems to be at least the case for exogenous attention (Smith and Schenk, 2012). When no eye movements could be planned to a part of the visual field, covert attentional allocation to this region was impaired (Craighero et al., 2004; Smith et al., 2010). Hence we can further test effects of the intervention on attentional allocation: When eye movements are not impossible but made less frequent on one side than the other, does this also have an influence on subsequent covert attentional allocation as would be suggested by the premotor theory of attention?

This intervention based on the gaze-contingent removal of stimuli combines several positive aspects: First, it operates with implicit feedback without the need for explicit scanning instructions. The latter depend on the conscious cooperation and effort of the patient, which are not always a given (Robertson and Manly, 2002). Second, learning that stimuli on the preferred (ipsilesional) side disappear upon looking there could alleviate the disengage deficit, since their competition with the stimuli on the usually neglected side is weakened. In this regard it has been demonstrated that the absence of stimuli on the ipsilesional side decreases neglect symptoms (Mark et al., 1988; Schnider et al., 2011).

Before applying the proposed intervention to neglect patients, we tested its effects on healthy participants.

Healthy participants, interestingly, show the opposite (albeit much smaller) effect to neglect patients: they tend to have a small preference for the left, which manifests itself in a leftward saccadic bias in visual search tasks, especially for early eye movements (Nuthmann and Matthias, 2014; Zelinsky, 1996) which is possibly due to a lateralization in the spatial attention network (Thiebaut de Schotten et al., 2011). Hence, in the current study with groups of healthy participants, the stimuli were removed on the left side when gaze coordinates crossed the (invisible) delimiter to the left while the participants were searching for a tilted line among vertical distractors (see Fig. 1). Similarly, healthy participants also show the opposite pattern to neglect patients in line bisection. Healthy participants bisect lines slightly to the left of the center of the line, a phenomenon that has been termed pseudoneglect (Bowers and Heilman, 1980), while in neglect patients the underrepresentation of the left side is reflected in bisection errors far to the right of the center of the line (Heilman and Valenstein, 1979; Schenkenberg et al., 1980).

To test the effect of the gaze contingent intervention, several tasks

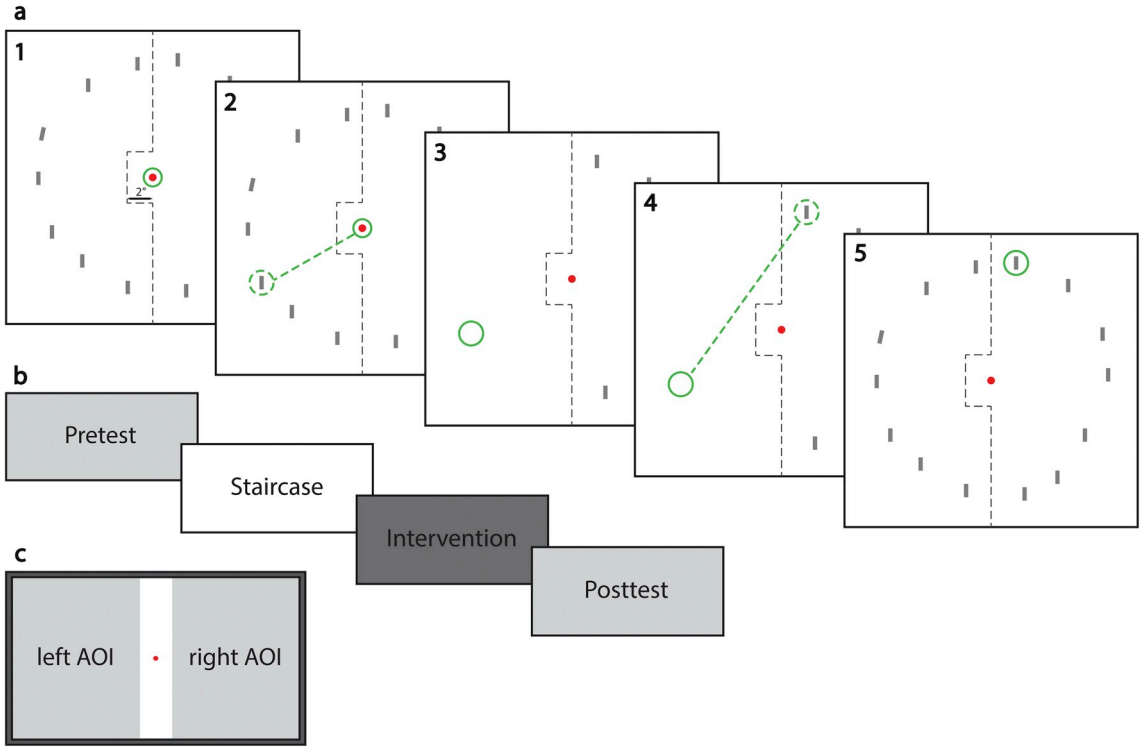

Fig. 1. a) Schematic illustration of the gaze-contingent intervention. If the gaze coordinates crossed the black dashed line (this delimiter was not displayed in the experiment) to the left, all stimuli on the left were removed. 1) In this example, the participant is still maintaining fixation. 2) The next saccade will cross the delimiter. 3) Once the saccade lands on the left, the stimuli have already been removed. 4) The next saccade will cross the delimiter to the right. 5) When the gaze coordinates are right of the delimiter, the stimuli on the left are displayed again. b) Procedure: The respective pretest was followed by the adaptive paradigm (staircase) in which the optimal tilt of the target line was determined individually. In case of the feature search task, the staircase preceded the pretest. The intervention was followed by a posttest which was always identical to the pretest (except for practice trials). c) Two areas of interest (AOIs) were created for the analysis of the eye tracking data. Here they are shown on the PC screen.

were measured before and after the intervention: (1) A first group of participants was tested in a visual search task that was identical to the task in the intervention, except that no stimuli were removed in a gaze-contingent manner. This was designed as a first test of whether overt attentional allocation remained affected by the intervention after it was stopped. (2) A second group of participants carried out a conjunction search task; the rationale of this experiment was to test whether the effect of the intervention generalized to a different search task or whether it was limited to the same task. (3) The pre- and posttest of a third group of participants was a Posner paradigm. This aimed at testing whether the intervention also affected covert attentional allocation. (4) With a fourth group of participants, a replication of this Posner task was carried out. (5) A fifth group of participants was tested with a line bisection task to assess whether there was a transfer to a more clinical task typically used in neglect diagnostics.

2. Gaze-contingent intervention

2.1. Methods

2.1.1. Participants

All participants were right-handed and naïve to the purpose of the study. They gave informed written consent to participate in the study, which was approved by the local ethics committee of the psychology department of the Ludwig-Maximilians-Universität München.

As all participants of Experiment 1–5 completed the intervention, their results are summarized in this section. The results are further displayed separately for each experimental group in the supplement. Some exclusion criteria applied in experiments 1–4, but in the present analysis of the gaze-contingent intervention, the data of all participants is included. In exchange for 8€ per hour or course credit, 137 participants (73 female, mean age: 25.43, range: 18 to 44, standard deviation (SD): 5.53) without psychiatric or neurological preconditions agreed to take part in the experiments; 103 were right-eye dominant, 34 were left-eye dominant.

2.1.2. Apparatus

Stimuli were created with MATLAB R2015a (MathWorks, Natick, MA) and the Psychophysics Toolbox Version 3 (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997) and presented on a BenQ XL2420Z, 24″ monitor at 144 Hz via an IBM compatible computer. The distance from the eyes to the monitor was 92.5 cm. Gaze position was recorded with an Eyelink 1000 Plus (SR Research) with a temporal resolution of 2000 Hz. A 9-point calibration (grey ring on black background) was carried out at the beginning of each experiment and repeated when necessary (see description of the experiments). When the deviation between calibration and validation was at least below 1° visual angle for each point, the calibration was accepted. Eye movements that exceeded either the velocity criterion (30°/s) or the acceleration criterion (8000°/s^2) and were larger than 0.1°, were labeled as saccades and all data periods that were not labeled as saccades or blinks were classified as fixations. When possible, the dominant eye (as measured with the hole-in-the-card test) was tracked. Button presses were recorded on a PST Serial Response Box.

2.1.3. Stimuli and procedure

The participants had to search for a target (tilted line) among distractors (vertical lines) and indicate by button press whether the target was present (first button) or not (second button). In half of the trials the target was present. Whenever the participants' gaze went further than 2° visual angle to the left of the fixation dot or left and more than 2° above or below the fixation dot (see delimiter in Fig. 1), the stimuli on the left side disappeared. When the gaze position returned to the right of these boundaries, the stimuli reappeared. The participants were instructed to try to carry out the task despite the disappearance of the stimuli and to find a strategy to do it as well as possible. Strategies aimed at disabling the gaze-contingent mechanism (e.g., closing the tracked eye or squinting) were not allowed and participants were told not to use them whenever such attempts were detected. This was, however, only rarely the case.

When the participants had given their answer, the display disappeared and was followed by a 500 ms blank display (+fixation dot). Each trial started with a 799 ms fixation period (+blue fixation dot) during which the calibration was checked. When the gaze position had drifted outside of a 2° × 2° window around the fixation point, the calibration procedure was repeated. All 14 lines subtended 0.4° and were arranged in a circle (radius 8°) around the fixation dot (0.3°) and could deviate up to 1° from the equidistant theoretical positions on the circle (spatial jitter), see Fig. 1. The arrangement of the stimuli was thus chosen, so that all stimuli could potentially be covertly scanned, with a high (although not perfect) chance of detecting the target in the periphery. Since the left stimuli could never be overtly scanned, this measure aimed at preventing frustration in the participants.

The stimuli were presented on a black background. The target occurred equally often at all possible locations. If the intervention did not follow the feature search task, it included 20 practice trials at the beginning during which feedback about the answer was given. All lines were light grey (82 cd/m^2). The tilt of the target-line was determined in an adaptive paradigm separately for each participant. The target could be tilted to the left or to the right (randomized across trials).

With the help of an artificial eye (Bernard et al., 2007) the delay between gaze position change and dis-/reappearance of the stimuli on the screen was measured to be 12–20 ms. Each participant completed 308 trials.

2.1.3.1. Adaptive paradigm. The staircase procedure served to individually adjust the tilt of the target line so that the task was neither easy enough to be carried out perfectly without eye movements nor too hard to lead to frustration when the stimuli on the left disappeared during the intervention. Indeed, participants were still able to detect 81.84% of the targets on the left during the intervention and were not discouraged from making eye movements to the right.

The staircase was based on a temporal 2AFC-task in which one of two subsequent displays contained the target (the tilted line). The displays were created in the same way as in the feature search task and were presented for 500 ms each and separated by a 903 ms blank display. After the presentation of the two displays, the participants had to indicate which display contained the target. The response was followed by a 1 s intertrial interval before the next trial started. The tilt started at 21° (of arc, measured from the vertical) and decreased after three correct answers and increased after one incorrect answer. For the first 8 reversals the tilt increased and decreased in steps of 5°, then 1°. After 14 reversals the staircase stopped and the values after the 10th reversal were averaged to obtain the threshold estimate. The staircase was repeated twice and the lower threshold estimate was used in the intervention (and in the feature search task). In the group that was tested with the feature search task, the adaptive paradigm was measured before the first search task, in all other groups it was tested before the intervention.

2.1.4. Analysis

As there were some extreme outliers, values above three standard deviations above the mean were excluded from the reaction time analysis.

For the analysis of the eye tracking data, two areas of interest (AOIs) were created. Gaze positions further left than 2° visual angle from the midline of the screen were counted towards the left AOI, the right AOI started 2° right from the midline of the screen, see Fig. 1c. For the dependent variable "first fixation", the first fixation that fell into either AOI was counted; the trial, however, usually started with a fixation on or near the fixation dot.

2.2. Results and discussion

Data of participants in which the intervention did not lead to the desired outcome (more fixations on the right than on the left in the second half of the intervention (inclusion criterion)) or who fulfilled other exclusion criteria were not analyzed in the pre-post tasks (Experiment 1–4). Here, however, the results of all participants are summarized.

We could demonstrate that the task was still feasible, even when the targets were on the left side, where the stimuli disappeared: The participants detected 81.84% of the targets on the left side. This is lower than the detection rate of targets on the right side (93.46%) but suggests that the aim of the adaptive paradigm was met. 11.15% of the target-absent trials were incorrectly labeled as target-present trials, resulting in overall 88.25% of correct trials, see Fig. 2d.

The aim of the intervention was to reduce the dwell time (sum of all fixation durations) in the left AOI relative to the right AOI. Fig. 2a shows that the participants started with a slight left bias in dwell times (average of first 20 trials: proportion in left AOI: 52.78%), which can be in part explained by the participants' curiosity of what happened when looking to the left. The proportion of dwell time in the left AOI then steadily decreased to merely 22.24% (average of the last 20 trials). Plotting the percentage of first fixations in the left AOI (see Fig. 2b) shows a similar picture. The results were structurally comparable for all experimental groups, see Supplemental Figs. 1–5.

Only 5 of the 137 participants did not meet the inclusion criterion (see above). Over all participants 25.80% of the fixations in either AOI and only 11.55% of the first fixations occurred on the left in the second half of the intervention. The reason that the inclusion criterion was not met was either that they kept on looking to the left despite or possibly because of the intervention (3 cases), that they disregarded that target detection on the right was also important (also leading to selectively low target detection on the right, 1 case), or that the tilt of the search target was too high and that they had to make hardly any saccades to find it (1 case).

Correct reaction times for targets on the left side (2.35 s) were larger than for targets on the right side (1.51 s) but both were shorter than in target-absent trials (3.92 s), see Fig. 2c.

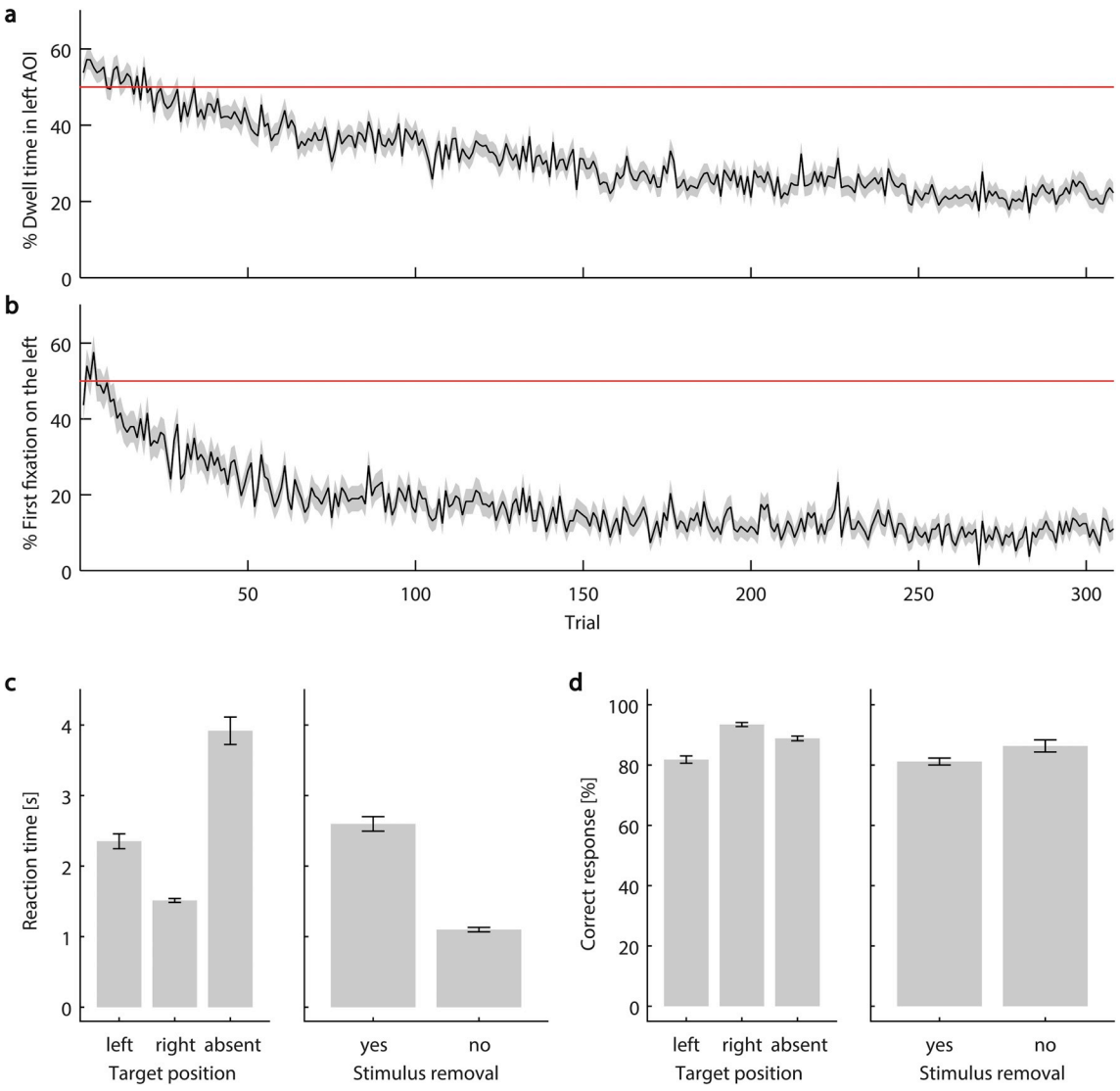

Fig. 2. Results of the intervention based on data from all 137 participants. a) The percentage of dwell time in the left AOI (left dwell time/(left dwell time + right dwell time)) over the course of the 308 trials. b) Percentage of trials in which the first fixation that fell into either AOI was on the left. c & d) Correct reaction times and target detection performance during the intervention, respectively. Left/right: % of detected targets. Absent: Correct rejection in trials without a target. Stimulus removal: for the bar diagrams in the right panel of c & d, respectively, data from the trials with targets on the left side have been split into two groups: group "yes" represents data from trials where the stimuli on the left were removed at least once during the trial (due to the participant moving their eyes to the left); group "no" represents data from all other trials. Grey area and error bars: ±1 SEM.

97.76% of the participants with valid answers (data from 134 of 137 participants) used a strategy – as instructed – to solve the task despite the disappearance of the stimuli. They named strategies such as "search the right field then fixate in the middle to detect irregularities on the left", "check right side, then use "intuition" for the left side", "gave up looking on the left", but also "always looked in the middle" or "tried to be faster than the eyetracker, which didn't work". 55.22% of the participants indicated that they changed the strategy over the course of the intervention.

To find out whether the intervention's effects were rather implicit or explicit, we asked whether the participants noticed that their strategy influenced them during the posttest. 42.22% (values from 135 participants) answered yes. Many described unspecific effects like "I had the feeling that I had become better than at the beginning.", but a few participants reported side-specific effects, e.g.: "one still has the 'looking to the right'-habit, but then it changed again" (Feature search), "first checked the right side (in most cases)" (Conjunction search), "I had the impression that I had to admonish myself not to look to the right" (Posner replication), "I think I approached more from the right with the mouse than the first time" (Line bisection). All quotes are translated from German.

The data demonstrate that – with the exception of five participants – the intervention worked as intended. Fewer eye movements were planned to and within the left half of the search display compared to the right. Also, for the vast majority of participants, the individual adjustment of the tilt through the adaptive paradigm seems to have met the goal of making the task hard enough to encourage eye movements while the above chance task performance shows that the participants did not just "give up" on searching for the target.

3. Experiment 1 – feature search

The aim of the first experiment was to establish whether the eye movement pattern established during the intervention, namely fewer fixations in the left half of the search display, continued when the gaze-contingent removal of the stimuli on the left side was stopped. Hence the feature search task in Experiment 1 was the same as during the intervention but without any stimulus removals.

3.1. Methods

3.1.1. Participants

The data from 21 of 23 participants passed the intervention inclusion criterion and were included in the analysis. The mean age of the participants was 29.33 years (range: 19 to 44, SD: 6.70) and 12 were female.

3.1.2. Stimuli and procedure

After giving informed consent and having their eye dominance measured, the participants were tested – in this order – in the adaptive paradigm, the feature search task, the intervention, and again in the feature search task. The tilt that was determined in the adaptive paradigm was used in both the feature search tasks and the intervention. The feature search task differed from the intervention only in that the stimuli did not disappear and that it lasted for 112 trials. In 20 practice trials at the beginning of the feature search, participants were able to familiarize themselves with the task.

3.1.3. Analysis

Here and in the following experiments the data were analyzed with paired-sample t-tests or repeated measures ANOVAs. When the assumptions of parametric testing were violated and a standard non-parametric alternative was available, the alternative was used. Whenever there was a directional hypothesis, one-sided tests were used. Partial η^2 (η_p^2) is given as a measure of the effect size in the ANOVAs and Cohen's d for the t-tests. For the Wilcoxon signed-rank test the effect size estimate r was calculated by dividing the z-value by the squareroot of the number of observations. For comparability, the measure of central tendency is always the mean, both in the figures and in the text.

The amount of outliers (>3 SD) was negligible (not more than 2 per participant per pre/post measurement) so the reaction time analyses are based on all values.

3.2. Results and discussion

In the feature search task, target detection was consistently high both before and after the intervention and both for targets on the left and the right side (all conditions > 96%). Correct rejections were also high (>98%), resulting in 98.04% correct responses before and 98.30% correct responses after the intervention.

Correct responses to targets were significantly faster after the intervention (before: left: 1.84 s, right: 1.79 s; after: left: 1.52 s, right: 1.50 s; factor time: $F(1,20) = 21.26$, $p < .001$, $\eta_p^2 = 0.52$), but there was neither a significant effect of side ($F(1,20) = 0.40$, $p = .535$, $\eta_p^2 = 0.02$) nor a significant interaction between the factors time and side ($F(1,20) = 0.06$, $p = .804$, $\eta_p^2 = 0.00$), meaning that at the level of reaction times, the intervention had no side-specific effects. Response times in target-absent trials were longer than in target-present trials both before and after the intervention (before: absent: 3.19 s, present: 1.81 s, $p < .001$, $r = 0.76$; after: absent: 2.94 s, present: 1.51 s; $p < .001$, $r = 0.76$), a standard finding in serial visual search tasks (Treisman, 1988).

After the intervention, the percentage of trials in which the eyes first fixated somewhere in the left AOI (37.88%) was significantly lower than beforehand (49.91%, $p < .001$, $r = 0.50$), see Fig. 3a. Similarly, the proportion of the dwell time in the left AOI (dwell time left/(dwell time left + dwell time right)) decreased after the intervention (before: 48.38%, after: 46.47%, $t(20) = 1.92$, $p = .034$, $d = 0.42$). Fig. 3f shows the horizontal gaze position data over the course of the trial, averaged over all trials per participant and then over all participants: before the intervention one can observe a small initial left bias; after the intervention this is reversed to an initial right bias.

Next we tested whether the effect of the intervention was driven by the first trials after the intervention or whether it was also detectable at the end of the posttest. Looking at the percentage of first fixations in the left AOI, both the first half (35.12%, $p = .001$, $r = 0.47$) and the second half (40.65%, $t(20) = 2.93$, $p = .004$, $d = 0.64$) of the posttest differed significantly from the pretest (49.91%).

We also tested whether the effect only occurred in participants who stated in the debriefing questionnaire that they had noticed that the strategy they chose during the intervention had influenced them also during the posttest. In a mixed ANOVA with the factors time (pre/post) and group (noticed vs. not noticed) and the percentage of first fixations in the left AOI as the dependent variable, we found no significant interaction of these factors ($F(1,19) = 2.29$, $p = .146$, $\eta_p^2 = 0.11$). Both groups showed a significant pre-post difference in the first fixation location (noticed: before: 51.79%, after: 36.29%, $t(13) = 3.29$, $p = .006$, $d = 0.88$; not noticed: before: 46.17%, after: 41.07%, $t(6) = 2.85$, $p = .029$, $d = 1.08$). We further checked how many trials it took the participants to notice that the gaze-contingent stimulus removal had stopped during the posttest. The majority of participants (16) already made a fixation in the left AOI during the first trial of the posttest, thereby noticing that the gaze-contingent mechanism was not at work anymore and that the left half could potentially be explored normally. By the third trial, all participants had looked to the left AOI.

The data show that even after the gaze-contingent removal of stimuli stopped, the imbalance in fixations on the left and right of fixation continued, with proportionally less first fixations occurring in the left AOI and a decrease in dwell time in the left compared to the right AOI. Importantly, the effect on the first fixation was not short-lived but could be demonstrated also in the second half of the posttest. Thus the intervention significantly influenced eye movements after its discontinuation – at least in a task that closely resembled it. Also, the participants noticed early on in the posttest that they did not need to avoid the left side

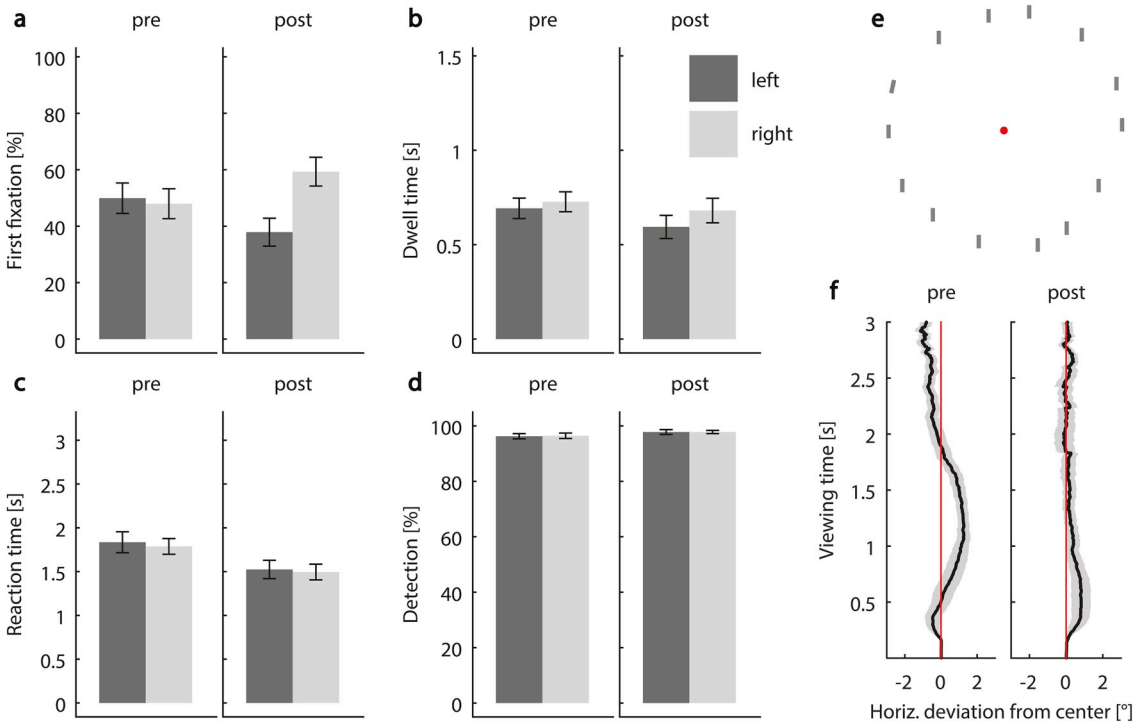

Fig. 3. Results of Experiment 1 – Feature search. (a) Proportion of trials in which the first fixation was in the left or right AOI, respectively. In some trials no fixations occurred in either AOI (usually because the gaze stayed close to the fixation dot); hence the numbers do not add up to 100%. (b) Dwell time: Sum of all fixation durations in left and right area of interest, respectively. (c) Reaction time in seconds to left and right targets averaged over all correct trials. (d) Detection rate of left and right targets before and after the intervention. (e) Example display of feature search. In the figure, stimuli are enlarged for better visibility; in the experiment they were presented on a black background. (f) Raw gaze position data (horizontal) averaged over all trials for each ms of viewing time. 0: center of the screen (fixation dot), negative values: left of center, positive values: right of center. Error bars and shaded grey areas: ±1 SEM.

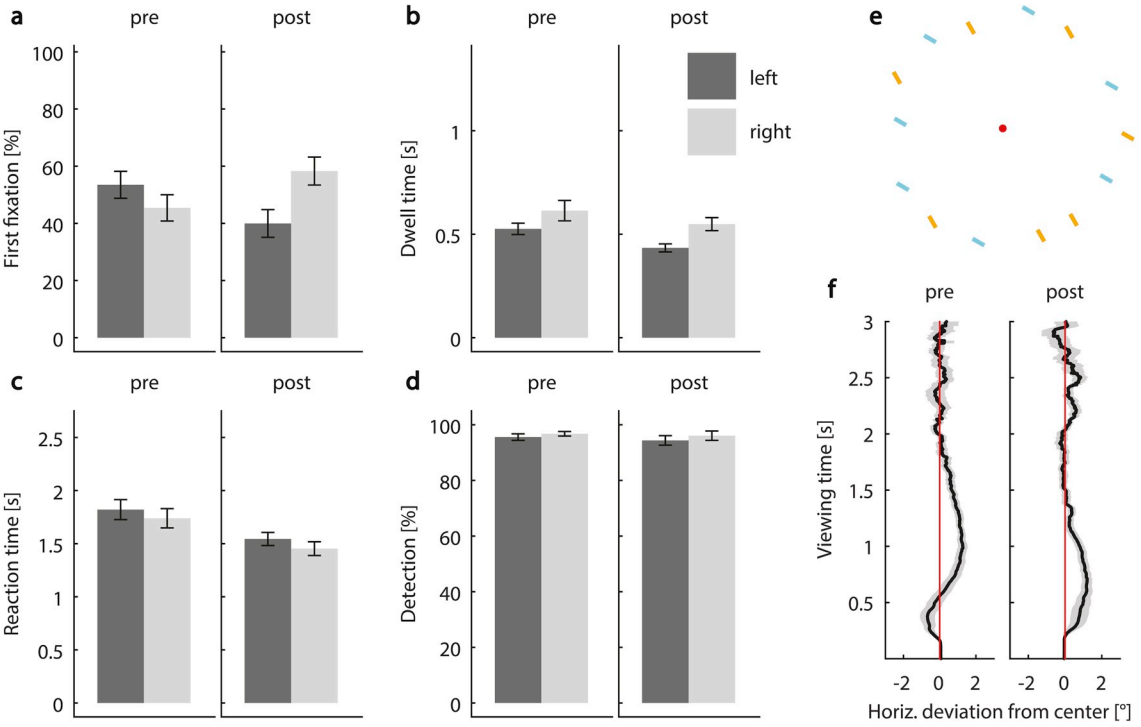

Fig. 4. Results of Experiment 2 – Conjunction search. (a) Proportion of trials in which the first fixation was in the left or right AOI, respectively. Again, in some trials no fixations occurred in either AOI. (b) Dwell time: Sum of all fixation durations in left and right area of interest, respectively. (c) Reaction time in seconds to left and right targets averaged over all correct trials. (d) Detection rate of left and right targets before and after the intervention. (e) Example display of conjunction search. The target was a 60°-tilt yellow line among blue lines of the same tilt and 30°-tilt yellow lines. Half of the displays contained a target. In the figure, stimuli are enlarged for better visibility; in the experiment they were presented on a black background. (f) Raw gaze position data (horizontal) averaged over all trials for each ms of viewing time. 0: center of the screen (fixation dot), negative values: left of center, positive values: right of center. Error bars and shaded grey areas: ±1 SEM.

anymore. Thus a false assumption of a continued gaze-contingent mechanism during the posttest cannot explain the results. We rather suspect that a new habit had formed that operated despite the participants' awareness that there were no more obstacles to exploring the left half. Furthermore, it was not necessary for the participants to notice the influence of their behavior during the intervention on the posttest for the effect to occur.

4. Experiment 2 – conjunction search

In the second experiment we wanted to test whether the effects of the intervention on overt attentional allocation also persisted if the type of visual search task was changed or whether they were limited to the same task and stimuli. We chose a conjunction search task in which the participants had to search for a target with a specific conjunction of features among distractors that all shared one of the features with the target.

4.1. Methods

4.1.1. Participants

After the exclusion of one participant due to the intervention criterion, data of 21 participants (11 female, mean age: 25.81 years, range: 18 to 39, SD: 4.86) were analyzed.

4.1.2. Stimuli and procedure

The target was a yellow line with a 60° (of arc, measured from the vertical) tilt and distractors were either yellow lines with a 30° tilt or blue lines with a 60° tilt, see Fig. 4e; the colors were chosen to be physically isoluminant (150 cd/m^2). Like the feature search task, it consisted of 112 trials, preceded by 20 practice trials in the measurement before the intervention.

4.2. Results and discussion

As in the feature search, target detection (all conditions > 94%) and correct rejections (all > 98%) and thus the proportion of correct answers (97.87% before and 97.11% after) were at ceiling.

The reaction times of correct responses decreased significantly from pretest to posttest (before: left: 1.82 s, right: 1.74 s; after: left: 1.54 s, right: 1.45 s; factor time: $F(1,20) = 22.54$, $p < .001$, $\eta_p^2 = 0.53$) and were faster to targets on the right side (factor side: $F(1,20) = 7.13$, $p = .015$, $\eta_p^2 = 0.26$), but there was no significant interaction between the factors time and side ($F(1,20) = 0.03$, $p = .868$, $\eta_p^2 = 0.00$), suggesting that – as in the previous experiment – the intervention had no side-specific effects on reaction times. Responses in trials without a target were again slower than in target-present trials (before: absent: 2.34 s, present: 1.78 s, $p < .001$, $r = 0.73$; after: absent: 2.07 s, present: 1.50 s; $t(20) = 7.64$, $p < .001$, $d = 1.67$).

The proportion of first fixations in the left AOI decreased significantly from before (53.49%) to after the intervention (39.97%, $t(20) = 3.53$, $p = .001$, $d = 0.77$), see Fig. 4a. The same was found for the proportion of the left dwell time (before: 46.95%, after: 44.62%, $t(20) = 2.27$, $p = .017$, $d = 0.49$). Fig. 4f shows – as for the feature search task - an initial left bias before the intervention and an initial right bias after the intervention.

Again, the effect on the position of the first fixation was detectable in both the first (36.82%, $t(20) = 3.88$, $p < .001$, $d = 0.85$) and the second half (43.11%, $t(20) = 2.67$, $p = .007$, $d = 0.58$) of the posttest (compared to the pretest: 53.49%).

As in the first experiment, we tested whether the effect only occurred in participants who had noticed any influence of their chosen strategy during the intervention on their behavior in the posttest. We analyzed the percentage of first fixations in the left AOI in a mixed ANOVA with the factors time (pre/post) and group (noticed vs. not noticed). We found no significant interaction of these factors ($F(1,19) = 0.31$, $p = .583$, $\eta_p^2 = 0.02$). Both groups showed a significant pre-post difference in the percentage of left first fixations (noticed: before: 52.23%, after: 36.43%, $t(9) = 2.58$, $p = .030$, $d = 0.81$; not noticed: before: 54.63%, after: 43.18%, $t(10) = 2.32$, $p = .042$, $d = 0.70$).

Again we checked how long it took the participants to notice that the gaze-contingent stimulus removal was not at work during the posttest. The majority of participants (18) already had a chance to detect this during the first trial of the posttest, as they made a fixation in the left AOI. The remaining participants (3) did so in the second trial.

Finding an effect on another visual search task demonstrates that the change in visual search behavior caused by the intervention is not limited to the exact same task and stimuli but transfers to another search task with different stimuli. The effect could also be detected in the second half of the posttest, which indicates that the effect of the intervention does not ebb away as soon as the gaze-contingent removal is stopped. The effect also occurred independent of whether participants felt that their behavior in the posttest was influenced by that during the intervention.

It is highly unlikely that the participants showed the imbalance in visual exploration because they thought that the gaze-contingent mechanism also penalized certain eye movements during the posttest. Already at the very beginning of the posttest, all participants had ventured with their eyes into the left AOI, thereby noticing that the stimulus removal had stopped. This is supported by the high target detection performance in the posttest. We rather assume that participants had formed a habit during the intervention that they continued in the posttest although it was not necessary anymore.

Also, before the intervention a left bias was found in the first fixations (see Fig. 4a) and as seen in the averaged horizontal gaze position over time (see Fig. 4f), which is in line with Nuthmann and Matthias' (2014) findings of pseudoneglect in visual exploration.

5. Experiment 3 – Posner task

The third experiment was carried out to test whether the intervention also had an effect on covert attentional allocation. A Posner task with exogenous cues was applied for this purpose. The cue (highlighting of a frame around the possible target locations, see Fig. 5) could either be valid (indicating the correct side of target occurrence), neutral (highlighting both sides), or invalid (indicating the non-target side) and reaction times to the target were measured in a discrimination task (see

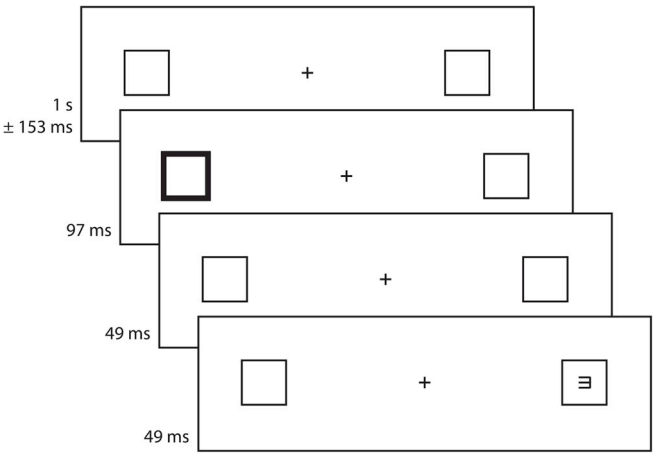

Fig. 5. Exemplary trial of the Posner task (in the experiment white on black background). After a fixation interval, a cue – i.e. highlighting of one of the surrounding boxes (valid or invalid trial) or both (neutral trial) – appeared. After a blank interval, the target was shown. The target could appear on the same side as the cue (valid trial) or on the other side (invalid trial, as depicted here). The participants had to carry out a discrimination task on the target, namely where the "E" was open (or closed, respectively, the instruction was randomly assigned to participants).

Fig. 5).

Neglect patients show a very specific pattern in similar Posner tasks, namely the disengage deficit. After the initial orienting of attention to a cue on their preferred (ipsilesional, usually the right) side, they have problems disengaging their attention from this cue. When the following target then appears on the other (contralesional/left) side (i.e. when the cue was invalid), reaction times are slow due to the disengage deficit (Losier and Klein, 2001). In contrast, when the attention is cued to the left but the target appears on the right side, latencies are significantly shorter – despite the fact that both trials constitute invalid trials.

Assuming that the intervention leads to a right-sided attentional bias in the healthy participants, since most eye movements are made to and within the right half of the search display, we hypothesized that we would find a disengage deficit similar to that shown by neglect patients (albeit weaker) after the intervention. This would present itself as increased reaction times to left targets after cues on the right.

Further we hypothesized that reaction times to right targets would be shorter relative to reaction times to left targets after the intervention, resulting in an interaction of target side (left vs. right) and measurement time (pre vs. post).

5.1. Methods

5.1.1. Participants

Of 29 participants, one was excluded due to the intervention criterion, one due to poor execution of the task (<80% correct performance), and five participants were excluded because they failed to maintain fixation in a sufficient amount of trials (i.e. in more than 20% of the trials in one of the conditions (valid, invalid, neutral) either before or after the intervention). The remaining 22 participants (14 female) were on average 26.64 years old (range: 21 to 37, SD: 4.39).

5.1.2. Stimuli and procedure

The participants' task was to indicate the open or closed side (constant for each participant) of an "E" – the target – which could face either left or right. The target could appear either 7° visual angle to the left or to the right of fixation and measured 0.5° × 0.4°. The display consisted of a fixation cross (0.5° × 0.5°) and two square outlines (2° × 2°, 7° left and right of fixation). Each trial started with a 1 s (+/− up to 153 ms) fixation period, then one of the outlines or both outlines increased in width for 97 ms (cue). Thus the target position could be validly cued (cue position equals target positon), invalidly cued (different cue and target position) or neutrally cued (cue on both sides). Each of these three conditions occurred with the same probability. 49 ms after the disappearance of the cue, the target appeared for 49 ms. All stimuli were white (on black background). Throughout the whole trial, participants were required to maintain central fixation. This was controlled via eye tracking and trials in which participants looked at the cue or the target were excluded from the analysis. The calibration was repeated after the practice trials and every 60 trials, when necessary.

Overall, the participants completed 36 practice trials and a further 180 trials which were included in the analysis.

5.1.3. Analysis

Only trials with correct target identification and good fixation were included in the analysis. Trials with reaction times below 150 ms and more than 2.5 standard deviations above the average response time within the pre- or the posttest for a given participant were excluded as well.

The disengage deficit was calculated as in Losier and Klein (2001), RT = reaction time:

(1) ((RT target left, invalid cue)-(RT target left, valid cue))-((RT target right, invalid cue)-(RT target right, valid cue))

This is assuming that disengaging attention from the right side would be more difficult after the intervention (thus particularly difficult in trials with invalid cues on the right, i.e. affecting reaction times to targets on the left after invalid cues).

Positive values indicate that reaction times to the target on the left are particularly slowed after cues on the right, according to the theory because it is difficult to disengage attention from those cues (Losier and Klein, 2001) – in neglect patients due to their preference for ipsilesional stimuli; here in our healthy participants due to the possible preference induced by the intervention.

When necessary, the results of the ANOVAs were Greenhouse-Geisser corrected.

5.2. Results and discussion

Before testing our hypotheses, we examined the quality of our paradigm, i.e. whether it produced a significant Posner effect in participants before the start of the intervention. To be precise, we tested for the pre-intervention performance whether reaction times to targets after valid cues were faster than after neutral cues and if those, in turn, were faster than after invalid cues. For this we performed a repeated measures ANOVA with the factor 'validity'. This analysis confirmed the existence of a Posner effect: the validity of the cue significantly influenced the reaction times to the target in the expected pattern (valid: 531.21 ms, neutral: 548.64 ms, invalid: 576.88 ms, $F(1.42,29.73) = 40.17$, $p < .001$, $\eta_p^2 = 0.66$), and all conditions were different from each other as tested in post-hoc t-tests using Bonferroni correction, all $p < .001$.

In fact, as can be seen in Supplemental Fig. 6, we found a traditional Posner effect both before and after the intervention and for both left and right targets.

To test our hypothesis that the intervention might affect performance in the Posner paradigm, we first analyzed whether the disengage deficit had increased from pre to post measurement, which was not the case (pre: 27.70 (SD: 39.14), post: −2.14 (SD: 54.76), $p = .960$ (two-sided: $p = .085$), $r = 0.26$), see Supplemental Fig. 6. Our hypothesis of more "neglect-like" behavior of healthy observers after the intervention, i.e. an increased disengage deficit could thus not be confirmed. Neither did the participants show a typical pattern (i.e. slowed reaction times to left targets following (invalid) right cues) after the intervention, see Supplemental Fig. 6c, nor did the calculated disengage deficit increase, see Supplemental Fig. 6d.

Then we tested whether the overall reaction times became faster on the right compared to the left after the intervention. An ANOVA with the factors 'time of measurement (pre/post)' and 'side (left/right)' revealed no significant interaction ($F(1,21) = 0.91$, $p = .352$, $\eta_p^2 = 0.04$; after exclusion of one participant, the data were normally distributed, yielding a similar result: $F(1,20) = 0.80$, $p = .781$, $\eta_p^2 = 0.00$), showing that reactions to targets on the right did not profit from the intervention as compared to reactions to targets on the left.

Next we explored whether our assumption about a side-dependent effect of the intervention was true in trials without (partially) misleading cues. This was done by restricting the analysis to valid trials. Indeed, we found a significant interaction effect of the factors pre/post and side in valid trials ($F(1,21) = 7.33$, $p = .013$, $\eta_p^2 = 0.26$; after exclusion of one participant, the data were again normally distributed, yielding a similar result: $F(1,20) = 6.25$, $p = .021$, $\eta_p^2 = 0.24$), see Supplemental Fig. 6. This means that in the subsample of valid trials, we indeed found a side-dependent effect of the intervention, i.e. reaction times became faster on the right compared to the left after the intervention. While this was also in line with the underlying assumptions, it was not part of the a priori hypotheses. Thus we carried out a replication of the experiment based on a power calculation of the effect of the valid cues. The η_p^2-value of the interaction term of the ANOVA was 0.259 which resulted – given an alpha error probability of 0.05 and a desired power of 0.9 – in a required minimum sample size of 33 as calculated by G*Power 3.1 (Faul et al., 2007).

6. Experiment 4 – Posner replication

6.1. Methods

6.1.1. Participants

Of 41 participants, one was excluded due to the intervention criterion and seven participants were excluded because they did not keep fixation in a sufficient amount of trials, i.e. they lost more than 20% of the trials in one of the conditions (valid, invalid, neutral) either before or after the intervention due to this fixation criterion. The remaining 33 participants (17 female) were on average 23.24 years old (range: 18 to 42, SD: 4.84).

All other methods were as described in Experiment 3.

6.2. Results and discussion

Again, the results before the intervention showed a traditional Posner effect ($\chi^2(2) = 43.70$, $p < .001$, Kendall's $W = 0.94$, demonstrated here with a Friedman Test due to violation of the assumption of normality), see Supplemental Fig. 7. All conditions were different from each other as tested in post-hoc t-tests using Bonferroni correction, all $p < .05$.

As for the hypotheses, we first tested whether the effect that we were aiming to replicate, namely a side-dependent effect of the intervention in the subsample of valid trials, also manifested itself in the new sample of participants. This was not the case as there was no significant interaction of the factors 'time of measurement (pre/post)' and 'side (left/right)' for valid trials ($F(1,32) = 0.15$, $p = .700$, $\eta_p^2 = 0.01$), see Supplemental Fig. 7b.

Next we tested whether our original hypotheses were confirmed in this larger sample. As in the first experiment, overall reaction times did not become significantly faster to right compared to left targets after the intervention ($F(1,32) = 2.03$, $p = .163$, $\eta_p^2 = 0.06$). However there was a trend towards an increase of the disengage deficit from pre to post measurement (pre: −11.21 ms, post, 5.14 ms), $t(32) = -1.68$, $p = .052$, $d = -0.29$.

To conclude, we could not replicate the finding concerning the valid trials in this second sample. However, we now found a trend towards an increase of the disengage deficit. This pattern of results was – however – not present in the first sample. On the contrary, here the disengage deficit decreased from pre to post measurement.

To make use of the large sample size of both groups together and to further clarify the findings in this inconclusive situation, we carried out a joint analysis of both groups of participants using Bayesian statistics, which are better suited than frequentist statistical methods for post-hoc joining of samples.

6.3. Joint analysis of both groups of participants

The joint data of both groups is depicted in Fig. 6; part (a) shows all data split for side (left/right) and time (pre/post) and shows a traditional Posner effect for all combinations.

Using the program JASP (JASP-Team, 2019; Wagenmakers et al., 2018a, 2018b), we carried out JZS Bayes two-way repeated measures ANOVAs with default priors (Rouder et al., 2012) with the factors 'time of measurement' and 'side' for reaction times of all trials and for reaction times of valid trials only and a Bayesian paired samples *t*-test with default priors comparing the disengage deficit before and after the intervention.

The ANOVA over all reaction times revealed a highly influential factor of 'time' (Bayes Factor of the model 'time' over the Null model: $BF_{10} = 13049.39$), which was – looking at the data (see Fig. 6) – driven by faster response times after the intervention. However, adding the second main factor 'side' ($BF_{10} = 0.146$, time + side: $BF_{10} = 1937.41$) to the model reduced the support by a factor of 6.74 (13049.39/1937.41). Similarly, adding the interaction term ($BF10 = 441.11$) further reduced the support by a factor of 4.39 (1937.41/441.11). This – according to Jeffreys' classification (1961) modified by Lee and Wagenmakers (2013) – amounts to moderate evidence against including this factor in the model. Given that the inclusion of the interaction term is not warranted, we can conclude that the intervention did not selectively influence reaction times to targets depending on their side in the Posner task. However, reaction times significantly decreased from pre to post measurement, which is most probably due to a simple practice effect.

The ANOVA over reaction times in valid trials also revealed a highly influential factor of 'time' (Bayes Factor of the model 'time' over the Null model: $BF_{10} = 107.28$). Adding the second main factor 'side' ($BF_{10} = 0.16$, time + side: $BF_{10} = 17.61$) to the model reduced the support by a factor of 6.09 (107.28/17.61). Similarly, adding the interaction term ($BF_{10} = 4.55$) further reduced the support by a factor of 3.87 (17.61/4.55), which is again moderate evidence against including this factor in the model. Thus we can conclude that the intervention did not

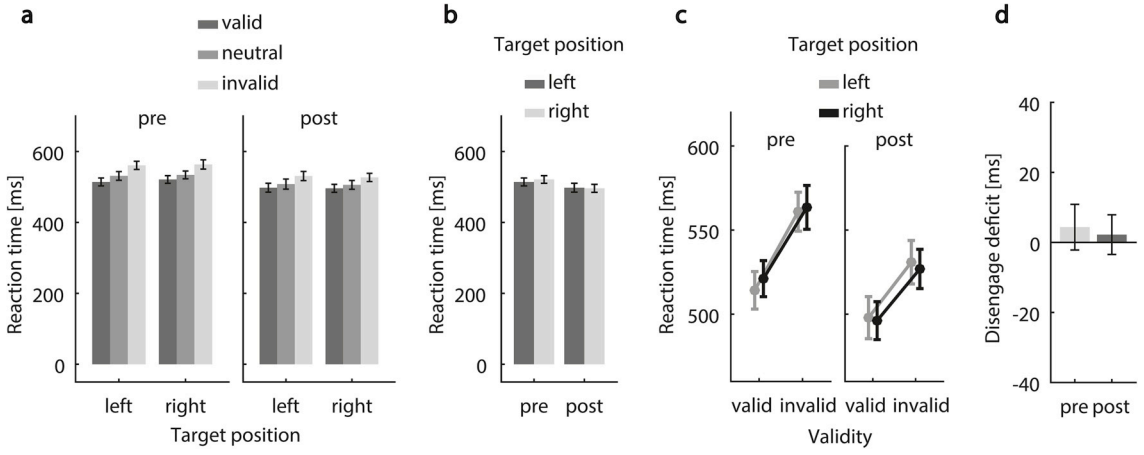

Fig. 6. Results of Experiment 3 and 4 combined – Posner task. (a) Reaction times to targets split for target position, validity of the cue and measurement (pre/post). A Posner effect (RT invalid > neutral > valid) can be seen for every combination of conditions. (b) Only valid trials: In experiment 3 there was an indication that the intervention changed reaction times after valid cues, dependent on which side they appeared. This was however not replicated in experiment 4 and for both data sets together this effect cannot be seen. (c) Reaction times in ms to targets after valid and invalid cues. No disengage deficit, i.e. no increased reaction times for invalidly cued targets on the left can be detected after the intervention. (d) The disengage deficit was calculated as follows: ((RT target left, invalid cue)-(RT target left, valid cue))-((RT target right, invalid cue)-(RT target right, valid cue)), i.e. a disengage deficit is reflected in positive values. Over all participants from experiment 3 and 4, no modulation due to the intervention can be observed.

selectively influence reaction times after valid cues depending on their side in the Posner task. This also becomes apparent in Fig. 6b.

Last we compared the disengage deficit before and after the intervention (Fig. 6c and 6d). Across all participants the disengage deficit did not change in the hypothesized direction (pre: 4.35 ms, post: 2.23 ms). The Bayes Factor of 0.12 indicates moderate evidence for the null hypothesis; see also the Bayes factor robustness check, Supplemental Fig. 8.

To sum up, none of our hypotheses regarding the effect of the intervention on performance in the Posner task could be confirmed. On the contrary, analyzing the two groups of participants together gave us moderate evidence in favor of the null hypothesis in each case, suggesting that the intervention had no effect on covert attentional orienting as measured in this variant of the Posner paradigm.

7. Experiment 5 – line bisection task

In a fifth experiment, our aim was to see whether the intervention had an effect on a task often used in a clinical setting for the diagnosis of neglect – line bisection.

Interestingly – contrary to the errors made by neglect patients – healthy participants have been shown to bisect lines slightly to the left of the middle (Bowers and Heilman, 1980).

7.1. Methods

7.1.1. Participants

Twenty-two participants (11 female, mean age: 22.86 years, range: 18 to 30, SD: 3.55) took part in this experiment, none were excluded.

7.1.2. Stimuli and procedure

In each trial a line (8° × 0.3°, 12° × 0.45°, 16° × 0.6°, or 20° × 0.75° visual angle: sizes at central position) appeared at one of three x-positions on the screen (−3°, 0°, or 3° from the middle; y position: always in the middle of the screen). The lines were light grey (82 cd/m^2) presented on a black background. The participants were instructed to move a triangular cursor (1.28°) to the perceived middle of the line, confirming their choice with a mouse click. The start position of the cursor was at the bottom of the screen at −4° or 4° from the middle. All possible combinations of line sizes, cursor, and line positions were presented four times, resulting in 96 trials. Each line was presented until the mouse click and trials were separated by an inter-trial-interval of 500 ms.

7.2. Results and discussion

In line with the literature (for a review see Jewell and McCourt (2000)), our participants bisected the lines slightly left of the middle, a phenomenon that has been named "pseudoneglect" (Bowers and Heilman, 1980). Before the intervention, the perceived midpoint of the line was at −0.80% (the left endpoint of the line was labeled −50% and the right endpoint +50%), see Fig. 7, which differed significantly from zero ($p < .001$, $r = -0.70$). The line bisection positions before and after the intervention, however, did not differ significantly from each other (after: −0.68%, $t(21) = -1.12$, $p = .138$, $d = -0.24$).

Neglect patients' rightwards errors in line bisection usually increase with line length (Ishiai et al., 2006) while the same is true for leftwards errors in healthy participants (McCourt and Jewell, 1999). Both respective errors have been found to be larger, the more leftward the lines lie in the visual field (McCourt and Jewell, 1999; Nichelli et al., 1989).

Both the effect of length ($F(2.08,43.63) = 16.58$, $p < .001$, $\eta_p^2 = 0.44$) and the effect of position ($F(1.08,22.77) = 5.96$, $p = .021$, $\eta_p^2 = 0.22$) could be replicated in our sample of participants, calculated for the pre-intervention data, see Fig. 7. The interaction was also significant ($F(2.39,50.30) = 3.07$, $p = .047$, $\eta_p^2 = 0.13$). When excluding one outlier to make the data more normally distributed, both main effects stayed highly significant, the interaction did not ($p = .094$).

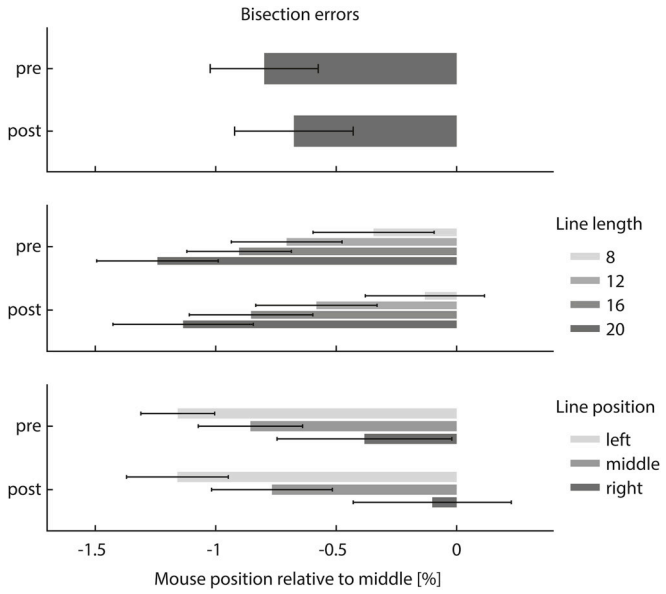

Fig. 7. Results of Experiment 5 – Line bisection task. Bisection errors in %, (bisection at the leftmost point of the line would lead to an error of −50%, bisection at the rightmost point to +50%) over all trials (top), split for line length (middle), and for line position (bottom). There were no significant effects of the intervention on line bisection performance.

Given that the strongest pseudoneglect is found for long lines positioned on the left (McCourt and Jewell, 1999; Nichelli et al., 1989, also see Fig. 7) and hence the largest possibility for change through the intervention, we tested those lines specifically. We did not find a significant change in the line bisection error either for the longest line (pre: −1.24%, post: −1.14%, $t(21) = -0.91$, $p = .187$, $d = -0.19$) or for the left line (pre: 1.16%, post: −1.16%, $t(21) = 0.01$, $p = .504$, $d = 0.00$). In an ANOVA with the factors pre/post, line length, and line position, there was neither a significant main effect of the factor pre/post ($F(1,21) = 1.25$, $p = .277$, $\eta_p^2 = 0.06$), nor any significant interaction including this factor (all $p > .134$).

We further tested how stable the line bisection errors were and calculated Spearman's rank-order correlation. Data from before the intervention (average over all lines) correlated highly with data from after the intervention, $r_s = 0.88$, $p < .001$.

Although we could confirm previous findings of line bisection in healthy participants, namely an effect of pseudoneglect (Bowers and Heilman, 1980) and its modification by line length and position (McCourt and Jewell, 1999; Nichelli et al., 1989), we did not find a significant influence of the intervention on the line bisection errors. Since this task is the furthest removed from the intervention, it is perhaps not surprising that the relatively short intervention could not influence the line bisection performance in healthy participants more strongly. Furthermore the line bisection errors proved to be very stable as shown by a strong positive correlation between the values before and after the intervention. This demonstrates that the bias might not be easily manipulable.

8. General discussion

In this series of experiments we tested the effects of an intervention in which left stimuli were removed dependent on gaze coordinates on several attentional tasks.

As a first step, we checked whether this gaze-contingent stimulus removal led to the desired eye movement behavior during the intervention. This was the case: over the course of the intervention, fixations and particularly first fixations on the left became relatively more sparse

thus leading to an imbalance between the two halves of the search display with more fixations in the right half.

This successful rebiasing of the visual exploration pattern allowed us to test its effect on different tasks.

Experiment 1 served to establish whether the left/right-imbalance induced during the intervention continued after the stimulus removal stopped; the task therefore was the same as during the intervention, namely a search for a tilted line among vertical distractors (feature search), but without stimulus removal. Indeed, the new right bias continued and was even detectable in the second half of the posttest, meaning that the effect was not short-lived but survived at least several minutes without stimulus removal.

Experiment 2 confirmed that the effect of the intervention transferred to another visual search task, namely a conjunction search. Here we also found that the effect was still present in the second half of the posttest.

These results can be viewed in an operant conditioning framework (Skinner, 1953): the gaze-contingent stimulus removal on the left serves as a punishment for eye movements towards and within the left half and thus decreases their frequency. Similarly, Lucas and colleagues (2013) found that coupling left-sided (but not right-sided) targets with reward led to increasing left exploration biases both in healthy participants and neglect patients. In monkeys it has been demonstrated that saccades in the rewarded compared to the non-rewarded direction were faster, started earlier and were less error-prone (Takikawa et al., 2002). Related or additional explanations, respectively, could be habituation or an explicit strategy change. With respect to the latter it is worth mentioning that the effect occurred independent of whether participants noticed an influence of their behavior during the intervention on the posttest. Thus, an explicit reflection on the behavior during the experiment was not necessary for the effect of the intervention. Also, the participants noticed early on in the posttest that the gaze-contingent mechanism had stopped. If their behavior was only a consequence of an explicit strategy during the posttest, they should have stopped it after noticing that it was no longer necessary. We thus maintain that an implicit change in exploration habits is a more likely explanation of the effects.

A possible further factor is that the participants may have erroneously come to the conclusion that targets appear more frequently on the right than on the left side. We know from earlier work that such statistical asymmetries can lead to results not unlike those observed in our study (Walthew and Gilchrist, 2006). As a matter of fact, target detection was reduced for targets presented on the left side during the intervention. However, given that targets were in fact presented as often on the right as on the left and given that participants showed ceiling detection performance of targets on the left during the posttest, it seems more likely that the learning of the eye movement consequence and its effect on the participants' exploration habits was the stronger driving factor than the learning of (spurious) target occurrence statistics.

An open question is whether a different punishment "schedule" leads to weaker or stronger effects, i.e. if it is detrimental or beneficial when gaze shifts to the left are not being punished in every trial but only on average on every other trial. Furthermore it is worth exploring if repetitions of the intervention lead to a better outcome and if yes, for how long effects of the intervention can be measured. These questions are being addressed in current studies.

In the Posner task, no consistent effects of the intervention could be measured. As the Posner task served as our measure for exogenously cued covert attentional orienting, this seems to demonstrate the limit of the generalizability of the training effects from our intervention. In the following paragraphs we will attempt to give an explanation for why this might have been the case.

It is worth noting that the Posner task differs in two important aspects from the task used during training: in the Posner task, attention is attracted in an exogenous way by the presentation of a peripheral cue. Furthermore, participants in a Posner task are explicitly told that they should not move their eyes away from the fixation point. In contrast in our training task, no exogenous attentional cues were provided and participants were free to explore the visual display in any way they liked and were allowed to make eye movements. Both aspects, exogenous versus endogenous attentional guidance and covert versus overt attentional allocation, could explain why our training did not produce significant changes in the Posner task.

Given that our intervention was partly inspired by the premotor theory, which predicts that interference with eye movement plans should also interfere with covert shifts of attention, it is surprising that our gaze-contingent intervention had no effect on covert shifts of attention in the Posner task. Indeed, other attempts to test the premotor theory using a manipulation of overt eye movements found effects on Posner tasks. In the eye abduction paradigm, the eye rotation is such that the target location on one side cannot be reached by a saccade. This also leads to deficits in allocating attention covertly to this side (Craighero et al., 2004; Smith et al., 2012). The same has been demonstrated for patients who are restricted in their ability to make saccades, such as in the case of ophthalmoplegia (Smith et al., 2004), oculomotor palsy (Craighero et al., 2001), or Duane retraction syndrome (Gabay et al., 2010).

One difference to these previous empirical tests of the premotor theory of attention is that in our intervention participants were still able to carry out eye movements to the left. We merely introduced a manipulation that discouraged them from performing eye movements to one half of the visual display. This might not have had a strong enough effect on covert attention. First, the intervention may not have prevented the planning but merely the execution of saccades to the left. Second, it is probable that by making it impossible to overtly scan the left side of the search display for the target the participants switched to covertly scanning the left and thus to also deploy attention – although covertly – to the left side. This might explain why covert shifts to the left seemed as uninfluenced by the intervention as shifts to the right. Another possibility is that the intervention indeed produced a lateral bias in covert attention but the measurement was not sensitive enough to pick up on it or the highly salient exogenous cues overrode the bias.

But perhaps the premotor theory of attention or rather the assumption that covert shifts of attention are limited to where eye movements are or can be carried out needs to be revised. Contrary to previous findings using the eye abduction paradigm, Hanning et al. (2019) showed that attention could indeed be deployed to exogenously cued locations outside the oculomotor range, as measured by enhanced target discrimination (compared to uncued locations).

Next we tested line bisection performance before and after the intervention. While we could not find a significant effect of the intervention on line bisection, we could replicate a finding of Bowers and Heilman (1980), namely pseudoneglect (bisection errors to the left of the center of the line), both before and after the intervention. This pseudoneglect was dependent on line length and position as reported by McCourt and Jewell (1999) and Nichelli et al. (1989).

How can this absence of significant modulation of line bisection performance by the intervention be explained? Since this is a relatively easy task for healthy participants, it might be unsurprising that it is not easily changeable with our relatively brief intervention. Moreover, the line bisection error in healthy participants is far smaller than in neglect patients, indicating that the sensitivity to manipulation is also more modest in healthy participants. It will be interesting to see whether the intervention has an effect on line bisection in neglect patients who have a larger potential for change. Furthermore the line bisection errors proved to be quite stable from pre to post measurement, which points towards a certain immunity towards manipulation.

It also must be added that line bisection and the intervention target different aspects of neglect. Line bisection is sensitive in picking up a bias in the egocentric reference frame, whereas the intervention aims at correcting the explorational deficits in neglect. This might explain why prism adaptation, which is aimed at correcting the shifted egocentric reference frame in neglect, can also influence line bisection performance

in healthy observers (Colent et al., 2000; Michel et al., 2003; Schintu et al., 2014). In general, the usefulness of line bisection in neglect diagnosis has been questioned (Ferber and Karnath, 2001). In healthy participants, recent data further corroborate that maybe no transfer from changes in eye movement behavior to line bisection performance was to be expected. Foulsham et al. (2018) reported a lack of correlation between eye movement biases and line-bisection performance. In a similar vein, Learmonth and colleagues (2015) demonstrated that tasks measuring left-right biases (including line bisection) in healthy observers correlate at best weakly with each other.

Another possibility is that we failed to pick up on more subtle effects by not measuring eye movements during this task. Foulsham and colleagues (2013) measured the effect of an asymmetrical gaze-contingent window during a trial of scene viewing on a line bisection task in a subsequent trial (without field of view restrictions). They found an effect on the eye movements towards central lines, but also no effect on behavioral line bisection performance.

This relatively brief application of the intervention is only to be thought of as a proof of principle. Interventions applied in neglect rehabilitation typically include multiple sessions (Kerkhoff and Schenk, 2012), so further tests are needed to determine the longevity of effects, whether they are strengthened by repeating the intervention, and – most importantly – how the intervention fares when applied to treat spatial neglect.

Overall, however, the change in overt attentional allocation – namely visual search behavior – through the current intervention is promising for the application in patients. The rebiasing of exploration behavior could allow neglect patients to venture further into their neglected side. It could possibly also allow hemianopic patients with neglect to better compensate for their visual field defect (Ishiai et al., 1987). In contrast to neglect patients, healthy participants have nothing to gain (quite the opposite) from the behavioral change induced by the intervention. With the exception of alleviating the slight left bias, their exploration of the visual world can only suffer from the intervention. Nevertheless its influence could also be detected after many trials of unimpaired visual search. Neglect patients, on the contrary, could benefit from a further reinforcing factor that sustains the effects of the intervention for longer, namely that they discover more items by attending to a larger portion of the visual field if their right bias (Husain et al., 2001; Niemeier and Karnath, 2000) is reduced. Given that there currently is no intervention for spatial neglect with unequivocal support of its long-lasting effectiveness (Kerkhoff and Schenk, 2012), research in this field remains important and the application of the proposed intervention in neglect patients the next logical step.

8.1. Conclusion

A new intervention using gaze-contingent stimulus removal in one half of the search display changed the bias in visual exploration patterns in healthy participants both during the application of the intervention and afterwards. Although covert attentional allocation as measured in a Posner task and line bisection performance were not significantly affected by the intervention, the transfer of the effect to a different search task shows that it is not narrowly restricted to the context in which it was applied. This effect might be used to work against the existing explorational bias in patients with spatial neglect.

Declaration of competing interest

The authors declare no financial or personal conflicts of interest.

CRediT authorship contribution statement

Karin Ludwig: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration. **Doris Schmid:** Methodology, Software, Investigation, Data curation, Writing - review & editing. **Thomas Schenk:** Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

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Appendix A. Supplementary data

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References

Behrmann, M., Ghiselli-Crippa, T., Dimatteo, I., 2001. Impaired initiation but not execution of contralesional saccades in hemispatial neglect. Behav. Neurol. 13, 39–60.
Bernard, J.B., Scherlen, A.C., Castet, E., 2007. Page mode reading with simulated scotomas: a modest effect of interline spacing on reading speed. Vis. Res. 47, 3447–3459.
Bowers, D., Heilman, K.M., 1980. Pseudoneglect: effects of hemispace on a tactile line bisection task. Neuropsychologia 18, 491–498.
Brainard, D.H., 1997. The psychophysics Toolbox. Spat. Vis. 10, 433–436.
Colent, C., Pisella, L., Bernieri, C., Rode, G., Rossetti, Y., 2000. Cognitive bias induced by visuo-motor adaptation to prisms: a simulation of unilateral neglect in normal individuals? Neuroreport 11, 1899–1902.
Craighero, L., Carta, A., Fadiga, L., 2001. Peripheral oculomotor palsy affects orienting of visuospatial attention. Neuroreport 12, 3283–3286.
Craighero, L., Nascimben, M., Fadiga, L., 2004. Eye position affects orienting of visuospatial attention. Curr. Biol. 14, 331–333.
Craighero, L., Rizzolatti, G., 2005. The premotor theory of attention. In: Itti, L., Rees, G., Tsotsos, J.K. (Eds.), Neurobiology of Attention. Elsevier Academic Press, Burlington, MA, pp. 181–186.
Faul, F., Erdfelder, E., Lang, A.G., Buchner, A., 2007. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav. Res. Methods 39, 175–191.
Ferber, S., Karnath, H.O., 2001. How to assess spatial neglect–line bisection or cancellation tasks? J. Clin. Exp. Neuropsychol. 23, 599–607.
Foulsham, T., Frost, E., Sage, L., 2018. Stable individual differences predict eye movements to the left, but not handedness or line bisection. Vis. Res. 144, 38–46.
Foulsham, T., Gray, A., Nasiopoulos, E., Kingstone, A., 2013. Leftward biases in picture scanning and line bisection: a gaze-contingent window study. Vis. Res. 78, 14–25.
Gabay, S., Henik, A., Gradstein, L., 2010. Ocular motor ability and covert attention in patients with Duane Retraction Syndrome. Neuropsychologia 48, 3102–3109.
Girotti, F., Casazza, M., Musicco, M., Avanzini, G., 1983. Oculomotor disorders in cortical lesions in man: the role of unilateral neglect. Neuropsychologia 21, 543–553.
Grattan, E.S., Skidmore, E.R., Woodbury, M.L., 2018. Examining anosognosia of neglect. OTJR (Thorofare N J) 38, 113–120.
Hanning, N.M., Szinte, M., Deubel, H., 2019. Visual attention is not limited to the oculomotor range. Proc. Natl. Acad. Sci. U. S. A. 116, 9665–9670.
Heilman, K.M., Valenstein, E., 1979. Mechanisms underlying hemispatial neglect. Ann. Neurol. 5, 166–170.
Husain, M., Mannan, S., Hodgson, T., Wojciulik, E., Driver, J., Kennard, C., 2001. Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. Brain 124, 941–952.
Ishiai, S., Furukawa, T., Tsukagoshi, H., 1987. Eye-fixation patterns in homonymous hemianopia and unilateral spatial neglect. Neuropsychologia 25, 675–679.
Ishiai, S., Koyama, Y., Seki, K., Hayashi, K., Izumi, Y., 2006. Approaches to subjective midpoint of horizontal lines in unilateral spatial neglect. Cortex 42, 685–691.
JASP-Team, 2019. JASP ([Computer software]), Version 0.9.2.
Jeffreys, H., 1961. The Theory of Probability, 3rd ed. Oxford University Press, Oxford.
Jewell, G., McCourt, M.E., 2000. Pseudoneglect: a review and meta-analysis of performance factors in line bisection tasks. Neuropsychologia 38, 93–110.
Karnath, H.O., Niemeier, M., Dichgans, J., 1998. Space exploration in neglect. Brain 121, 2357–2367.
Karnath, H.O., Schenkel, P., Fischer, B., 1991. Trunk orientation as the determining factor of the 'contralateral' deficit in the neglect syndrome and as the physical anchor of the internal representation of body orientation in space. Brain 114 (Pt 4), 1997–2014.
Kerkhoff, G., 2001. Spatial hemineglect in humans. Prog. Neurobiol. 63, 1–27.
Kerkhoff, G., Schenk, T., 2012. Rehabilitation of neglect: an update. Neuropsychologia 50, 1072–1079.

Kleiner, M., Brainard, D., Pelli, D., 2007. What's New in Psychtoolbox-3? *Perception*, vol. 36 (ECVP Abstract Supplement).
Learmonth, G., Gallagher, A., Gibson, J., Thut, G., Harvey, M., 2015. Intra- and inter-task reliability of spatial attention measures in pseudoneglect. PLoS One 10, e0138379.
Lee, M.D., Wagenmakers, E.-J., 2013. Bayesian Cognitive Modeling - A Practical Course. Cambridge University Press.
Losier, B.J.W., Klein, R.M., 2001. A review of the evidence for a disengage deficit following parietal lobe damage. Neurosci. Biobehav. Rev. 25, 1–13.
Lucas, N., Schwartz, S., Leroy, R., Pavin, S., Diserens, K., Vuilleumier, P., 2013. Gambling against neglect: unconscious spatial biases induced by reward reinforcement in healthy people and brain-damaged patients. Cortex 49, 2616–2627.
Mark, V.W., Kooistra, C.A., Heilman, K.M., 1988. Hemispatial neglect affected by non-neglected stimuli. Neurol. 38, 1207–1211.
McCourt, M.E., Jewell, G., 1999. Visuospatial attention in line bisection: stimulus modulation of pseudoneglect. Neuropsychologia 37, 843–855.
Michel, C., Pisella, L., Halligan, P.W., Luaute, J., Rode, G., Boisson, D., Rossetti, Y., 2003. Simulating unilateral neglect in normals using prism adaptation: implications for theory. Neuropsychologia 41, 25–39.
Nichelli, P., Rinaldi, M., Cubelli, R., 1989. Selective spatial attention and length representation in normal subjects and in patients with unilateral spatial neglect. Brain Cogn. 9, 57–70.
Niemeier, M., Karnath, H.O., 2000. Exploratory saccades show no direction-specific deficit in neglect. Neurol. 54, 515–518.
Nuthmann, A., Matthias, E., 2014. Time course of pseudoneglect in scene viewing. Cortex 52, 113–119.
Pelli, D.G., 1997. The VideoToolbox software for visual psychophysics: transforming numbers into movies. Spat. Vis. 10, 437–442.
Ptak, R., Golay, L., Muri, R.M., Schnider, A., 2009. Looking left with left neglect: the role of spatial attention when active vision selects local image features for fixation. Cortex 45, 1156–1166.
Rizzolatti, G., Riggio, L., Dascola, I., Umilta, C., 1987. Reorienting attention across the horizontal and vertical meridians: evidence in favor of a premotor theory of attention. Neuropsychologia 25, 31–40.
Robertson, I.H., Manly, T., 2002. Cognitive routes to the rehabilitation of unilateral neglect. In: Karnath, H.O., Milner, A.D., Vallar, G. (Eds.), The Cognitive and Neural Bases of Spatial Neglect. Oxford University Press, Oxford.
Rouder, J.N., Morey, R.D., Speckman, P.L., Province, J.M., 2012. Default Bayes factors for ANOVA designs. J. Math. Psychol. 56, 356–374.
Schenkenberg, T., Bradford, D.C., Ajax, E.T., 1980. Line bisection and unilateral visual neglect in patients with neurologic impairment. Neurol. 30, 509–517.
Schintu, S., Pisella, L., Jacobs, S., Salemme, R., Reilly, K.T., Farne, A., 2014. Prism adaptation in the healthy brain: the shift in line bisection judgments is long lasting and fluctuates. Neuropsychologia 53, 165–170.
Schnider, A., Durbec, V.B., Ptak, R., 2011. Absence of visual feedback abolishes expression of hemispatial neglect in self-guided spatial completion. J. Neurol. Neurosurg. Psychiatry 82, 1279–1282.
Skinner, B.F., 1953. Science and Human Behavior. Macmillan, New York.
Smith, D.T., Ball, K., Ellison, A., Schenk, T., 2010. Deficits of reflexive attention induced by abduction of the eye. Neuropsychologia 48, 1269–1276.
Smith, D.T., Rorden, C., Jackson, S.R., 2004. Exogenous orienting of attention depends upon the ability to execute eye movements. Curr. Biol. 14, 792–795.
Smith, D.T., Schenk, T., 2012. The Premotor theory of attention: time to move on? Neuropsychologia 50, 1104–1114.
Smith, D.T., Schenk, T., Rorden, C., 2012. Saccade preparation is required for exogenous attention but not endogenous attention or IOR. J. Exp. Psychol. Hum. Percept. Perform. 38, 1438–1447.
Sprenger, A., Kömpf, D., Heide, W., 2002. Visual search in patients with left visual hemineglect. Prog. Brain Res. 140, 395–416.
Takikawa, Y., Kawagoe, R., Itoh, H., Nakahara, H., Hikosaka, O., 2002. Modulation of saccadic eye movements by predicted reward outcome. Exp. Brain Res. 142, 284–291.
Thiebaut de Schotten, M., Dell'Acqua, F., Forkel, S.J., Simmons, A., Vergani, F., Murphy, D.G.M., Catani, M., 2011. A lateralized brain network for visuospatial attention. Nat. Neurosci. 14, 1245–1246.
Treisman, A., 1988. Features and objects: the fourteenth Bartlett memorial lecture. Q. J. Exp. Psychol. 40, 201–237.
Wagenmakers, E.J., Love, J., Marsman, M., Jamil, T., Ly, A., Verhagen, J., Morey, R.D., 2018a. Bayesian inference for psychology. Part II: example applications with JASP. Psychon. Bull. Rev. 25, 58–76.
Wagenmakers, E.J., Marsman, M., Jamil, T., Ly, A., Verhagen, J., Love, J., Morey, R.D., 2018b. Bayesian inference for psychology. Part I: theoretical advantages and practical ramifications. Psychon. Bull. Rev. 25, 35–57.
Walle, K.M., Nordvik, J.E., Becker, F., Espeseth, T., Sneve, M.H., Laeng, B., 2019. Unilateral neglect post stroke: eye movement frequencies indicate directional hypokinesia while fixation distributions suggest compensational mechanism. Brain Behav. 9, e01170.
Walthew, C., Gilchrist, I.D., 2006. Target location probability effects in visual search: an effect of sequential dependencies. J. Exp. Psychol. Hum. Percept. Perform. 32, 1294–1301.
Zelinsky, G.J., 1996. Using eye saccades to assess the selectivity of search movements. Vis. Res. 36, 2177–2187.

3. General Discussion

In the current dissertation, we evaluated, improved, and created tools for visual rehabilitation. In particular, we focused on two disorders: Homonymous visual field defect (HVFD) and neglect. In both cases, there is a lack of evidence for long-term effects of treatments and for the generalization of treatment effects to activities of daily living (ADL). Reasons for this are, among others, methodological issues of visual tests and trainings. Consequently, we directly addressed two methodological problems in HVFD-research. In the first manuscript, we confirmed that light scatter is sufficient to detect a target within the natural blind spot of healthy participants. Such artefacts could be misinterpreted as residual visual capacities (RVCs) in the blind field of patients. As a solution, we presented light-scatter-free paradigms for future application in patient studies. In the second manuscript, we estimated the diagnostic quality of the redundant target paradigm (RTP), a test frequently used to assess RVCs. The RTP avoids the problem of biased response criteria and has several further advantages compared to other RVC-tests. Our results showed that the RTP has poor sensitivity and reliability but a reasonable specificity. Moreover, the RTP does not satisfy the minimal configuration criterion (MCC) of RVCs. Next, we focused on unilateral neglect. In the third manuscript, we presented a new gaze-contingent intervention for neglect that is based on the premotor theory of attention and implicit approaches to rehabilitation. We showed the feasibility and short-term effectiveness of our intervention in healthy participants. In the following sections, we will discuss our results in light of previous literature and highlight the implications for theories of vision and visual rehabilitation.

3.1. Tools and techniques for visual rehabilitation of HVFDs

One approach in visual rehabilitation aims to restore visual functions in patients with HVFD. To create an effective treatment, studies need to measure visual functions and its changes with a test having high diagnostic quality. We identified four challenges to acquire such a test. Two of these challenges can be met by adequate experimental or technical choices. (1) Precise eye-tracking devices are available to ensure that targets of visual tests are presented at the intended location within the HVFD. (2) It is possible to avoid biased response criteria by forced-choice paradigms or tasks measuring visual functions indirectly. Still, the other two challenges persist. (3) There are no paradigms for which light-scatter artefacts were excluded with a thorough experimental investigation. Previous investigations had small sample sizes and often applied equipment that is out of use. Hence, previous results are not generalizable to subsequent experiments. (4) The diagnostic values, i.e. sensitivity, specificity, and reliability, have not been estimated for the vast majority of RVC-tests. Following this, we addressed these two open challenges in the first and second manuscript.

3.1.1. Light-scatter-free paradigms

The term light-scatter artefact describes above-chance performance within the HVFD of patients that is not due to RVCs but due to light-scatter (Campion et al., 1983). Light is elicited by targets presented within the HVFD. On its way to the retina, light scatters and could hence fall on retinal areas corresponding to the sighted visual field (Campion et al., 1983). In the first manuscript, we conducted a comprehensive review showing that experimental features influence the strength of light scatter. In particular, light scatter gets stronger the bigger and brighter a target is and the closer it is located towards the blind field border (Barbur et al., 1994; Campion et al., 1983). Additionally, decreased room illumination increases light scatter (Faubert et al., 1999). The most thorough way to test light-scatter artefacts is blind-spot testing (Cowey, 2010). If performance is high, even though the target is presented within the natural blind spot, participants used intra- and/or extra-ocular light scatter to solve the task. Following this, we applied the blind-spot method to three commonly used RVC-paradigms. Initially, we confirmed that light scatter can be sufficient to solve a task. Using a temporal two-alternative forced-choice task (2AFC), we found that participants could indicate correctly in which interval a white circle was presented on a black background in a dark room. Importantly, the white circle was presented within the blind spot. This result confirms previous reports about light-scatter artefacts. Light scatter was shown to enable target detection (Barbur et al., 1994; Campion et al., 1983; Danckert & Culham, 2010; Faubert & Diaconu, 2001; Stoerig & Cowey, 1991; Wilson, 1968; Zihl & Werth, 1984), localization (Campion et al., 1983), and discrimination of target orientation (Campion et al., 1983). In summary, there is convincing evidence that light scatter can mimic RVCs. Hence, it is necessary to apply light-scatter-free paradigms for RVC-tests and treatments.

Besides this deliberately strong light-scatter condition, we tested two conditions less prone to create light scatter in an illuminated room, namely white or black targets on a grey background. In both cases, temporal detection was at chance level. Additionally, we measured black targets in a task requiring movement direction discrimination and in a RTP. Light scatter did not influence results in both paradigms. In conclusion, future studies can use these stimulus-paradigm combinations in an illuminated room without worrying about light-scatter artefacts (see second manuscript for details about experimental apparatus):

1a) Temporal 2AFC with white targets on a grey background
1b) Temporal 2AFC with black targets on a grey background
2) Movement direction discrimination with black targets on a grey background
3) Redundant target paradigm with black targets on a grey background

Our results agree with previous findings from blind-spot tests. Some studies showed that bright targets on a darker background did not elicit light-scatter (e.g. Huxlin et al., 2009;

Savina & Guitton, 2018). The same was true for dark targets on a brighter background (e.g. Danckert & Culham, 2010; Huxlin et al., 2009; Stoerig, 2010). Importantly, these results of previous blind-spot tests could not easily be generalized to new designs. One reason for this are small sample sizes of only four participants as maximum. Furthermore, experimental equipment, paradigms, type of stimuli, and room illumination varied. The combination of these factors influences light scatter in various ways. Consequently, until now it has been necessary to test light-scatter artefacts for every new experimental design.

In this light, our study constitutes an attempt to solve this issue. We tested the paradigms in a medium-size sample of healthy participants applying rigorous methods, for instance high precision eye-tracking. Additionally, we tested paradigms frequently used in RVC-research allowing a broad application. In the selection of paradigms, we payed close attention that biased response criteria are avoided (Azzopardi & Cowey, 1998; Cowey, 2010). Following this, we propose to use these specific light-scatter-free versions of the paradigms whenever the research question calls for such paradigms in future studies. With our study at hand, the pool of available light-scatter-free paradigms is still sparse, especially given the broad range of RVCs like affective blindsight (Celeghin, de Gelder, et al., 2015) or shape discrimination (Marcel, 1998). Hence, this pool should be expanded in the future. Furthermore, it is unclear how robust our findings are against small changes in the experimental apparatus. Therefore, further research should test the robustness of avoiding light-scatter artefacts for these versions of the paradigms. It is necessary to measure paradigms in large groups of healthy participants. Additionally, light-scatter artefacts could be measured using the blind spot within the sighted field of HVFD-patients. Such investigations could be done, for instance, in a multi-lab study applying the same experimental program but using the monitor and laboratory room at hand.

Applying light-scatter-free paradigms in evaluating novel treatment approaches can help to improve visual rehabilitation and will also provide more reliable evidence to evaluate neuroscientific theories of vision. Light-scatter artefacts are particularly problematic in vision restitution trainings (VRT; e.g. Marshall et al., 2010; Zihl & von Cramon, 1979). This approach aims to enlarge the sighted field by stimulating the blind field with light targets. As targets are bright and usually presented close to the blind field border, there is a high probability for light scatter. Hence, instead of a true visual field enlargement, patients could learn to utilize light-scatter information more efficiently. With sound testing of light-scatter artefacts, the latter explanation can be ruled out. Whenever a light target on dark background is used, the problem of light-scatter is also an issue for trainings aimed at increasing sensitivity within a given portion of the HVFD (e.g. Larcombe et al., 2018).

Importantly, the maximum contrast, i.e. white targets on a black background, is not necessary for the restoration of visual functions. Visual sensitivity training (VST) was shown to be effective with targets being black random dots on a mid-grey background (e.g. Saionz et al., 2020). This luminance-paradigm combination was free of light-scatter artefacts in our study. Consequently, light-scatter-free paradigms should be preferred in future studies investigating restoration training.

Light-scatter artefacts are also relevant for RVC-research and addressing those artefacts could help to resolve some inconsistencies found in the past research on RVCs. Here is an example. Danckert and Culham (2010) observed a counter-intuitive finding about pointing-behavior in patient *DC.* Authors initially assumed a '*novel form of blindsight'* (page 98). Surprised by the lack of any neuronal activation in fMRI, several control experiments revealed that performance was based on light-scatter artefacts (Danckert & Culham, 2010). As fMRI is not measured by default in RVC-studies, there is an excellent chance that light-scatter artefacts may have produced numerous false-positive findings on RVC, thereby potentially leading to erroneous conclusions and faulty models of the neuronal organization of the visual system.

To conclude, the validity of rehabilitation studies and of vision theories would improve if light-scatter artefacts were consistently controlled for. We hope that vision scientists will expand and utilize the pool of light-scatter free paradigms in the future.

3.1.2. Low diagnostic quality of the redundant target paradigm

In the second manuscript, we addressed another open methodological issue: The diagnostic quality of most RVC-tests is unclear. In the context of RVCs, the diagnostic quality defines how accurate patients can be classified as having RVCs or not. We evaluated this question for one RVC-test: the RTP.

The RTP is a test frequently used in measuring RVCs in HVFD-patients (e.g. Marzi et al., 1986). The RTP attracted attention because it has several advantages compared to other RVC-tests. Firstly, the RTP avoids biased response criteria as it measures RVC indirectly. Secondly, conducting a RTP has no specific technical requirements and can thus be implemented in basically equipped vision laboratories. Thirdly, compliance in patients is high as the task is easy and does not emphasize their deficits. Lastly, the RTP is a potential candidate to test whether the minimal configuration criterion (MCC) for RVCs is satisfied in a given patient (e.g. Striemer et al., 2018). The MCC defines the behavioral and neuronal correlates that underlie all types of RVCs. However, the diagnostic quality of the RTP has not yet been evaluated. Ideally, the diagnostic quality should be evaluated in a large number of patients testing the RTP multiple times. To estimate the reliability, performance is compared between test sessions. Furthermore, results should be compared to the outcome of a gold

standard RVC-test to define specificity and sensitivity (Lalkhen & McCluskey, 2008). However, such a gold standard does not yet exist. Since we do not have any objective reference for RVCs, we do not know whether RVCs are truly present or not. Hence, the direct way to estimate the diagnostic quality of a RVC-test is not possible. Following this, it is necessary to estimate the diagnostic quality in an indirect way by testing healthy participants and the sighted field in HVFD-patients. In our attempt, we relied on previously published results as well as on our own empirical data.

Initially, we calculated a meta-analysis to investigate the effect underlying the RTP in healthy participants. The redundant target effect (RTE) is present if reaction times are shorter in response to two identical targets (double condition) compared to one target (single condition; Raab, 1962). In RVC-research, the double condition consists of one target presented in the sighted and one target simultaneously presented in the blind visual field of HVFD-patients. RVC is present if this bilateral configuration leads to shorter reaction times than a single target in the sighted field (Marzi et al., 1986). In the meta-analysis, we showed that the prediction interval for the RTE with a bilateral configuration is above zero in healthy participants. This means, that we can expect to see a positive RTE if we conduct subsequent studies with the same paradigm. This was true for our own experiment using the RTP in a large sample of healthy participants. It is worth noting that the publication bias might have increased the summary effect size. Hence, future studies should re-evaluate our analysis with pre-registered studies counteracting the publication bias.

Next, we evaluated the diagnostic quality of the RTP for its application in HVFD-patients. It is worth noting that the level of analysis changed. In the meta-analysis, we calculated the average effects size of the RTE on group level. However, in patients, it is critical that the diagnostic decision can be rendered for each individual patient. Tests that produce reliable results only on group level are therefore not useful when employed in single-case studies or in a diagnostic context. Therefore, it was important to also explore how RTP fares when applied to the classification or diagnosis of single cases.

Initially, we estimated the sensitivity, i.e. how good the RTP detects the presence of visual functions. Visual functions are present in healthy participants as well as in the sighted field of patients. In these cases, the RTP had a positive result in 18.18%-77.27% of participants. The broad range of values might emerge for several reasons. Starting with the highest value, 77.27% of healthy participants showed a RTE in a double unilateral condition, i.e. two targets within one hemifield (Schärli et al., 1999). Intriguingly, in the meta-analysis unilateral target configurations (including Schärli et al., 1999) showed a higher summary effect size than bilateral target configurations. In our sample of healthy participants, sensitivity estimates were considerably lower. Still, there were more significant RTEs for the unilateral (32.08%)

than the bilateral (30.19%) target configuration. Hence, the percentage found by Schärli et al. (1999) might overestimate the sensitivity of the bilateral RTP used in RVC-research.

Reviewing the literature, sensitivity was 41.67% within the sighted field of HVFD-patients. In contrast, the lowest estimate (18.18%) occurred in our HVFD-patient sample. As researchers often recruited patients with known RVCs, values might be positively biased. In our study, RVCs of patients were unknown.

In general, sensitivity estimates based on patient data were lower than those based on healthy participants. This could be explained by impaired visual functions within the sighted field of HVFD-patients. These perceptual impairments have been termed '*sightblindness*' (page 1; Bola et al., 2013b). They concern contour integration (Paramei et al., 2017), categorization of natural scenes (Cavezian et al., 2015), and the useful field of view (Woutersen et al., 2020). Furthermore, Hess and Pointer (1989) reported lower contrast sensitivity in the sighted field of HVFD-patients. With respect to reaction times, Bola et al. (2013a) showed that processing speed is reduced within the sighted field of patients with pre- and post-chiasmatic lesions. In particular, reaction times in a detection paradigm (perimetry) were prolonged if targets were closer to the visual field border (Bola et al., 2013a). To summarize, visual functions can be impaired within the sighted field of HVFD-patients. As some of these visual functions are also relevant for the RTP, sensitivity estimates might be underestimated. Importantly, to measure RVCs, tests have to detect remnants of visual functions. Hence, they need to have a high sensitivity despite visual impairments. As a consequence, we recommend investigating the sensitivity of RVC-tests in healthy participants and within the sighted field of HVFD-patients.

To illustrate what these percentages mean for the interpretation of results, we imagine a sample of 100 HVFD-patients. Regarding sensitivity, we will rely on the estimate of 41.67% based on the HVFD-patients in the literature. If 100 patients truly have RVCs, the RTP would only detect the RVCs in 41.67% of these patients thereby underestimating the RVC-prevalence tremendously. In conclusions, the sensitivity of the RTP is poor.

Next, we estimated the specificity which indicates how good the RTP detects the absence of visual functions. To our knowledge, no previous study measured the specificity. Hence, we could only rely on data of the first manuscript about light scatter. We re-analyzed RTP-data in which we presented the second, redundant target within the blind spot. In humans, we know that there are no visual functions within the natural blind spot (Jonas et al., 1991). Following this, none of the participants should have a RTE in this condition. The single-case analysis showed that the RTP detected the absence of visual function in 89.47% of healthy participants. To illustrate the meaning of this result, we stick to our example. If 100 patients are truly blind, only 10.53% show a false positive RTE. This implies that a positive RTE

indicates the presence of RVCs with high probability. Notably, this analysis was post-hoc. Consequently, our result should be replicated in a confirmatory, at best pre-registered study.

The value of reliability shows how good tests correspond between sessions if the function of interest does not change. In healthy participants, it is clear that visual capacities are present and stable. In our dataset, we compared results of healthy participants between target configurations (bilateral versus unilateral) by two statistical measures, namely correspondence of results from single-case analysis and intra-class correlations (ICC). Both statistical measures indicated poor reliability (correspondence of positive results in single-case analysis = 15.09%). We already know from the meta-analysis and from the analysis at group level that the summary effect size varies across different target configurations. Accordingly, those values computed on the basis of comparisons between different target configurations might underestimate reliability but still indicate to what extent the RTE is susceptible to rather minor modifications in the setup. Nevertheless, to improve the precision of the reliability estimate, future studies should test the same target configuration of the RTE in healthy participants in multiple sessions.

Regarding patients, we used reports in the literature and data from our own clinical sample to compare results of the double bilateral configuration (RVC-condition) between test sessions. In our sample, no patient showed consistent positive results (correspondence of positive results in single-case analysis = 0%). In the literature, only 33.33% of patients had a positive RTE in all test sessions indicating a low retest-reliability of the RTP. Low reliability values in patients could, however, also mean that RVCs changed over the course of time. On the one hand, RVCs might improve due to spontaneous recovery or training (e.g. Saionz et al., 2020). On the other hand, RVCs might get lost due to trans-synaptic retrograde degeneration (TRD) which affects also the pathways relevant for RVCs (Ajina et al., 2015; Cowey et al., 2011). These reasons suggest that the reliability values taken from patients measured across longer temporal intervals might underestimate the true reliability of the RTP. So far, most RTP-studies did not report the exact time intervals between test sessions. Hence, it is unclear whether the current reliability estimate might be influenced by such processes. Future studies on intra-patient reliability should ideally test and compare the RTE within a relatively short period of time to avoid confounds with time-dependent physiological changes of RVCs (deterioration by TRD; spontaneous- or training-induced amelioration).

Taken together, results of healthy participants and HVFD-patients suggest that the reliability of the RTP is poor. This is not surprising given the poor sensitivity of the RTP. The RTP detects true RVCs only with low probability. This is true for every test session. Hence, it is also unlikely that the RTP detects RVCs in the same patient in all test sessions. This has implications for the interpretation of test results, for instance in the case of a dissociation. A

HVFD-patient with a lesion in a specific neuronal pathway has RVCs in task A but not in task B. We would conclude that the specific neuronal pathway is not necessary for task A but for task B. However, the lack of RVCs in task B might also be explained by its poor sensitivity and poor reliability. Following this, implications for visual rehabilitation or vision theories might vary depending on the sensitivity and reliability of a test.

Lastly, some studies suggested that the RTE might be used to test whether the MCC for RVCs are given in a certain patient (e.g. Striemer et al., 2018). Such a test would be useful to select patients that are promising candidates for theoretical studies on the neural basis of implicit processes in vision. Such a test might also prove useful to select patients that are most likely to benefit from restitution training. A patient having RVCs in this test would then fulfill the MCC. It follows that a patient must not show RVC within the blind field in any task if the MCC-test is negative. To evaluate whether the RTP is a MCC-test, we reviewed the literature. From previous studies, we evaluated results of HVFD-patients that were tested with the RTP and with other RVC-tests. Six patients showed no RTE but RVCs in other tasks. Consequently, we have to reject the assumption that the RTP is a MCC-test.

While the RTP has clear advantages compared to other RVC-tests, it may be less robust and powerful than previously thought. Its sensitivity and reliability are low. It has good specificity but cannot serve as a good test to check whether the MCC for RVCs are given in a certain patient. Thus, as a rule of thumb, we can state that the presence of a significant RTE likely indicates RVCs, but its absence does not exclude the existence of RVCs.

These findings have implications for vision theories that were based on the RTP-results. We will illustrate this with two examples. Firstly, the well-known model from Milner and Goodale (1995, 2008) describes two cortical systems: The dorsal stream providing *'vision for action'* and the ventral stream providing *'vision for perception'*. On the one hand, the model predicts that the outcome of ventral processes affects the content of our visual awareness. On the other hand, the outcome of dorsal processes affects behaviour, but not the content of visual awareness (Milner & Goodale, 1995, 2008). Striemer et al. (2009) confirmed this prediction in one HVFD-patient showing obstacle avoidance without awareness of the obstacles. In contrast, Ross et al. (2018) could not replicate this finding in six HVFD-patients. Striemer et al. (2018) argued against the finding of Ross et al. (2018) because only one of the six HVFD-patients showed RVCs in a RTP. This argument is challenged in view of the current findings. As the RTP is no MCC-test, it is not valid to rule out RVCs on the basis of a negative finding in the RTP. Our findings on the sensitivity of the RTP point in the same direction. Poor sensitivity of the RTP means we cannot conclude absence of RVCs on the basis of absence of a significant RTE. Following this, it is possible that the other five HVFD-patients of Ross et al. (2018) truly had RVCs but these remained undetected by the

RTP. In conclusion, the results of Ross et al. (2018) cannot simply be dismissed as irrelevant just because the RTP did not yield evidence of RVCs in the blind field.

Secondly, RTP-findings were frequently used to support models about the neuronal pathways underlying RVCs and factors influencing RVCs. In particular, Leh et al. (2006) as well as Marzi et al. (2009) tested the RTP in different color conditions. Results showed the presence of the RTE for certain color conditions but not for others. Marzi et al. (2009) stated that RVCs depended on specific wavelengths potentially because certain cell types are less affected by TRD. Leh et al. (2006) concluded that RVCs are mediated by the superior colliculi (SC). They found no RTE if targets activated only S-cones which should not input to the SC. However, a recent study showed that the S-cones do activate the SC questioning the previous conclusion (Hall & Colby, 2014). In light of the estimated diagnostic quality, the lack of a significant RTE in certain color conditions could also be due to the poor reliability, in particular given the small sample size of the studies (N = 5, Leh et al., 2006; N = 1, Marzi et al., 2009). This should be considered when discussing these and related implication of RVC-results.

In general, previous results of the RTP and their implications for vison theories or visual rehabilitation should be re-evaluated considering the poor sensitivity and poor reliability found in the current study.

Importantly, our findings about the low diagnostic quality of the RTP do not only affect research in HVFD-patients. The results of healthy participants are also relevant for the application of the RTP in other clinical groups. Only 25 of 53 healthy participants (47.17%) tested in our study showed a significant RTE in single-case analysis in at least one condition (double unilateral and/or double bilateral). Thereof, only 8 healthy participants (15.09%) showed a significant RTE in both conditions. Thus, there is a poor sensitivity and reliability of the RTP on single-case level in healthy participants. This should be considered in interpreting findings of all studies that intend to detect certain (visual) functions with the RTP.

As an example, Ouimet et al. (2009) used the RTP to investigate sensory-motor integration in eight patients with complete or partial callosotomy. Single-case analysis showed a significant bilateral RTE in six patients but only three patients had a significant RTE in the unilateral and vertical condition respectively. This difference was attributed to the dissociation between subcortical and cortical pathways (Ouimet et al., 2009). Given the poor sensitivity found in our study with healthy participants, the absence of the RTE in the unilateral and vertical condition does not indicate the absence of (visual) functions. Consequently, such dissociations in the RTP cannot be uncritically used to determine the relevance and role of affected brain structures in the processing of visual information.

The RTP has also been employed in investigating several other clinical groups like schizophrenia (e.g. Florio et al., 2008) or unilateral neglect (e.g. Müller-Oehring et al., 2009). Not all research findings are necessarily undermined by the low diagnostic quality of the RTP. However, the knowledge of RTP's low sensitivity certainly requires a critical re-evaluation of many clinical findings obtained with the RTP.

3.1.3. Possible ways to enhance the diagnostic quality of the redundant target paradigm

Due to the advantages of the RTP, it is worth thinking about ways to improve its diagnostic quality, in particular increase its sensitivity and reliability. In the current state, reaction times are compared between the single-target, i.e. baseline condition, and the double-target, i.e. RVC-condition. If the RTE is present, reaction times are faster in response to two targets. Given the low sensitivity, the difference in reaction times induced by this manipulation is not strong enough to reliably detect the presence of vision. Hence, it might be possible to either additionally slow down reaction times in the baseline condition or further speed up reaction times in the RVC-condition. Research about the RTP in healthy participants and in HVFD-patients offers clues about potential ways to enhance the diagnostic quality of the RTP.

In particular, we evaluated the following experimental manipulations. Slowing down of reaction times in the baseline condition could be achieved by stimuli within the HVFD that counteract the intention to press the button. In the other direction, speeding up of reaction times in the RVC-condition could be achieved by stimuli within the HVFD that promote the intention to press the button. In brief, such stimuli could be (1) multiple redundant targets, (2) Gestalt-targets, (3) emotional faces, as well as (4) specifically tuned gratings.

Two studies showed prolongation of reaction times in the single condition by distractors. In Grice and Gwynne (1987), presenting noise letters increased reaction times in the single-target condition. Ben-David et al. (2014) confirmed this finding. They showed that a distractor in the single-target condition increased the redundancy gain (no distractor in the redundant target condition; Ben-David et al., 2014). Interestingly, both studies used a two-choice paradigm which led to the lowest summary effect size of the RTE in the meta-analysis. The strongest average RTE was present for detection paradigms. Following this, future studies should investigate whether distractors or noise stimuli can also be implemented in detection paradigms to increase the redundancy gain.

With respect to the acceleration of reaction times by redundant-target stimuli, several studies in healthy participants presented more than two identical stimuli. Grice and Gwynne (1987) investigated reaction times in response to one, two, three, or four targets. Results of the two-choice task showed reduced reaction times with increasing number of targets.

Descriptively, the biggest difference occurred between one target with noise and four targets without noise (Grice & Gwynne, 1987). Theeuwes (1994) investigated one, two, or three targets in a go/no-go paradigm. Again, reaction times accelerated with increasing number of targets (Theeuwes, 1994). However, redundancy gain for two or more targets was not compared statistically in either study. Hence, from these studies it is unclear whether presenting two versus three targets increases the redundancy gain significantly. Allen et al. (1993) replicated the main effect of target number (one, two, and three). However, comparing reaction times directly showed a significant difference between one target and two or three targets but no difference between two and three targets. This was true for a go/no-go paradigm as well as for a two-choice task (Allen et al., 1993). Taking these findings together, there is promising, yet not compelling, evidence that more than two redundant targets increase the redundancy gain significantly. In the future, researchers may investigate how many redundant targets consistently lead to a higher redundancy gain.

Regarding research in HVFD-patients, studies showed that certain target types are processed easier within the blind field thus promoting RVCs. Identifying and using these target types for the RTP could improve its diagnostic quality. In particular, there is evidence for the special role of Gestalt-laws, fearful faces, as well as for the spatial and temporal properties of gratings.

Gestalt-laws were important in Celeghin, Savazzi, et al. (2015) who presented either one or four targets within the blind field of HVFD-patients. Interestingly, the group-level reaction times were significantly reduced with four targets in the blind field but only if they followed the Gestalt-laws (e.g. diamond configuration; Celeghin, Savazzi, et al., 2015). This finding was replicated in a subsequent study testing two hemispherectomized patients with known RVCs (Georgy et al., 2016). In contrast, the pattern of results differed regarding the sighted field. In Celeghin, Savazzi, et al. (2015), it did not matter whether the four stimuli were positioned randomly or in a Gestalt. However, in Georgy et al. (2016), reaction times had a similar pattern than in the blind field meaning that reaction times were reduced only for four targets in a Gestalt but not in random configuration.

There is a long line of research about the visual processing of targets following the Gestalt laws. A recent example for this is the study by Marini and Marzi (2016) who investigated reaction times and ERPs in response to congruent or incongruent presentation of bilateral targets in healthy participants. There could be a Gestalt target at the left, at the right, at both, or at none of the positions. In the conditions with none or a single Gestalt-target, there was a non-Gestalt target at the remaining position(s). As the instruction was simple detection of targets, the task was similar to a RTP with an additional distractor in the single-target condition. However, there were no differences in reaction times. In the EEG, Gestalt-targets

lead to enhanced amplitudes of several ERPs that are associated with attentional capture (Marini & Marzi, 2016). Even though effects of Gestalt-targets on reaction times were inconsistent, EEG-results confirmed the special visual processing of Gestalt-targets. Following this, cognitive scientists still need to ascertain the experimental conditions under which reaction times capture this effect consistently.

Another target type especially suitable for RVCs are emotional faces and in particular fearful faces. Herein, there might be another potential to improve the diagnostic quality of the RTP. De Gelder et al., (2001) used a variant of the RTP by presenting one half of a face in the sighted and the other half in the blind hemifield. Face halves could be emotionally congruent or incongruent. Patient *GY* showed faster reaction times in response to the face half in his sighted field if the face half in the blind field showed the same emotion. In a subsequent experiment, this effect was confirmed with full faces in each hemifield (de Gelder et al., 2001).

Bertini et al. (2013) applied the RTP in three go/no-go tasks in which HVFD-patients had to respond to: (1) a specific emotion of faces, (2) a specific gender of faces, or (3) a specific geometrical shape. The targets in the sighted field were paired with the identical target, a scrambled version of the target, or an alternative target (other emotion, gender, or shape). Intriguingly, in the emotion task reaction times were not fastest when emotionally congruent faces were presented but when a happy face in the sighted field was coupled with a fearful face in the blind field. The second experiment confirmed the facilitating effect of fearful faces in the blind field, in this case coupled with a neutral face in the sighted field. It is worth noting that participants should respond to the gender of the face in the sighted field making the emotional content irrelevant for the task (Bertini et al., 2013).

The special role of fearful faces is supported by further studies. In the EEG study of Cecere et al. (2014), results showed no effects in reaction times. However, there was an enhanced ERP for the combination of happy faces in the sighted and fearful faces in the blind field for patients with left hemisphere lesions (Cecere et al., 2014). Hence, the EEG study supports the peculiarity in the neuronal processing of emotional faces even though behavioral results are not consistent. Moreover, a recent study showed that fearful faces did not only facilitate responses to other faces but also to geometric shapes. In Bertini et al. (2019), patients with left-hemisphere lesions showed faster reaction times in response to Gabor patches in the sighted field if they were coupled with fearful faces in the blind field. This facilitation effect was not present for happy or neutral faces within the blind field (Bertini et al., 2019).

All three studies (Bertini et al., 2019; Bertini et al., 2013; Cecere et al., 2014) also investigated RVCs using a detection task and three discrimination tasks. None of the patients showed above-chance detection or discrimination (emotion, gender, and shapes).

Importantly, this analysis was done on single-case level. In contrast, analysis of reaction times in the RTPs or of EEG was done on group-level. Hence, it is doubtful that all patients would have had the reaction-time effect or EEG-effect of the fearful faces on single-case level. Still, it seems possible that the RTPs with fearful faces were more sensitive to pick up RVCs.

There is at least one further target type that showed particularly promising results for RVCs. Multiple investigations in HVFD-patients varied parameters of Gabor patches systematically and measured its detection within the blind fields. They showed a maximum sensitivity for a spatial frequency of 1 cycle/° (Sahraie et al., 2008; Sahraie et al., 2003; Sahraie et al., 2002). In the conditions with spatial frequencies above 4 cycle/°, none of the patients showed above-chance performance (Sahraie et al., 2003; Sahraie et al., 2002; exception: Trevethan et al., 2007). Regarding the temporal frequency, the maximum performance occurred at 10 Hz (Sahraie et al., 2008). Furthermore, the minimum target size required for detection ranged from 4° to 10° diameter (Sahraie et al., 2008).

Subsequently, a number of studies used grating targets with roughly these properties (spatial frequency: 1 cycle/°; temporal frequency: 10Hz) for RVC-research (e.g Ajina et al., 2015). Importantly, these grating properties were also used for a sensitivity training presented by the Sahraie-group (Sahraie et al., 2013). During the training, task difficulty was adapted by reducing target contrast. In four out of five patients, training led to improved sensitivity and increased awareness (Sahraie et al., 2013). In a recent study, results confirmed the training effect, showed its influence on neuronal activity, and demonstrated generalization on the detection and discrimination of moving dots (Ajina et al., 2021).

Grating targets were also applied in RTPs. Leh et al. (2006) used grating targets (static, 1 cycle/°) to measure RVCs in five hemispherectomized patients and in 16 healthy participants. Results for achromatic gratings showed a significant RTE at group level in healthy participants but only for the three patients with previously reported RVCs. Hence, the RTE is present with gratings but it is unclear if this effect is stronger compared to other target types.

To conclude, we identified several possibilities to enhance the RTE and thus improve the sensitivity and reliability of the RTP. Two ways could slow down reaction times in the single condition: Presentation of (1) a noise stimulus or (2) a counteracting distractor in the blind field. Four ways could further accelerate reaction times in the redundant condition: Presentation of (1) more than two redundant targets, (2) targets following the Gestalt-laws, (3) fearful faces, and (4) spatially and temporally tuned gratings in the blind field. There might be even more possibilities that could be identified in the future. It is worth noting that most of the studies described above calculated the reaction-time effects on group level. In

RVC-research however, we like to draw conclusions about a single patient. Hence, it is necessary to investigate whether the effects of the experimental manipulations on the RTE are consistent on single-case level. Upcoming research should find the way that leads to the strongest RTE to benefit from the advantages of the RTP *and* have a high diagnostic quality.

Taking the first and second manuscript together, future research about RVCs and about treatments for HVFD should use paradigms with precise fixation control avoiding biased response criteria and light-scatter artefacts. Furthermore, the diagnostic quality of tests should ideally be evaluated and if possible improved. If experimental designs cannot comply with all requirements, they have to discuss results in light of these weaknesses. Following this approach, we hope that implications about RVCs and hence vision theories will be more precise. Regarding visual rehabilitation, these methodological precautions could contribute to a more valid evaluation of effects thereby improving treatments and hence quality of life in patients.

3.2. Tools and techniques for visual rehabilitation of unilateral neglect

In visual rehabilitation of unilateral neglect, there exist several treatment approaches (for a review see Kerkhoff & Schenk, 2012). As insight into impairments is often lacking in neglect patients (for a review see Jenkinson et al., 2011), it is advisable to base treatments on implicit learning and not on explicit exploration strategies. Still, there is a lack of evidence for long-term effects and for the generalization to ADLs of current implicit training approaches (Kerkhoff & Schenk, 2012). This could be due to inconsistencies in applying treatments. As an example, findings about optokinetic stimulation (OKS) varied depending on the presence or absence of a fixation symbol. Salillas et al. (2009) showed an effect of OKS presented together with a fixation symbol on number-space representation whereas Pitteri et al. (2015) could not replicate this effect but they also used a different configuration without a fixation symbol. Furthermore, some treatments have unpleasant side effects, for instance nausea after caloric vestibular stimulation (CVS; Been et al., 2007). Thus, implicit approaches show promise but their efficacy is not yet proven and the side effects of some are sufficiently unpleasant to warrant the search for alternatives. For this reason, we decided to explore another implicit intervention strategy that might be effective while avoiding the problems described above.

The described treatments all assume that the core-deficit in neglect is the orientation bias towards the right sight (Kerkhoff & Schenk, 2012). As neglect types are diverse (Brozzoli et al., 2006; Buxbaum et al., 2004), it might be promising to target another symptom, for instance the bias in attentional allocation. In particular, patients show a so-called disengage deficit (Losier & Klein, 2001). If patients attend to targets within the preferred side, they have problems disengaging the attention and then relocating the attention to a target within the

neglected side (Losier & Klein, 2001). Rizzolatti et al. (1987) proposed a link between covert attentional allocation and eye movement planning. Experimental evidence supports this hypothesis (called the premotor theory) at least for exogenous attention (Smith & Schenk, 2012). In line with this, results showed impaired attentional allocation when eye movements were restricted to one side by employing an eye abduction intervention (for more details, see Smith et al., 2012). To conclude, a treatment aimed at changing the eye-movements of neglect patients might help to ameliorate neglect symptoms. Based on this idea, we created a novel training paradigm for neglect patients.

3.2.1. Gaze-contingent intervention: Short-term effects in healthy participants

In the third manuscript, we presented the new, gaze-contingent intervention. As a first step, we tested the feasibility of the intervention in healthy participants. For this, the training task was adapted to counteract pseudoneglect, i.e. a small bias towards the left, present in healthy participants (Bowers & Heilman, 1980). During the training, participants conducted a visual exploration task in which left search items (distractors and if applicable the target) vanished as soon as the gaze position reached the left hemifield of the screen. Like this, eye movements towards the left side were made useless. Initially, we showed that eye-movement behavior changed during the course of the intervention. In particular, the intervention induced a higher sum of fixation durations, i.e. dwell time, on the right compared to the left hemifield of the screen. Moreover, the first fixation fell more often into the right hemifield of the screen. This indicates that our intervention can counteract pseudoneglect in healthy participants.

In a series of five experiments, we investigated the short-term effect of the intervention on four visual tasks in healthy participants. In the first experiment, we tested the training effect on a feature search task similar to the intervention. In the second experiment, we tested the generalization of the training effect on a conjunction search task. Although search items did not vanish anymore, the changes in eye movement pattern persisted until the second half of the post-test in both visual search tasks. This demonstrates that there was a short-term effect of the intervention which generalized to a search task different from the intervention (conjunction search).

In two subsequent experiments, we measured the training effect on a Posner task. Relating to the premotor theory of attention, exogenous attention should dependent on (eye) movement planning (Craighero & Rizzolatti, 2005; Smith & Schenk, 2012). As the intervention led to reduced eye movements towards the left, we expected a change in exogenous attention measured by the Posner task. In particular, we hypothesized prolonged reaction times in response to targets on the left side if the cue indicated the right side, i.e. a disengage deficit (Losier & Klein, 2001). Data of the third experiment did not confirm this

hypothesis. Still, in valid trials there were significantly reduced reaction times for targets on the right. However, our attempt to replicate this finding (experiment 4) showed neither a disengage deficit nor the side-dependent effect. Hence, against the prediction, changes in eye movements did not influence exogenously driven covert attention measured in the Posner paradigm.

There are several possible explanations for the lack of a consistent training effect in the Posner paradigm. Firstly, the Posner paradigm might have been too distinct from the intervention paradigm. The intervention shifted attention overtly and endogenously. In contrast, the Posner paradigm measures covert attention with exogenous cues. Secondly, even if the intervention led to a shift in covert attentional allocation, this might have been outperformed by the exogenous cues in the Posner task. Thirdly, in previous studies about the premotor theory, eye movements were impossible towards one side (e.g. Smith et al., 2010). In contrast, we only made eye movements useless but they were still possible. Consequently, the Posner paradigm might not have been the optimal task to measure changes in attentional allocation.

One possible solution could be to measure the disengage deficit in a task more similar to the intervention. The disengage deficit was shown in a recent study investigating free viewing in neglect patients (Kaufmann et al., 2020). Neglect patients showed typical biases in visual exploration like a rightward shift in fixation locations and an increased dwell time in the right side of the screen. Authors operationalized the disengage deficit by '*capture fixations'* (page 1412, Kaufmann et al., 2020), i.e. a fixations whose area (1° diameter) overlapped with sequential fixations. Patients had significantly more capture fixations at the right side of the screen than at the left side (Kaufmann et al., 2020). Following this, capture fixations might be a useful variable in measuring the disengage deficit in a visual search paradigm. Future experiments could use this analysis to test the training effect on the attentional disengage deficit in a task more similar to the intervention.

In the last experiment, we tested the effect of the intervention on a line-bisection task. Herein, we replicated the effect of pseudoneglect in the pre-test (Bowers & Heilman, 1980). However, pseudoneglect was still present in the post-test indicating that the intervention could not counteract the natural bias in this task. Several reasons could explain the lack of a training effect on line bisection. It is possible that the pseudoneglect bias is too robust to be changed by a short intervention. Moreover, studies showed that line bisection and visual search tasks measure distinguishable symptoms in neglect (McIntosh et al., 2017). Traditionally, line bisection was used as an estimate for the subjective midpoint of the patient (McIntosh et al., 2017). In contrast, visual search measures a bias in exploration behavior (Karnath et al., 1998). This is in accordance with the finding that line-bisection did not

correlate with the eye-movement bias in a large sample of healthy participants (Foulsham et al., 2018). In these studies as well as in our manuscript, the outcome variable of line-bisection was the average bisection error. However, there might be other outcome variables that have a higher correlation with eye-movement patterns. McIntosh et al. (2017) suggested two new outcome measures regarding line-bisection: Endpoint weighting bias (EWB) and endpoint weighting sum (EWS; for formulas see page 150 in McIntosh et al., 2017; and page 838 in McIntosh et al., 2005). Authors assume that EWB indicates the bias in lateral attention. EWS indicates non-lateralized attentional allocation able to distinguish patients and healthy participants (McIntosh et al., 2005). Results showed that these measures overlapped better with other neglect tests than the traditional average bisection error (McIntosh et al., 2017). Following this, future studies could test whether our gaze-contingent intervention has an effect on EWB or EWS in the line-bisection task.

In summary, applying our intervention in healthy participants induced the intended change in eye movement patterns which had a short-term effect on two visual search tasks. The intervention did not influence outcome of a Posner task nor of a line-bisection task. As these tasks were more different to the intervention, other measures of covert attentional allocation or from line-bisection might be more sensitive to pick up the intervention effect.

Still, it is unclear whether the gaze-contingent intervention will be superior to other neglect treatment. At least, studies in healthy participants already showed certain advantages of the gaze-contingent intervention. Developing this intervention, we aimed to overcome methodological problems of current neglect trainings. In contrast to CVS (Been et al., 2007), our intervention did no lead to unpleasant side effects. Furthermore, awareness is not necessary for the effect of our gaze-contingent intervention. Although, the search task requires active participation, participants do not need an explicit exploration strategy. Even though participants recognized the stop of stimulus-removal already in the first trials of the post-test, the biased eye-movement pattern persisted in the second half of the post-test (feature search and conjunction search). In addition, results of the debriefing questionnaire showed that the training effect did not differ between those participants noticing the influence of the intervention on the post-test or not. Hence an explicit strategy was not necessary. Rather, the intervention induced a new habit by implicit learning.

With these promising results, we achieved the first step towards an intervention for neglect patients. As next steps, we will test the long-term effectiveness of the gaze-contingent intervention and its feasibility in neglect patients.

3.3. Conclusions

In this thesis, we aimed to provide tools and techniques for visual rehabilitation of neglect and HVFD. Regarding HVFD, we addressed two methodological issues. Firstly, we confirmed that light-scatter artefacts can mimic RVCs in HVFD. As a possible solution for future research, we provided three paradigms, thereof one paradigm in two versions, that avoid light-scatter artefacts:

1a) Temporal 2AFC with white targets on a grey background
1b) Temporal 2AFC with black targets on a grey background
2) Movement direction discrimination with black targets on a grey background
3) Redundant target paradigm with black targets on a grey background

Future studies should investigate these versions of the paradigms in large samples applying varying experimental equipment to test the generalizability of our results to other vision laboratories.

Secondly, we investigated the RTP, a frequently used RVC-test which has several advantages. The RTP avoids biased response criteria, has low technical requirements, and is easy to perform for HVFD-patients. The RTP is based on the RTE, meaning faster reactions times in response to two redundant compared to a single target. Initially, we calculated a meta-analysis demonstrating that the RTE has a positive summary effect size on group level in healthy participants. As the publication bias might have led to an overestimation of the average effect size, future RTP-studies should be pre-registered to allow a more valid evaluation of the RTE-strength.

On single-case level, the diagnostic quality of the RTP is sufficient for specificity but poor for sensitivity and reliability. Knowing this diagnostic quality, previous and subsequent RTP-results can be interpreted accordingly. In brief, the presence of a RTE indicates the presence of RVCs. In contrast, the absence of a RTE does not imply the absence of RVCs. Applying this to lesion studies in HVFD-patients implies that conclusions drawn from the absence of a RTE to the relevance of damaged neuronal pathways are invalid.

A variety of RVCs have been described in the literature. It might be possible that there are behavioral and neuronal preconditions, i.e. a minimal configuration criterion, underlying all RVC-types. Having a MCC-test would allow to select adequate rehabilitation strategies for a given patient and recruit suitable patients for RVC-research. However, our review showed that even though the RTP measures basal visual functions, it is no MCC-test.

It is worth noting that the low diagnostic quality of the RTP, as found in healthy participants, also has to be considered when applying the RTP to detect visual functions in other clinical

samples, for instance unilateral neglect or split-brain patients. Absence of a RTE in these clinical groups is hence not informative about the presence or absence of visual functions but might be explained by the low sensitivity of the RTP.

As one main limitation, we measured the RTP only in a small sample of patients and relied on reports in the literature. Herein, we cumulated results even though the experimental paradigms and analysis varied between previous patient studies. Following this, it is necessary to re-evaluate our estimates of the diagnostic quality in a large number of HVFD-patients measuring the RTP multiple times at brief intervals.

For the future application of the RTP, it is worth improving its diagnostic quality. Therefore, we identified several experimental manipulations potentially increasing the sensitivity and reliability of the RTP. As an example, the presentation of distractors in the baseline condition (single target) might prolong reaction times and the use of Gestalt-targets in the RVC-condition (bilateral redundant targets) might accelerate reaction times. In combination, the redundancy gain would increase, reinforcing the RTE, and thus improving the diagnostic quality of the RTP. Investigating the effects of such experimental manipulations will be the topic of subsequent studies.

We hope that applying light-scatter-free paradigms and tests with high diagnostic quality in HVFD-research will lead to more reliable evidence regarding vision theories and to more effective interventions for HVFD-patients.

A second disorder that plays a prominent role in visual rehabilitation is unilateral neglect. Here, one of the main challenges is to develop intervention strategies that work even for patients who have no insight into their own disorder. To address this problem, we aimed to develop an implicit training approach, i.e. a training that affects behavior in a positive way even if the patients themselves do not intentionally work towards this behavioral change.

For this purpose, we introduced a gaze-contingent intervention. Among others, neglect patients have problems exploring the contralesional, i.e. neglected, hemifield and disengaging their attention from targets on the ipsilesional, i.e. preferred, hemifield. The gaze-contingent intervention is based on a visual search task. Targets are removed on the preferred side hemifield of the screen if eye movements are made towards it. This manipulation should reduce exploration of the preferred hemifield and promote exploration of the neglected hemifield.

In our feasibility study with healthy participants, the intervention was adapted to counteract the pseudoneglect bias. Results showed a consistently reduced number of fixations within the punished hemifield. Furthermore, the training effect generalized to other visual tasks measuring overt attentional allocation. Unfortunately, the intervention did not change covert

attentional allocation in a Posner paradigm nor the bias in a line-bisection task. Hence, the training effect might be specific to overt attentional allocation. Alternatively, measures were not sensitive enough. Following this, prospective studies may test whether other outcome measures show a training effect on covert attentional allocation.

Importantly, explicit strategies were not necessary for the behavioral change in visual exploration behavior. Due to this implicit nature of the training effect, neglect patients might improve more than in conventional explicit exploratory trainings. Furthermore, there were no unpleasant side-effects during or after the gaze-contingent intervention. Subsequent studies will investigate the long-term effects of the gaze-contingent intervention and its application in neglect patients. Lastly, the effectiveness of the gaze-contingent intervention should be evaluated against other common neglect treatments to offer the most promising approach to neglect patients.

In conclusion, the three manuscripts presented in this thesis provided tools and techniques for visual rehabilitation. By this, we hope to contribute to the development of more effective treatments to finally improve quality of life in HVFD- and neglect patients.

4. References[1]

Aimola, L., Lane, A. R., Smith, D. T., Kerkhoff, G., Ford, G. A., & Schenk, T. (2014). Efficacy and feasibility of home-based training for individuals with homonymous visual field defects. *Neurorehabilitation and neural repair*, *28*(3), 207-218. https://doi.org/10.1177/1545968313503219

Ajina, S., & Bridge, H. (2018). Subcortical pathways to extrastriate visual cortex underlie residual vision following bilateral damage to V1. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2018.01.007

Ajina, S., Jünemann, K., Sahraie, A., & Bridge, H. (2021). Increased Visual Sensitivity and Occipital Activity in Patients With Hemianopia Following Vision Rehabilitation. *Journal of Neuroscience*.

Ajina, S., Pestilli, F., Rokem, A., Kennard, C., & Bridge, H. (2015). Human blindsight is mediated by an intact geniculo-extrastriate pathway. *Elife*, *4*. https://doi.org/10.7554/eLife.08935

Ajina, S., Pollard, M., & Bridge, H. (2020). The Superior Colliculus and Amygdala Support Evaluation of Face Trait in Blindsight. *Frontiers in neurology*, *11*, 769. https://doi.org/10.3389/fneur.2020.00769

Allen, P. A., Groth, K. E., Weber, T. A., & Madden, D. J. (1993). Influence of response selection and noise similarity on age differences in the redundancy gain. *Journal of Gerontology*, *48*(4), P189-P198.

Azzopardi, P., & Cowey, A. (1998). Blindsight and visual awareness. *Consciousness and Cognition*, *7*(3), 292-311. https://doi.org/10.1006/ccog.1998.0358

Barbur, J., Harlow, A. J., & Weiskrantz, L. (1994). Spatial and temporal response properties of residual vision in a case of hemianopia. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *343*(1304), 157-166. https://doi.org/10.1098/rstb.1994.0018

Barbur, J., Ruddock, K., & Waterfield, V. A. (1980). Human visual responses in the absence of the geniculo-calcarine projection. *Brain: a journal of neurology*, *103*(4), 905-928. https://doi.org/10.1093/brain/103.4.905

Been, G., Ngo, T. T., Miller, S. M., & Fitzgerald, P. B. (2007). The use of tDCS and CVS as methods of non-invasive brain stimulation. *Brain research reviews*, *56*(2), 346-361.

Ben-David, B. M., Eidels, A., & Donkin, C. (2014). Effects of aging and distractors on detection of redundant visual targets and capacity: do older adults integrate visual targets differently than younger adults? *PLoS One*, *9*(12), e113551. https://doi.org/10.1371/journal.pone.0113551

Bergsma, D. P., & van der Wildt, G. (2010). Visual training of cerebral blindness patients gradually enlarges the visual field. *British Journal of Ophthalmology*, *94*(1), 88-96. https://doi.org/10.1136/bjo.2008.154336

Bertini, C., Cecere, R., & Ladavas, E. (2019). Unseen fearful faces facilitate visual discrimination in the intact field. *Neuropsychologia*, *128*, 58-64.

Bertini, C., Cecere, R., & Làdavas, E. (2013). I am blind, but I "see" fear. *Cortex*, *49*(4), 985-993.

[1] This list comprises only the references for the General Introduction and General Discussion. The references of the manuscripts contained in this thesis are listed at the end of corresponding chapters (Chapters 2.1- 2.3).

Bola, M., Gall, C., & Sabel, B. A. (2013a). The second face of blindness: processing speed deficits in the intact visual field after pre-and post-chiasmatic lesions. *PLoS One*, *8*(5), e63700.

Bola, M., Gall, C., & Sabel, B. A. (2013b). "Sightblind": perceptual deficits in the "intact" visual field. *Frontiers in neurology*, *4*(80). https://doi.org/10.3389/fneur.2013.00080

Bosma, M. S., Nijboer, T. C., Caljouw, M. A., & Achterberg, W. P. (2020). Impact of visuospatial neglect post-stroke on daily activities, participation and informal caregiver burden: A systematic review. *Annals of physical rehabilitation medicine*, *63*(4), 344-358.

Bowen, A., Hazelton, C., Pollock, A., & Lincoln, N. B. (2013). Cognitive rehabilitation for spatial neglect following stroke. *Cochrane Database of Systematic Reviews*, *7*.

Bowen, A., McKenna, K., & Tallis, R. C. (1999). Reasons for variability in the reported rate of occurrence of unilateral spatial neglect after stroke. *Stroke*, *30*(6), 1196-1202.

Bowers, D., & Heilman, K. M. (1980). Pseudoneglect: Effects of hemispace on a tactile line bisection task. *Neuropsychologia*, *18*(4-5), 491-498.

Brozzoli, C., Demattè, M. L., Pavani, F., Frassinetti, F., & Farnè, A. (2006). Neglect and extinction: within and between sensory modalities. *Restorative neurology and neuroscience*, *24*(4-6), 217-232.

Buxbaum, L. J., Ferraro, M., Veramonti, T., Farne, A., Whyte, J., Ladavas, E., Frassinetti, F., & Coslett, H. (2004). Hemispatial neglect: Subtypes, neuroanatomy, and disability. *Neurology*, *62*(5), 749-756.

Campion, J., Latto, R., & Smith, Y. (1983). Is blindsight an effect of scattered light, spared cortex, and near-threshold vision? *Behavioral and Brain Sciences*, *6*(3), 423-448. https://doi.org/10.1017/S0140525X00016861

Cavanaugh, M. R., Barbot, A., Carrasco, M., & Huxlin, K. R. (2017). Feature-based attention potentiates recovery of fine direction discrimination in cortically blind patients. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2017.12.010

Cavanaugh, M. R., & Huxlin, K. R. (2017). Visual discrimination training improves Humphrey perimetry in chronic cortically induced blindness. *Neurology*, *88*(19), 1856-1864. https://doi.org/10.1212/wnl.0000000000003921

Cavezian, C., Perez, C., Peyrin, C., Gaudry, I., Obadia, M., Gout, O., & Chokron, S. (2015). Hemisphere-dependent ipsilesional deficits in hemianopia: Sightblindness in the 'intact' visual field. *Cortex*, *69*, 166-174. https://doi.org/10.1016/j.cortex.2015.05.010

Cecere, R., Bertini, C., Maier, M. E., & Làdavas, E. (2014). Unseen fearful faces influence face encoding: evidence from ERPs in hemianopic patients. *Journal of Cognitive Neuroscience*, *26*(11), 2564-2577.

Celeghin, A., de Gelder, B., & Tamietto, M. (2015). From affective blindsight to emotional consciousness. *Consciousness and Cognition*, *36*, 414-425. https://doi.org/10.1016/j.concog.2015.05.007

Celeghin, A., Savazzi, S., Barabas, M., Bendini, M., & Marzi, C. A. (2015). Blindsight is sensitive to stimulus numerosity and configuration: evidence from the redundant signal effect. *Experimental brain research*, *233*(5), 1617-1623. https://doi.org/10.1007/s00221-015-4236-6

Cicerone, K. D., Dahlberg, C., Kalmar, K., Langenbahn, D. M., Malec, J. F., Bergquist, T. F., Felicetti, T., Giacino, J. T., Harley, J. P., & Harrington, D. E. (2000). Evidence-based

cognitive rehabilitation: recommendations for clinical practice. *Archives of physical medicine and rehabilitation*, *81*(12), 1596-1615. https://doi.org/https://doi.org/10.1053/apmr.2000.19240

Cicerone, K. D., Goldin, Y., Ganci, K., Rosenbaum, A., Wethe, J. V., Langenbahn, D. M., Malec, J. F., Bergquist, T. F., Kingsley, K., & Nagele, D. (2019). Evidence-based cognitive rehabilitation: systematic review of the literature from 2009 through 2014. *Archives of physical medicine and rehabilitation*, *100*(8), 1515-1533. https://doi.org/https://doi.org/10.1016/j.apmr.2019.02.011

Corbetta, M., Marzi, C. A., Tassinari, G., & Aglioti, S. (1990). Effectiveness of different task paradigms in revealing blindsight. *Brain*, *113*, 603-616. https://www.ncbi.nlm.nih.gov/pubmed/2364262

Cowey, A. (2010). The blindsight saga. *Experimental brain research*, *200*(1), 3-24. https://doi.org/10.1007/s00221-009-1914-2

Cowey, A., Alexander, I., & Stoerig, P. (2011). Transneuronal retrograde degeneration of retinal ganglion cells and optic tract in hemianopic monkeys and humans. *Brain*, *134*, 2149-2157. https://doi.org/10.1093/brain/awr125

Craighero, L., Carta, A., & Fadiga, L. (2001). Peripheral oculomotor palsy affects orienting of visuospatial attention. *Neuroreport*, *12*(15), 3283-3286.

Craighero, L., Nascimben, M., & Fadiga, L. (2004). Eye position affects orienting of visuospatial attention. *Current Biology*, *14*(4), 331-333.

Craighero, L., & Rizzolatti, G. (2005). CHAPTER 31 - The premotor theory of attention. In L. Itti, G. Rees, & J. K. Tsotsos (Eds.), *Neurobiology of attention* (pp. 181-186). Academic Press. https://doi.org/https://doi.org/10.1016/B978-012375731-9/50035-5

Cubelli, R. (2017). Definition: Spatial neglect. *Cortex*, *92*, 320-321. https://doi.org/https://doi.org/10.1016/j.cortex.2017.03.021

Danckert, J., & Culham, J. C. (2010). Reflections on blindsight: Neuroimaging and behavioural explorations clarify a case of reversed localisation in the blind field of a patient with hemianopia. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale*, *64*(2), 86. https://doi.org/https://doi.org/10.1037/a0017426

Danckert, J., Tamietto, M., & Rossetti, Y. (2019). Definition: Blindsight. *Cortex*, *119*, 569-570. https://doi.org/10.1016/j.cortex.2019.01.027

de Gelder, B., Pourtois, G., van Raamsdonk, M., Vroomen, J., & Weiskrantz, L. (2001). Unseen stimuli modulate conscious visual experience: evidence from inter-hemispheric summation. *Neuroreport*, *12*(2), 385-391.

de Haan, G. A., Heutink, J., Melis-Dankers, B. J., Brouwer, W. H., & Tucha, O. (2015). Difficulties in Daily Life Reported by Patients With Homonymous Visual Field Defects. *Journal of Neuro-Ophthalmology*, *35*(3), 259-264. https://doi.org/10.1097/WNO.0000000000000244

de Haan, G. A., Melis-Dankers, B. J., Brouwer, W. H., Tucha, O., & Heutink, J. (2015). The Effects of Compensatory Scanning Training on Mobility in Patients with Homonymous Visual Field Defects: A Randomized Controlled Trial. *PLoS One*, *10*(8), e0134459. https://doi.org/10.1371/journal.pone.0134459

Diller, L., & Weinberg, J. (1977). Hemi-inattention in rehabilitation: the evolution of a rational remediation program. *Advances in Neurology*, *18*, 63–82.

Faubert, J., & Diaconu, V. (2001). Chapter 25 From visual consciousness to spectral absorption in the human retina. In *Progress in brain research* (Vol. 134, pp. 399-409). Elsevier. https://doi.org/https://doi.org/10.1016/S0079-6123(01)34026-8.

Faubert, J., Diaconu, V., Ptito, M., & Ptito, A. (1999). Residual vision in the blind field of hemidecorticated humans predicted by a diffusion scatter model and selective spectral absorption of the human eye. *Vision research*, *39*(1), 149-157. https://doi.org/https://doi.org/10.1016/S0042-6989(98)00107-2

Fellrath, J., & Ptak, R. (2015). The role of visual saliency for the allocation of attention: Evidence from spatial neglect and hemianopia. *Neuropsychologia*, *73*, 70-81. https://doi.org/10.1016/j.neuropsychologia.2015.05.003

Florio, V., Marzi, C. A., Girelli, A., & Savazzi, S. (2008). Enhanced redundancy gain in schizophrenics: a correlate of callosal dysfunction? *Neuropsychologia*, *46*(11), 2808-2815. https://doi.org/10.1016/j.neuropsychologia.2008.05.007

Florio, V., Savazzi, S., Conca, A., & Marzi, C. A. (2013). Differential impairment of interhemispheric transmission in bipolar disease. *Experimental brain research*, *230*(2), 175-185. https://doi.org/10.1007/s00221-013-3642-x

Foulsham, T., Frost, E., & Sage, L. (2018). Stable individual differences predict eye movements to the left, but not handedness or line bisection. *Vision research*, *144*, 38-46. https://doi.org/https://doi.org/10.1016/j.visres.2018.02.002

Gainotti, G., De Luca, L., Figliozzi, F., & Doricchi, F. (2009). The influence of distracters, stimulus duration and hemianopia on first saccade in patients with unilateral neglect. *Cortex*, *45*(4), 506-516. https://doi.org/https://doi.org/10.1016/j.cortex.2007.12.008

Georgy, L., Celeghin, A., Marzi, C. A., Tamietto, M., & Ptito, A. (2016). The superior colliculus is sensitive to gestalt-like stimulus configuration in hemispherectomy patients. *Cortex*, *81*, 151-161. https://doi.org/https://doi.org/10.1016/j.cortex.2016.04.018

Grattan, E. S., Skidmore, E. R., & Woodbury, M. L. (2018). Examining anosognosia of neglect. *OTJR: occupation, participation and health*, *38*(2), 113-120. https://doi.org/https://doi.org/10.1177/1539449217747586

Grice, G. R., & Gwynne, J. W. (1987). Dependence of target redundancy effects on noise conditions and number of targets. *Perception & Psychophysics*, *42*(1), 29-36. https://doi.org/https://doi.org/10.3758/BF03211511

Hall, N., & Colby, C. (2014). S-cone visual stimuli activate superior colliculus neurons in old world monkeys: implications for understanding blindsight. *Journal of Cognitive Neuroscience*, *26*(6), 1234-1256. https://doi.org/10.1162/jocn_a_00555

Hanna, K. L., Hepworth, L. R., & Rowe, F. J. (2017). The treatment methods for post-stroke visual impairment: A systematic review. *Brain and behavior*, *7*(5), e00682. https://doi.org/10.1002/brb3.682

Hess, R., & Pointer, J. (1989). Spatial and temporal contrast sensitivity in hemianopia: a comparative study of the sighted and blind hemifields. *Brain*, *112*(4), 871-894. https://doi.org/https://doi.org/10.1093/brain/112.4.871

Holé, J., Reilly, K. T., Nash, S., & Rode, G. (2020). Caloric Vestibular Stimulation Reduces the DirectionalBias in Representational Neglect. *Brain sciences*, *10*(6), 323. https://doi.org/https://doi.org/10.3390/brainsci10060323

Holmes, G. (1918). Disturbances of Vision by Cerebral Lesions. *British Journal of Ophthalmology*, *2*(7), 353-384. https://www.ncbi.nlm.nih.gov/pubmed/18167806

Hooge, I. T., Niehorster, D. C., Nyström, M., Andersson, R., & Hessels, R. S. (2018). Is human classification by experienced untrained observers a gold standard in fixation detection? *Behavior Research Methods*, *50*(5), 1864-1881. https://doi.org/https://doi.org/10.3758/s13428-017-0955-x

Hooge, I. T., Niehorster, D. C., Nyström, M., Andersson, R., & Hessels, R. S. (2021). Correction to:"Is human classification by experienced untrained observers a gold standard in fixation detection?". *Behavior Research Methods*, 1-2. https://doi.org/https://doi.org/10.3758/s13428-017-0955-x

Howard, C., & Rowe, F. J. (2018). Adaptation to poststroke visual field loss: A systematic review. *Brain and behavior*, *8*(8), e01041. https://doi.org/10.1002/brb3.1041

Huxlin, K. R. (2004). Training-induced Recovery of Visual Motion Perception after Extrastriate Cortical Damage in the Adult Cat. *Cerebral Cortex*, *14*(1), 81-90. https://doi.org/10.1093/cercor/bhg106

Huxlin, K. R., Martin, T., Kelly, K., Riley, M., Friedman, D. I., Burgin, W. S., & Hayhoe, M. (2009). Perceptual relearning of complex visual motion after V1 damage in humans. *Journal of Neuroscience*, *29*(13), 3981-3991. https://doi.org/10.1523/JNEUROSCI.4882-08.2009

Ishiai, S., Furukawa, T., & Tsukagoshi, H. (1987). Eye-fixation patterns in homonymous hemianopia and unilateral spatial neglect. *Neuropsychologia*, *25*(4), 675-679. https://www.ncbi.nlm.nih.gov/pubmed/3658150

Jacquin-Courtois, S., Bays, P. M., Salemme, R., Leff, A. P., & Husain, M. (2013). Rapid compensation of visual search strategy in patients with chronic visual field defects. *Cortex*, *49*(4), 994-1000. https://doi.org/10.1016/j.cortex.2012.03.025

Jenkinson, P. M., Preston, C., & Ellis, S. J. (2011). Unawareness after stroke: a review and practical guide to understanding, assessing, and managing anosognosia for hemiplegia. *Journal of Clinical Experimental Neuropsychology*, *33*(10), 1079-1093. https://doi.org/https://doi.org/10.1080/13803395.2011.596822

Johannsen, L., Ackermann, H., & Karnath, H.-O. (2003). Lasting amelioration of spatial neglect by treatment with neck muscle vibration even without concurrent training. *Journal of Rehabilitation Medicine*, *35*(6), 249-253. https://doi.org/10.1080/16501970310009972

Jonas, J. B., Gusek, G. C., & Fernández, M. C. (1991). Correlation of the blind spot size to the area of the optic disk and parapapillary atrophy. *American journal of ophthalmology*, *111*(5), 559-565. https://doi.org/https://doi.org/10.1016/S0002-9394(14)73698-0

Karnath, H.-O. (2001). New insights into the functions of the superior temporal cortex. *Nature Reviews Neuroscience*, *2*(8), 568-576. https://doi.org/https://doi.org/10.1038/35086057

Karnath, H.-O., & Dieterich, M. (2006). Spatial neglect—a vestibular disorder? *Brain*, *129*(2), 293-305. https://doi.org/https://doi.org/10.1093/brain/awh698

Karnath, H.-O., Fetter, M., & Dichgans, J. (1996). Ocular exploration of space as a function of neck proprioceptive and vestibular input—observations in normal subjects and patients with spatial neglect after parietal lesions. *Experimental brain research*, *109*(2), 333-342. https://doi.org/https://doi.org/10.1007/BF00231791

Karnath, H.-O., Niemeier, M., & Dichgans, J. (1998). Space exploration in neglect. *Brain*, *121*(12), 2357-2367. https://doi.org/ https://doi.org/10.1093/brain/121.12.2357

Karnath, H.-O., Rennig, J., Johannsen, L., & Rorden, C. (2011). The anatomy underlying acute versus chronic spatial neglect: a longitudinal study. *Brain*, *134*(3), 903-912.

Kasten, E., Wüst, S., Behrens-Baumann, W., & Sabel, B. A. (1998). Computer-based training for the treatment of partial blindness. *Nature medicine*, *4*(9), 1083-1087. https://doi.org/10.1038/2079

Kaufmann, B. C., Knobel, S. E. J., Nef, T., Müri, R. M., Cazzoli, D., & Nyffeler, T. (2020). Visual exploration area in neglect: a new analysis method for video-oculography data based on foveal vision. *Frontiers in Neuroscience*, *13*, 1412. https://doi.org/https://doi.org/10.3389/fnins.2019.01412

Keller, I., & Lefin-Rank, G. (2010). Improvement of visual search after audiovisual exploration training in hemianopic patients. *Neurorehabilitation and neural repair*, *24*(7), 666-673. https://doi.org/10.1177/1545968310372774

Kerkhoff, G. (2001). Spatial hemineglect in humans. *Progress in Neurobiology*, *63*(1), 1-27. https://doi.org/https://doi.org/10.1016/S0301-0082(00)00028-9

Kerkhoff, G. (2002). Neue Perspektiven in der Behandlung von Patienten mit multimodalem Neglect. *Ergotherapie & Rehabilitation*, 6-14.

Kerkhoff, G., Munssinger, U., Haaf, E., Eberle-Strauss, G., & Stogerer, E. (1992). Rehabilitation of homonymous scotomata in patients with postgeniculate damage of the visual system: saccadic compensation training. *Restorative neurology and neuroscience*, *4*(4), 245-254. https://doi.org/10.3233/RNN-1992-4402

Kerkhoff, G., & Schenk, T. (2012). Rehabilitation of neglect: an update. *Neuropsychologia*, *50*(6), 1072-1079. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2012.01.024

Koo, T. K., & Li, M. Y. (2016). A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *Journal of chiropractic medicine*, *15*(2), 155-163. https://doi.org/https://doi.org/10.1016/j.jcm.2016.02.012

Lalkhen, A. G., & McCluskey, A. (2008). Clinical tests: sensitivity and specificity. *Continuing Education in Anaesthesia Critical Care & Pain*, *8*(6), 221-223. https://doi.org/https://doi.org/10.1093/bjaceaccp/mkn041

Lane, A. R., Smith, D. T., Ellison, A., & Schenk, T. (2010). Visual exploration training is no better than attention training for treating hemianopia. *Brain*, *133*(Pt 6), 1717-1728. https://doi.org/10.1093/brain/awq088

Larcombe, S. J., Kulyomina, Y., Antonova, N., Ajina, S., Stagg, C. J., Clatworthy, P. L., & Bridge, H. (2018). Visual training in hemianopia alters neural activity in the absence of behavioural improvement: a pilot study. *Ophthalmic and Physiological Optics*, *38*(5), 538-549. https://doi.org/https://doi.org/10.1111/opo.12584

Leh, S. E., Mullen, K. T., & Ptito, A. (2006). Absence of S-cone input in human blindsight following hemispherectomy. *European Journal of Neuroscience*, *24*(10), 2954-2960. https://doi.org/ https://doi.org/10.1111/j.1460-9568.2006.05178.x

Lewald, J., Peters, S., Tegenthoff, M., & Hausmann, M. (2009). Dissociation of auditory and visual straight ahead in hemianopia. *Brain research*, *1287*, 111-117. https://doi.org/https://doi.org/10.1016/j.brainres.2009.06.085

Losier, B. J., & Klein, R. M. (2001). A review of the evidence for a disengage deficit following parietal lobe damage. *Neuroscience & Biobehavioral Reviews*, *25*(1), 1-13. https://doi.org/https://doi.org/10.1016/S0149-7634(00)00046-4

Marcel, A. J. (1998). Blindsight and shape perception: deficit of visual consciousness or of visual function? *Brain*, *121*(8), 1565-1588. https://doi.org/https://doi.org/10.1093/brain/121.8.1565

Marini, F., & Marzi, C. A. (2016). Gestalt perceptual organization of visual stimuli captures attention automatically: Electrophysiological evidence. *Frontiers in human neuroscience*, *10*, 446. https://doi.org/https://doi.org/10.3389/fnhum.2016.00446

Marshall, R. S., Chmayssani, M., O'Brien, K. A., Handy, C., & Greenstein, V. C. (2010). Visual field expansion after visual restoration therapy. *Clinical Rehabilitation*, *24*(11), 1027-1035. https://doi.org/10.1177/0269215510362323

Marzi, C. A., Mancini, F., Metitieri, T., & Savazzi, S. (2009). Blindsight following visual cortex deafferentation disappears with purple and red stimuli: A case study. *Neuropsychologia*, *47*(5), 1382-1385. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2009.01.023

Marzi, C. A., Tassinari, G., Aglioti, S., & Lutzemberger, L. (1986). Spatial summation across the vertical meridian in hemianopics: a test of blindsight. *Neuropsychologia*, *24*(6), 749-758. https://www.ncbi.nlm.nih.gov/pubmed/3808284

Mazzi, C., Bagattini, C., & Savazzi, S. (2016). Blind-Sight vs. Degraded-Sight: Different Measures Tell a Different Story. *Frontiers in psychology*, *7*, 901. https://doi.org/10.3389/fpsyg.2016.00901

Mazzi, C., Tagliabue, C. F., Mazzeo, G., & Savazzi, S. (2018). Reliability in reporting perceptual experience: Behaviour and electrophysiology in hemianopic patients. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2018.01.017

McIntosh, R. D., Ietswaart, M., & Milner, A. D. (2017). Weight and see: Line bisection in neglect reliably measures the allocation of attention, but not the perception of length. *Neuropsychologia*, *106*, 146-158. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2017.09.014

McIntosh, R. D., Schindler, I., Birchall, D., & Milner, A. D. (2005). Weights and measures: A new look at bisection behaviour in neglect. *Cognitive brain research*, *25*(3), 833-850. https://doi.org/https://doi.org/10.1016/j.cogbrainres.2005.09.008

Menozzi, M., Näpflin, U., & Krueger, H. (1999). CRT versus LCD: A pilot study on visual performance and suitability of two display technologies for use in office work. *Displays*, *20*(1), 3-10.

Milner, A., & Goodale, M. (1995). *The visual brain in action*. Oxford University Press New York.

Milner, A., & Goodale, M. (2008). Two visual systems re-viewed. *Neuropsychologia*, *46*(3), 774-785. https://doi.org/10.1016/j.neuropsychologia.2007.10.005

Mograbi, D. C., & Morris, R. G. (2018). Anosognosia. *Cortex*, *103*, 385-386. https://doi.org/https://doi.org/10.1016/j.cortex.2018.04.001

Müller-Oehring, E. M., Kasten, E., Poggel, D. A., Schulte, T., Strasburger, H., & Sabel, B. A. (2003). Neglect and hemianopia superimposed. *Journal of Clinical Experimental Neuropsychology*, *25*(8), 1154-1168. https://doi.org/https://doi.org/10.1076/jcen.25.8.1154.16727

Müller-Oehring, E. M., Schulte, T., Kasten, E., Poggel, D. A., Müller, I., Wüstenberg, T., & Sabel, B. A. (2009). Parallel interhemispheric processing in hemineglect: Relation to visual field defects. *Neuropsychologia*, *47*(12), 2397-2408. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2009.04.014

Nelles, G., Esser, J., Eckstein, A., Tiede, A., Gerhard, H., & Diener, H. C. (2001). Compensatory visual field training for patients with hemianopia after stroke. *Neuroscience Letters*, *306*(3), 189-192. https://www.ncbi.nlm.nih.gov/pubmed/11406327

Nuthmann, A., & Matthias, E. (2014). Time course of pseudoneglect in scene viewing. *Cortex*, *52*, 113-119. https://doi.org/https://doi.org/10.1016/j.cortex.2013.11.007

Ong, Y. H., Jacquin-Courtois, S., Gorgoraptis, N., Bays, P. M., Husain, M., & Leff, A. P. (2015). Eye-Search: A web-based therapy that improves visual search in hemianopia. *Annals of Clinical and Translational Neurology*, *2*(1), 74-78. https://doi.org/10.1002/acn3.154

Ouimet, C., Jolicœur, P., Miller, J., Ptito, A., Paggi, A., Foschi, N., Ortenzi, A., & Lassonde, M. (2009). Sensory and motor involvement in the enhanced redundant target effect: A study comparing anterior-and totally split-brain individuals. *Neuropsychologia*, *47*(3), 684-692. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2008.11.023

Overgaard, M. (2011). Visual experience and blindsight: a methodological review. *Experimental brain research*, *209*(4), 473-479. https://doi.org/10.1007/s00221-011-2578-2

Pambakian, A. L., Wooding, D. S., Patel, N., Morland, A. B., Kennard, C., & Mannan, S. K. (2000). Scanning the visual world: a study of patients with homonymous hemianopia. *Journal of Neurology, Neurosurgery & Psychiatry*, *69*(6), 751-759. https://www.ncbi.nlm.nih.gov/pubmed/11080227

Panico, F., Rossetti, Y., & Trojano, L. (2020). On the mechanisms underlying Prism Adaptation: A review of neuro-imaging and neuro-stimulation studies. *Cortex*, *123*, 57-71. https://doi.org/https://doi.org/10.1016/j.cortex.2019.10.003

Paramei, G. V., Favrod, O., Sabel, B. A., & Herzog, M. H. (2017). Pathological completion in the intact visual field of hemianopia patients. *Visual Cognition*, *25*(1-3), 169-183. https://doi.org/https://doi.org/10.1080/13506285.2017.1352056

Pasik, T., & Pasik, P. (1971). The visual world of monkeys deprived of striate cortex: effective stimulus parameters and the importance of the accessory optic system. *Vision research*, *11*, 419-IN455. https://doi.org/https://doi.org/10.1016/0042-6989(71)90055-1

Pettorossi, V. E., Panichi, R., Botti, F. M., Biscarini, A., Filippi, G. M., & Schieppati, M. (2015). Long-lasting effects of neck muscle vibration and contraction on self-motion perception of vestibular origin. *Clinical Neurophysiology*, *126*(10), 1886-1900. https://doi.org/https://doi.org/10.1016/j.clinph.2015.02.057

Pitteri, M., Kerkhoff, G., Keller, I., Meneghello, F., & Priftis, K. (2015). Extra-powerful on the visuo-perceptual space, but variable on the number space: Different effects of optokinetic stimulation in neglect patients. *Journal of neuropsychology*, *9*(2), 299-318. https://doi.org/ https://doi.org/10.1111/jnp.12051

Pizzamiglio, L., Fasotti, L., Jehkonen, M., Antonucci, G., Magnotti, L., Boelen, D., & Asa, S. (2004). The use of optokinetic stimulation in rehabilitation of the hemineglect disorder. *Cortex*, *40*(3), 441-450. https://doi.org/https://doi.org/10.1016/S0010-9452(08)70138-2

Pollock, A., Hazelton, C., Henderson, C. A., Angilley, J., Dhillon, B., Langhorne, P., Livingstone, K., Munro, F. A., Orr, H., Rowe, F., & Shahani, U. (2011). Interventions for Visual Field Defects in Patients With Stroke. *Stroke*, *43*(4), e37-e38. https://doi.org/10.1161/strokeaha.111.639815

Pöppel, E., Held, R., & Frost, D. (1973). Residual visual function after brain wounds involving the central visual pathways in man. *Nature*, *243*(5405), 295-296. https://doi.org/https://doi.org/10.1038/243295a0

Poppelreuter, W. (1917). *Die psychischen Schädigungen durch Kopfschu im Kriege 1914/1916 Vol. I: Die Störungen der niederen und höheren Sehleistungen durch Verletzungen des Okzipitalhirns.* Voss.

Portengen, B. L., Roelofzen, C., Porro, G. L., Imhof, S. M., Fracasso, A., & Naber, M. (2021). Blind spot and visual field anisotropy detection with flicker pupil perimetry across brightness and task variations. *Vision research*, *178*, 79-85. https://doi.org/https://doi.org/10.1016/j.visres.2020.10.005

Raab, D. H. (1962). Statistical facilitation of simple reaction times. *Transactions of the New York Academy of Sciences*, *24*, 574-590.

Redding, G. M., & Wallace, B. (2006). Generalization of prism adaptation. *Journal of Experimental Psychology: Human Perception Performance*, *32*(4), 1006. https://doi.org/https://doi.org/10.1037/0096-1523.32.4.1006

Reinhard, J., Schreiber, A., Schiefer, U., Kasten, E., Sabel, B. A., Kenkel, S., Vonthein, R., & Trauzettel-Klosinski, S. (2005). Does visual restitution training change absolute homonymous visual field defects? A fundus controlled study. *British Journal of Ophthalmology*, *89*(1), 30-35. https://doi.org/10.1136/bjo.2003.040543

Richards, W. (1973). Visual processing in scotomata. *Experimental brain research*, *17*(4), 333-347. https://doi.org/https://doi.org/10.1007/BF00234098

Riddoch, G. (1917). DISSOCIATION OF VISUAL PERCEPTIONS DUE TO OCCIPITAL INJURIES WITH ESPECIALL REFERENCE TO APPRECIATION OF MOVEMENT. *Brain*, *40*(1), 15-57. https://doi.org/https://doi.org/10.1093/brain/40.1.15

Rizzolatti, G., Riggio, L., Dascola, I., & Umiltá, C. (1987). Reorienting attention across the horizontal and vertical meridians: evidence in favor of a premotor theory of attention. *Neuropsychologia*, *25*(1), 31-40. https://doi.org/https://doi.org/10.1016/0028-3932(87)90041-8

Robertson, I. H., & Manly, T. (2002). Cognitive routes to the rehabilitation of unilateral neglect. In H. O. Karnath, A. D. Milner, & G. Vallar (Eds.), *The cognitive and neural bases of spatial neglect* (pp. 365). Oxford University Press.

Ross, A. I., Schenk, T., Billino, J., Macleod, M. J., & Hesse, C. (2018). Avoiding unseen obstacles: Subcortical vision is not sufficient to maintain normal obstacle avoidance behaviour during reaching. *Cortex*, *98*, 177-193. https://doi.org/https://doi.org/10.1016/j.cortex.2016.09.010

Roth, T., Sokolov, A. N., Messias, A., Roth, P., Weller, M., & Trauzettel-Klosinski, S. (2009). Comparing explorative saccade and flicker training in hemianopia: a randomized controlled study. *Neurology*, *72*(4), 324-331. https://doi.org/10.1212/01.wnl.0000341276.65721.f2

Rowe, F. J., Conroy, E. J., Bedson, E., Cwiklinski, E., Drummond, A., Garcia-Finana, M., Howard, C., Pollock, A., Shipman, T., Dodridge, C., MacIntosh, C., Johnson, S., Noonan, C., Barton, G., & Sackley, C. (2017). A pilot randomized controlled trial comparing effectiveness of prism glasses, visual search training and standard care in hemianopia. *Acta Neurologica Scandinavica*, *136*(4), 310-321. https://doi.org/10.1111/ane.12725

Rowe, F. J., Wright, D., Brand, D., Jackson, C., Harrison, S., Maan, T., Scott, C., Vogwell, L., Peel, S., Akerman, N., Dodridge, C., Howard, C., Shipman, T., Sperring, U., Macdiarmid, S., & Freeman, C. (2013). A prospective profile of visual field loss following stroke: prevalence, type, rehabilitation, and outcome. *BioMed research international*, *2013*, 719096. https://doi.org/10.1155/2013/719096

Rudolph, K. K., & Pasternak, T. (1996). Lesions in cat lateral suprasylvian cortex affect the perception of complex motion. *Cerebral Cortex*, *6*(6), 814-822. https://doi.org/https://doi.org/10.1093/cercor/6.6.814

Sahraie, A., Trevethan, C. T., & MacLeod, M. J. (2008). Temporal properties of spatial channel of processing in hemianopia. *Neuropsychologia*, *46*(3), 879-885. https://doi.org/10.1016/j.neuropsychologia.2007.11.008

Sahraie, A., Trevethan, C. T., MacLeod, M. J., Murray, A. D., Olson, J. A., & Weiskrantz, L. (2006). Increased sensitivity after repeated stimulation of residual spatial channels in blindsight. *Proceedings of the National Academy of Sciences*, *103*(40), 14971-14976. https://doi.org/10.1073/pnas.0607073103

Sahraie, A., Trevethan, C. T., Macleod, M. J., Weiskrantz, L., & Hunt, A. R. (2013). The continuum of detection and awareness of visual stimuli within the blindfield: from blindsight to the sighted-sight. *Investigative ophthalmology & visual science*, *54*(5), 3579-3585. https://doi.org/10.1167/iovs.12-11231

Sahraie, A., Trevethan, C. T., Weiskrantz, L., Olson, J., MacLeod, M. J., Murray, A. D., Dijkhuizen, R. S., Counsell, C., & Coleman, R. (2003). Spatial channels of visual processing in cortical blindness. *European Journal of Neuroscience*, *18*(5), 1189-1196. https://doi.org/10.1046/j.1460-9568.2003.02853.x

Sahraie, A., Weiskrantz, L., Trevethan, C. T., Cruce, R., & Murray, A. D. (2002). Psychophysical and pupillometric study of spatial channels of visual processing in blindsight. *Experimental brain research*, *143*(2), 249-256. https://doi.org/10.1007/s00221-001-0989-1

Saionz, E. L., Tadin, D., Melnick, M. D., & Huxlin, K. R. (2020). Functional preservation and enhanced capacity for visual restoration in subacute occipital stroke. *Brain*, *143*(6), 1857-1872. https://doi.org/10.1093/brain/awaa128

Saj, A., Honore, J., Braem, B., Bernati, T., & Rousseaux, M. (2012). Time since stroke influences the impact of hemianopia and spatial neglect on visual-spatial tasks. *Neuropsychology*, *26*(1), 37-44. https://doi.org/10.1037/a0025733

Salillas, E., Granà, A., Juncadella, M., Rico, I., & Semenza, C. (2009). Leftward motion restores number space in neglect. *Cortex*, *45*(6), 730-737. https://doi.org/https://doi.org/10.1016/j.cortex.2008.09.006

Savazzi, S., & Marzi, C. A. (2004). The superior colliculus subserves interhemispheric neural summation in both normals and patients with a total section or agenesis of the corpus callosum. *Neuropsychologia*, *42*(12), 1608-1618. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2004.04.011

Savina, O., & Guitton, D. (2018). The primitive retino-tecto-reticular pathway is functional in hemidecorticate patients. *Current Biology*, *28*(20), R1184-R1186. https://doi.org/10.1016/j.cub.2018.09.006

Schärli, H., Harman, A. M., & Hogben, J. H. (1999). Blindsight in subjects with homonymous visual field defects. *Journal of Cognitive Neuroscience*, *11*(1), 52-66. https://doi.org/https://doi.org/10.1162/089892999563247

Schindler, I., Kerkhoff, G., Karnath, H.-O., Keller, I., & Goldenberg, G. (2002). Neck muscle vibration induces lasting recovery in spatial neglect. *Journal of Neurology, Neurosurgery & Psychiatry*, *73*(4), 412-419. https://doi.org/http://dx.doi.org/10.1136/jnnp.73.4.412

Schmidt, L., Utz, K. S., Depper, L., Adams, M., Schaadt, A.-K., Reinhart, S., & Kerkhoff, G. (2013). Now you feel both: galvanic vestibular stimulation induces lasting improvements in the rehabilitation of chronic tactile extinction. *Frontiers in human neuroscience*, *7*, 90. https://doi.org/https://doi.org/10.3389/fnhum.2013.00090

Schnider, A., Durbec, V. B., & Ptak, R. (2011). Absence of visual feedback abolishes expression of hemispatial neglect in self-guided spatial completion. *Journal of Neurology, Neurosurgery & Psychiatry*, *82*(11), 1279-1282. https://doi.org/http://dx.doi.org/10.1136/jnnp-2011-300656

Schröder, A., Wist, E. R., & Hömberg, V. (2008). TENS and optokinetic stimulation in neglect therapy after cerebrovascular accident: a randomized controlled study. *European journal of neurology*, *15*(9), 922-927. https://doi.org/https://doi.org/10.1111/j.1468-1331.2008.02229.x

Schuett, S., Heywood, C. A., Kentridge, R. W., Dauner, R., & Zihl, J. (2012). Rehabilitation of reading and visual exploration in visual field disorders: transfer or specificity? *Brain*, *135*(Pt 3), 912-921. https://doi.org/10.1093/brain/awr356

Serino, A., Barbiani, M., Rinaldesi, M. L., & Ladavas, E. (2009). Effectiveness of prism adaptation in neglect rehabilitation: a controlled trial study. *Stroke*, *40*(4), 1392-1398. https://doi.org/https://doi.org/10.1161/STROKEAHA.108.530485

Smith, D. T., Ball, K., Ellison, A., & Schenk, T. (2010). Deficits of reflexive attention induced by abduction of the eye. *Neuropsychologia*, *48*(5), 1269-1276. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2009.12.028

Smith, D. T., & Schenk, T. (2012). The premotor theory of attention: time to move on? *Neuropsychologia*, *50*(6), 1104-1114. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2012.01.025

Smith, D. T., Schenk, T., & Rorden, C. (2012). Saccade preparation is required for exogenous attention but not endogenous attention or IOR. *Journal of Experimental Psychology: Human Perception Performance*, *38*(6), 1438. https://doi.org/https://doi.org/10.1037/a0027794

Sprenger, A., Kömpf, D., & Heide, W. (2002). Visual search in patients with left visual hemineglect. *Progress in brain research*, *140*, 395-416. https://doi.org/https://doi.org/10.1016/S0079-6123(02)40065-9

Stoerig, P. (2010). Cueless blindsight. *Frontiers in human neuroscience*, *3*, 74. https://doi.org/10.3389/neuro.09.074.2009

Stoerig, P., & Cowey, A. (1991). Increment-threshold spectral sensitivity in blindsight: evidence for colour opponency. *Brain*, *114*(3), 1487-1512. https://doi.org/https://doi.org/10.1093/brain/114.3.1487

Stoerig, P., Hübner, M., & Pöppel, E. (1985). Signal detection analysis of residual vision in a field defect due to a post-geniculate lesion. *Neuropsychologia*, *23*(5), 589-599. https://doi.org/https://doi.org/10.1016/0028-3932(85)90061-2

Stone, S., Patel, P., Greenwood, R., & Halligan, P. (1992). Measuring visual neglect in acute stroke and predicting its recovery: the visual neglect recovery index. *Journal of*

Neurology, Neurosurgery & Psychiatry, *55*(6), 431-436. https://doi.org/http://dx.doi.org/10.1136/jnnp.55.6.431

Striemer, C. L., Chapman, C. S., & Goodale, M. A. (2009). "Real-time" obstacle avoidance in the absence of primary visual cortex. *Proceedings of the National Academy of Sciences*, *106*(37), 15996-16001. https://doi.org/10.1073/pnas.0905549106

Striemer, C. L., Chapman, C. S., & Goodale, M. A. (2018). The role of non-conscious visual processing in obstacle avoidance: A commentary on Ross et al. (2016). *Cortex*, *98*, 269-275. https://doi.org/10.1016/j.cortex.2017.03.024

Szalados, R., Leff, A. P., & Doogan, C. E. (2021). The clinical effectiveness of Eye-Search therapy for patients with hemianopia, neglect or hemianopia and neglect. *Neuropsychological Rehabilitation*, 1-12. https://doi.org/https://doi.org/10.1080/09602011.2020.1751662

Theeuwes, J. (1994). The effects of location cuing on redundant-target processing. *Psychological Research*, *57*(1), 15-19. https://doi.org/https://doi.org/10.1007/BF00452991

Trevethan, C. T., Sahraie, A., & Weiskrantz, L. (2007). Can blindsight be superior to 'sighted-sight'? *Cognition*, *103*(3), 491-501. https://doi.org/10.1016/j.cognition.2006.04.011

Utz, K. S., Keller, I., Kardinal, M., & Kerkhoff, G. (2011). Galvanic vestibular stimulation reduces the pathological rightward line bisection error in neglect—a sham stimulation-controlled study. *Neuropsychologia*, *49*(5), 1219-1225. https://doi.org/https://doi.org/10.1016/j.neuropsychologia.2011.02.046

Vaina, L. M., Soloviev, S., Calabro, F. J., Buonanno, F., Passingham, R., & Cowey, A. (2014). Reorganization of retinotopic maps after occipital lobe infarction. *Journal of Cognitive Neuroscience*, *26*(6), 1266-1282. https://doi.org/10.1162/jocn_a_00538

Vilimovsky, T., Chen, P., Hoidekrova, K., Petioky, J., & Harsa, P. (2021). Prism adaptation treatment to address spatial neglect in an intensive rehabilitation program: A randomized pilot and feasibility trial. *PLoS One*, *16*(1), e0245425. https://doi.org/https://doi.org/10.1371/journal.pone.0245425

Volkening, K., Kerkhoff, G., & Keller, I. (2018). Effects of repetitive galvanic vestibular stimulation on spatial neglect and verticality perception—a randomised sham-controlled trial. *Neuropsychological Rehabilitation*, *28*(7), 1179-1196. https://doi.org/https://doi.org/10.1080/09602011.2016.1248446

von der Gablentz, J., Könemund, I., Sprenger, A., Heide, W., Heldmann, M., Helmchen, C., & Machner, B. (2019). Brain activations during optokinetic stimulation in acute right-hemisphere stroke patients and hemispatial neglect: an fMRI study. *Neurorehabilitation and neural repair*, *33*(7), 581-592. https://doi.org/https://doi.org/10.1177/1545968319855038

Walker, R., Findlay, J. M., Young, A. W., & Welch, J. (1991). Disentangling neglect and hemianopia. *Neuropsychologia*, *29*(10), 1019-1027. https://doi.org/https://doi.org/10.1016/0028-3932(91)90065-G

Walle, K. M., Nordvik, J. E., Becker, F., Espeseth, T., Sneve, M. H., & Laeng, B. (2019). Unilateral neglect post stroke: Eye movement frequencies indicate directional hypokinesia while fixation distributions suggest compensational mechanism. *Brain and behavior*, *9*(1), e01170. https://doi.org/ https://doi.org/10.1002/brb3.1170

Weiskrantz, L. (1999). *Consciousness lost and found: A neuropsychological exploration*. OUP Oxford.

Weiskrantz, L., Warrington, E. K., Sanders, M. D., & Marshall, J. (1974). Visual capacity in the hemianopic field following a restricted occipital ablation. *Brain*, *97*(4), 709-728. https://www.ncbi.nlm.nih.gov/pubmed/4434190

Wilson, M. E. (1968). The detection of light scattered from stimuli in impaired regions of the visual field. *Journal of Neurology, Neurosurgery & Psychiatry*, *31*(5), 509. https://doi.org/10.1136/jnnp.31.5.509

Woutersen, K., Geuzebroek, A. C., van den Berg, A. V., & Goossens, J. (2020). Useful Field of View Performance in the Intact Visual Field of Hemianopia Patients. *Investigative ophthalmology & visual science*, *61*(5), 43-43. https://doi.org/https://doi.org/10.1167/iovs.61.5.43

Wüst, S., Kasten, E., & Sabel, B. A. (2002). Blindsight after optic nerve injury indicates functionality of spared fibers. *Journal of Cognitive Neuroscience*, *14*(2), 243-253. https://doi.org/https://doi.org/10.1162/089892902317236876

Zhang, X., Kedar, S., Lynn, M. J., Newman, N. J., & Biousse, V. (2006). Natural history of homonymous hemianopia. *Neurology*, *66*(6), 901-905. https://doi.org/10.1212/01.wnl.0000203338.54323.22

Zihl, J. (1995). Visual scanning behavior in patients with homonymous hemianopia. *Neuropsychologia*, *33*(3), 287-303. https://www.ncbi.nlm.nih.gov/pubmed/7791997

Zihl, J. (2010). *Rehabilitation of visual disorders after brain injury* (2 ed.). Psychology Press.

Zihl, J., & Kennard, C. (2003). Disorders of higher visual function. In *Neurological Disorders* (pp. 255-263). Elsevier.

Zihl, J., Samann, P., Schenk, T., Schuett, S., & Dauner, R. (2009). On the origin of line bisection error in hemianopia. *Neuropsychologia*, *47*(12), 2417-2426. https://doi.org/10.1016/j.neuropsychologia.2009.04.009

Zihl, J., & von Cramon, D. (1979). Restitution of visual function in patients with cerebral blindness. *Journal of Neurology, Neurosurgery & Psychiatry*, *42*(4), 312-322. https://www.ncbi.nlm.nih.gov/pubmed/458478

Zihl, J., & von Cramon, D. (1985). Visual field recovery from scotoma in patients with postgeniculate damage. A review of 55 cases. *Brain*, *108 (Pt 2)*, 335-365. https://www.ncbi.nlm.nih.gov/pubmed/4005527

Zihl, J., & Werth, R. (1984). Contributions to the study of “blindsight”—I. Can stray light account for saccadic localization in patients with postgeniculate field defects? *Neuropsychologia*, *22*(1), 1-11. https://doi.org/https://doi.org/10.1016/0028-3932(84)90002-2

List of Publications

Friedrich, E. V., Berger, B., Minarik, T., Schmid, D., Peylo, C., & Sauseng, P. (2019). No enhancing effect of fronto-medial tDCS on working memory processes. *Journal of Cognitive Enhancement*, 3(4), 416-424. https://doi-org.emedien.ub.uni-muenchen.de/10.1007/s41465-019-00136-5

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Author contributions

Friedrich, E. V., Berger, B., Minarik, T., Schmid, D., Peylo, C., & Sauseng, P. (2019). No enhancing effect of fronto-medial tDCS on working memory processes. *Journal of Cognitive Enhancement*, 3(4), 416-424. https://doi-org.emedien.ub.uni-muenchen.de/10.1007/s41465-019-00136-5

Elisabeth V. C. Friedrich:	Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration.
Barbara Berger:	Conceptualization, Methodology, Software, Formal analysis, Data curation, Visualization, Writing - review & editing
Tamas Minarik:	Software, Formal analysis, Data curation, Writing - review & editing
Doris Schmid:	Investigation, Data curation, Writing - review & editing
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Ludwig, K., Schmid, D., & Schenk, T. (2020). Gaze-contingent stimulus removal leads to subsequent changes in overt attentional allocation. *Neuropsychologia*, 139, 107297. https://doi.org/10.1016/j.neuropsychologia.2019.107297

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Doris Schmid:	Methodology, Software, Investigation, Data curation, Writing - review & editing.
Thomas Schenk:	Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Schmid, D., Schneider, S. & Schenk, T. (in preparation). How to test blindsight without light scatter artefacts?

Doris Schmid:	Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration.
Sebastian Schneider:	Investigation, Data curation, Writing - review & editing, Visualization
Thomas Schenk:	Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Schmid, D., Hesse, C., & Schenk, T. (in preparation). Blindsight and residual vision: How reliable is the redundant target effect as a diagnostic tool?

Doris Schmid:	Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration.
Constanze Hesse:	Methodology, Writing - review & editing
Thomas Schenk:	Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Eidesstattliche Versicherung/ Affidavit

Hiermit versichere ich an Eides statt, dass ich die vorliegende Dissertation *Sharpening our tool-kits for visual rehabilitation - An investigation into the diagnosis and treatment of patients with homonymous visual field defect or unilateral neglect* selbstständig angefertigt habe, mich außer der angegebenen keiner weiteren Hilfsmittel bedient und alle Erkenntnisse, die aus dem Schrifttum ganz oder annähernd übernommen sind, als solche kenntlich gemacht und nach ihrer Herkunft unter Bezeichnung der Fundstelle einzeln nachgewiesen habe.

I hereby confirm that the dissertation *Sharpening our tool-kits for visual rehabilitation - An investigation into the diagnosis and treatment of patients with homonymous visual field defect or unilateral neglect* is the result of my own work and that I have only used sources or materials listed and specified in the dissertation.

München, den 09. August 2021 Doris Schmid
Munich, 09. August 2021

Unterschrift signature