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Diagnosing and Treating Compressive-Optic-Neuropathy in Thyroid Eye Disease (TED-CON)

Habilitationsschrift

zum Erwerb der Venia Legendi für das Fach Augenheilkunde

vorgelegt von

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To my family

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Diagnosing Compressive-Optic-Neuropathy in Thyroid Eye Disease

1. Introduction

This cumulative postdoctoral thesis focuses on the topic of diagnosing optic nerve compression - a severe complication of Thyroid Eye Disease (TED). Beyond the analysis of the diagnostic methods, the publications included in thesis help us to detect subclinical cases and understand the treatment methods to preserve the vision in such patients.

Although observed rarely, optic nerve compression in TED (TED-CON) patients, or so-called dysthyroid optic neuropathy (DON), affects 4-8% of patients with the Graves' orbitopathy (GO). [1,2] GO is an immune-mediated inflammatory disease attributed to glycosaminoglycan depositions by fibroblasts into the retrobulbar tissues resulting in fibrosis. [3] The disease causes an enlargement of the extraocular muscles and increased volume of the orbital fat. [4] GO can be classified as mild, moderate to severe or sight threatening.[5] According to the Consensus Statement of the European Group on Graves' Orbitopathy (EUGOGO), sight-threatening GO is described as TED-CON and/or corneal breakdown requiring immediate intervention to preserve vision. [5]

Lack of standardised diagnostic criteria is a major impediment to timely diagnosis and treatment of TED-CON. Existing diagnostic tools, such as visual field (VF) examination, color vision, visual acuity tests, not only require patient cooperation but also are largely subjective, and easily influenced by coexisting corneal problems and motility of the eye (e.g., double vision) in patients with GO. Therefore, it is very challenging to detect patients with optic nerve compression and give them the best treatment for preserving their visual acuity.

The first line of treatment in TED-CON involves steroid-pulse treatment, also known as medical decompression. Severe cases of DON that do not respond to this initial therapy are often treated with surgical orbital decompression. In this postdoctoral thesis we identify diagnostic tools for detecting the disease in the subclinical phase and compare existing treatment methods of TED-CON in order to provide the best treatment to patients as early as possible.

2. Published own work on the topic:

2.1 Subclinical dysthyroid optic neuropathy: tritan deficiency as an early sign of dysthyroid optic neuropathy.

Aylin Garip Kuebler, Kathrin Halfter , Lukas Reznicek, Annemarie Klingenstein, Siegfried Priglinger, Christoph Hintschich

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doi:10.1136/bjophthalmol-2020-316433

Normal human vision is trichromatic and involves three types of cones sensitive to short (S), medium (M) and long (L) wavelengths, respectively. The red-green channel uses cones sensitive to L and M wavelengths, whereas the blue-yellow channel uses cones sensitive to S signals. [6] Pathologies on color vision can be congenital or acquired, with the latter occurring secondary to a pathology in the visual pathway. There is a broad spectrum of methods for assessing acquired color vision deficiency. In our case series, we used the color vision test by Arden.

Our goal in this paper was to identify potential pathological signs in patients prior to the DON diagnosis to detect the optic nerve compression as early as possible. We examined the medical charts of all patients with a definitive diagnosis of DON overseen by the Plastic and Reconstructive Surgery Section at the Department of Ophthalmology, Ludwig-Maximilians-University between 2008 and 2019. Our sample included 24 patients and 32 eyes. Our statistical analysis examined the data of the visit prior to the definitive diagnosis of DON, which was called the subclinical phase (V0), where the patients presented in our clinic due to worsening of their symptoms related to GO and/or due to the routine control examination in active GO cases. We documented and analysed the findings of the visit at the time of the DON diagnosis and compared them to the findings at the time of the subclinical phase.

Strikingly, we discovered that the earliest pathological sign in the subclinical cases was tritan deficiency in color vision test. In all cases but one, regardless of the VF defects, the tritan value was pathological (based on a threshold of 8%). Interestingly, this is the first publication to describe color vision findings in patients with DON. The mean tritan value was 19.12% (range 6.9–80.8%) at the time of the subclinical phase and 32.16% (range 6.3–100.0%) at the time of the diagnosis of DON. The sensitivity of the color vision test was 20% for protan and 96.67% for tritan in the subclinical phase. At the time of the definitive diagnosis of DON, the sensitivity of protan was 48.15% compared to 96.30% for tritan.

In this paper, we found changes to vision of blue-yellow (tritan) colors to be an early sign of DON resulting from the compression of the optic nerve in patients later diagnosed with the

disease. Crucially, these changes were observed even in patients with normal VF tests. Our data suggest that in cases of suspected but not yet diagnosed DON, a color vision test that can detect tritan deficiency is an essential tool for the adequate assessment, diagnosis and treatment of this condition.

2.2 A sensitive, new pathological indicator for Dysthyroid Optic Neuropathy: Tritan Deficiency, Ludwig-Maximilians-University Experience.

Aylin Garip Kuebler, Kathrin Halfter , Lukas Reznicek, Annemarie Klingenstein, Siegfried Priglinger, Günther Rudolph, Christoph Hintschich

Graefe's Archives for Clinical and Experimental Ophthalmology 2021; 259:3421-3426. doi:10.1007/s00417-021-05227-8

After discovering the importance of color vision, especially tritan deficiency in subclinical cases, in this research project, we investigated the sensitivity of the color vision test by Arden in patients with a definitive diagnosis of DON using a larger case series. In this observational, retrospective study, we included the medical records of 92 eyes (48 patients) with a diagnosis of DON between 2008 and 2019 in order to evaluate the full spectrum of findings from the color vision test by Arden. Thirty-five patients were female, and 13 patients were male. The mean age was 58.0 years (range: 34–79) at the time of the DON diagnosis.

Interestingly, in this case series, forty-one eyes displayed relatively good best-corrected visual acuity (BCVA) with ≤ 0.2 LogMAR, which is very good visual acuity for patients with optic nerve compression. We found a protan value exceeding the threshold of ≥ 8% in 57 eyes (30 patients) at the time of the diagnosis. The sensitivity of protan was 61.9% (95% CI 51.2–71.8%), while that of tritan was a striking 98.9% (95% CI 94.1–99.9%). We discovered one pathological sign, tritan deficiency (based on a threshold of ≥ 8%) consistently in all eyes but one at the time of the diagnosis, regardless of the visual field defects or any changes in BCVA. The diagnosis of DON is especially challenging for patients who display no or minimal change in BCVA and visual field (VF). This study evaluated color vision tests as an alternative tool for identifying neuro-ophthalmic pathology, which can be missed in tests for visual acuity or visual field.

This study presents evidence for the potential importance of tritan deficiency in the diagnosis of DON. Most importantly, we showed that tritan deficiency can help detect DON even in cases with little vision loss. A total of 17 DON patients (41 eyes) in our data had a relatively good BCVA score of ≤ 0.2 LogMAR, but they all showed pathological tritan values. Clinical diagnostics could use tritan tests to confirm a suspected DON diagnosis and also to potentially detect patients before they display any signs of vision loss.

Research suggests tritan deficiency to be one of the most common forms of acquired vision loss. Therefore, our results might be relevant to a broader area of diseases which cause changes in color vision especially tritan deficiency such as optic neuritis, macular diseases, media opacity, dominantly inherited juvenile optic atrophy (DIJOA), and amblyopia. [7,8] It is important to mention that there is a broad spectrum of hereditary diseases strongly related with blue-yellow deficiency such as DIJOA and congenital tritanopia. [8] For example, Almog et al. documented color vision loss as an outcome of optic neuropathy even among patients with a good-to-moderate visual acuity (VA).[7] This finding is all the more striking given that the authors rely on Ishihara plates for testing color vision, which is limited in identifying

acquired color deficiency. Although the focus of our study detailed above was on a different condition (DON) and relied on a different color vision test (by Arden), we observed a similar pattern. Ninety-one eyes (out of 92 eyes) in our data display pathological values of tritan, even the 41 eyes that had a relatively good BCVA of ≤ 0.2 LogMAR.

We conclude that tritan deficiency may indicate optic nerve compression in patients with DON.

2.3 Evaluation of visual evoked potentials in dysthyroid optic neuropathy.

Aylin Garip Kübler, Kathrin Halfter, Lukas Reznicek, Annemarie Klingenstein, Siegfried Priglinger, Günther Rudolph, and Christoph Hintschich

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In search of an objective method to detect patients with an optic nerve compression, in this study, we consider visual evoked potentials (VEP) and evaluate the findings of VEP and its usefulness in the diagnosis of DON.

Visual evoked potentials have been suggested as an alternative method for objective evaluation of optic neuropathy in patients with TED. VEP measures the change of the electrical signal in the occipital cortex in response to a visual stimulus. Theoretically, any disturbance or pathology along the visual pathway or the visual cortex should result in a prolongation of the latency and/or a decrease in the amplitude of the VEP.

Recent work has relied on two types of VEP in DON patients. Pattern-VEP captures the response to a checkerboard pattern stimulation, covering 15° of the visual field. Flash-VEP, by contrast, engages the entire retinal response to a flashlight stimulation (while potentially missing a localized abnormal response along the visual pathway). There are two major components of VEP reported to be affected in patients with optic neuropathy: P100 latency and P100 amplitude.[10]

Many studies have investigated the changes in VEP in patients with DON. Some studies have compared the *p*-VEP latency and amplitudes among TED patients with and without optic nerve compression, and a control group.[10-13] All of these studies report a significant prolongation of the P100 latency and decrease in P100 amplitudes in patients with optic nerve compression. While these comparisons are useful to understand the disease, their results are not immediately applicable to clinical decisions.

In this case series we observed 22 patients and 40 eyes. We included all the patients with an existing VEP examination, and a diagnosis of DON observed between (2010-2014) in our clinic.

All patients underwent a pattern-VEP (*p*-VEP). In cases with no reproducible responses to the p-VEP, we also performed a flash-VEP (f-VEP). 3 eyes of 3 patients had non-reproducible p-VEP documented (due to low BCVA); therefore, a f-VEP was performed instead. Surprisingly, in our case series, in almost half of the cases (43.2%, 16 out of 37 eyes with *p*-VEP) P100 latency was documented as normal. More strikingly, in 27 out of 37 eyes (72.97%), no pathology in P100 amplitudes could be detected. Even in cases with an optic disc swelling (12 out of 40 eyes), which is an important sign for optic nerve involvement, 4 eyes showed no prolongation of P100 latency with values completely in the normal range. Similarly, 8 of those 12 eyes indicated no reduced P100 amplitudes.

Our study had the advantage of detecting early-DON patients due to availability of CT findings and color vision tests for tritan deficiency. We observed 36 out of 40 eyes with a pathological tritan value and 33 eyes with an apical crowding as documented by a radiologist. This pattern could explain why 10 out of 16 eyes display a relatively good BCVA (≤0.2 LogMAR) among patients with normal p100 latency in pVEP. By contrast, in McKeag et al.'s research, 80% of the patients with a DON diagnosis had a BCVA ≤0.6 and 73% of the cases had an abnormal VEP latency. [14] Therefore, based on the rates of apical crowding detected in CT and tritan deficiency observed in color vision test, we speculate that our study might be capturing patients in early or subclinical phase of optic nerve compression.

In light of this research, it is possible to conclude that in patients with a relative good BCVA (defined as ≤0.2 LogMAR), VEP might miss the cases with optic nerve compression. Our findings should alert clinicians to shortcomings of VEP for detecting optic nerve compression in DON patients especially those with a relatively good BCVA.

2.4 Classification of the Visual Field Defects in Thyroid Eye-Disease-Compressive Optic Neuropathy according to American Ophthalmological Society (AOS) Thesis in 100 Eyes; Ludwig-Maximilians-University Experience.

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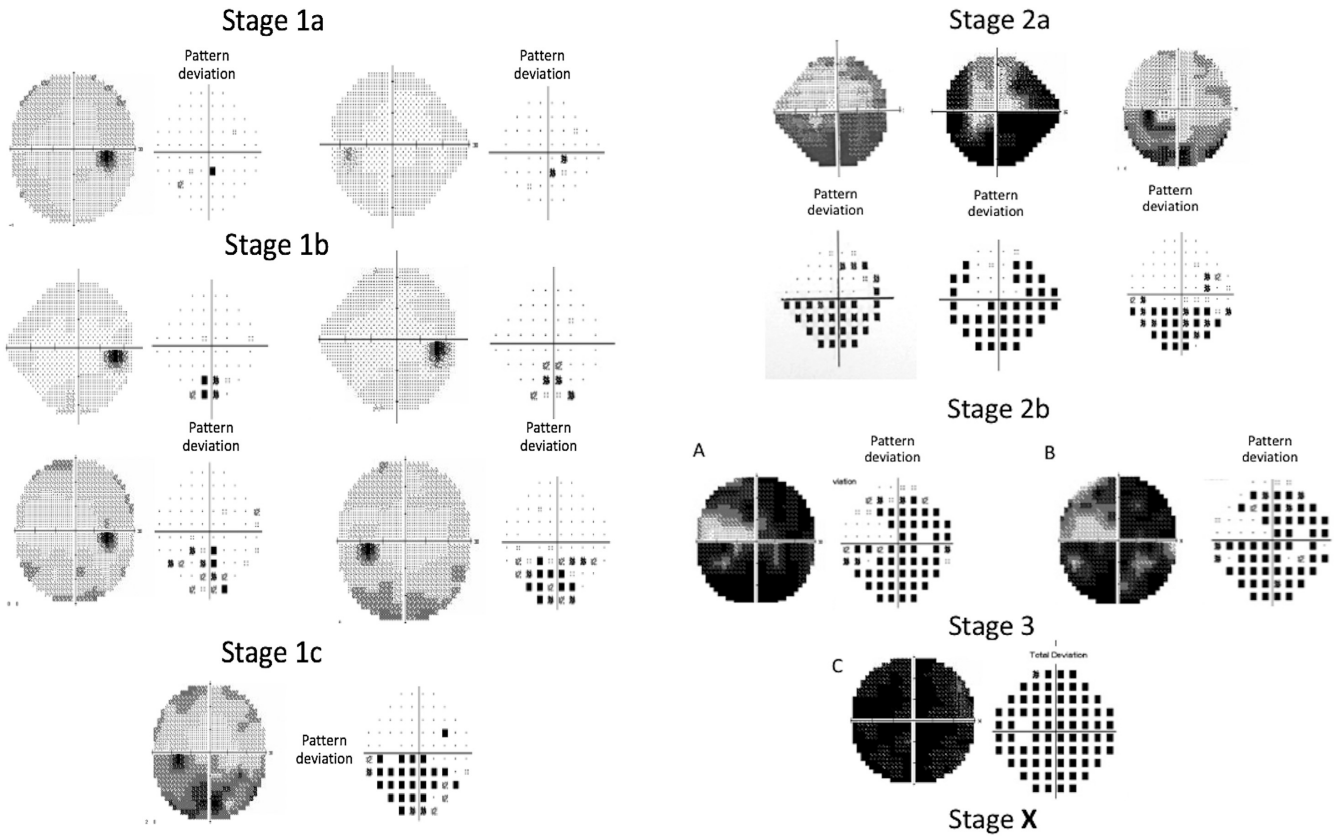
Recent years have witnessed several important publications on the diagnosis, monitoring, and treatment of TED-CON. There has been a significant effort to improve diagnostic findings in TED-CON patients pointing out the importance of additional features such as changes in color vision and VF, even in subclinical cases. Freitag and Tanking's (FT hereafter) work, in particular, has made a key contribution with its classification of VF defects in describing the progression of the disease. This work offers two important advantages in daily clinical life. First, the classification alerts us to the very first changes in the inferior part of the VF, which can be an early sign of the optic nerve compression. Second, the classification allows us to understand and categorize the progression of the disease in a standardized way. [15]

The classification is summarized below. [15]

Figure 1. Classification of Visual Field Defects in Thyroid Eye-Disease-Compressive Optic Neuropathy according to American Ophthalmological Society (AOS) Thesis



Stage 1 defects are the earliest changes seen in VF in TED-CON patients.

Stage 1a is described as a small inferior paracentral hemifield abnormality involving 1– 4 consecutive points and having at least 1 point at <0.5 or <1%.

Stage 1b is described as a large inferior paracentral hemifield defect including 5– 29 consecutive points, not involving the entire inferior hemifield, with at least one point being <1%.

Stage 1c is described as an inferior altitudinal defect showing a severe VF loss on the entire inferior hemifield mostly respecting the horizontal midline, with 70% of the points having $p < 0.5$ on pattern deviation plot.

Stage 2 defects can be described in 2 levels of severity and involves an altitudinal VF defect which crosses the horizontal midline and extends to the superior region.

Stage 2a is described as an inferior altitudinal defect with superior advancement involving the entire hemifield with a superior extension with 1– 15 points crossing the horizontal midline nasally, temporally, or both.

Stage 2b is described as an inferior altitudinal plus superior arcuate defect involving the entire inferior hemifield with a superior extension above the horizontal line in an arcuate form.

Stage 3 involves total loss, defined as a widespread VF loss in 4 quadrants (MD > 20.00 dB).

Stage X involves less common VF defects including the following patterns:

Superior defect (VF defect in the superior hemifield), central/ paracentral (VF defect predominantly at macular/ perimacular region but not contiguous with the blind spot in 15° fixation), enlarged blindspot (VF defect contiguous with the blindspot), and scatter (diffuse VF loss in ≥ 3 quadrants, but also having minimum 1 point at <2% in ≥ 2 quadrants).

In our study, our goal was to apply the FT classification to VF examinations from 51 patients (96 eyes) at the time of TED-CON diagnosis. We also wanted to evaluate this classification in terms of its reliability across examiners, and its reproducibility by the same examiner at different times. To that end, we de-identified patient records, randomized their ordering, and asked two examiners to classify VF defects independently. After a month of this initial reading, we re-numbered patient records (while keeping them anonymous) and asked each reader to re-do the classification. By analysing the resulting data, we assessed both interreader agreement and intrareader reproducibility of this important classification scheme for TED-CON. We found that a wide distribution of our patients (eyes) across the ten stages of VF defects identified in the FT classification. The most frequent VF defects at

the time of the diagnosis involved, what FT call, stage 1b (large inferior paracentral hemifield defect). These defects accounted for 34.4% of the eyes in reader 1's classification, and 35.4% of the eyes in reader 2's classification. The second most frequent defects were stage 2b (inferior altitudinal plus superior arcuate defect), making up 10.4% of cases for reader 1 and 14.6% cases for reader 2. The third most frequent defects belonged to stage 3 (total loss), including 10.4% cases for both readers.

It is worth emphasizing that BCVA would not have been a good predictor of TED-CON in our data. We had 44 eyes (45.8%) with a BCVA LogMAR ≤ 0.2, that is, half of cases had a good VA. Even more striking is the fact that about a fourth of our cases (22 eyes) had a BCVA LogMAR ≤ 0.1, indicating minimal-to-no worsening in BCVA. This pattern points to the need for performing other tests, such as VF examination, in suspected TED-CON patients as soon as possible. Similar to FT, our findings show the most frequent VF defect in TED-CON patients to be stage 1b defects. Therefore, clinicians should remain alert to small defects in inferior region (stage 1a/1b) of the VF examination, which might indicate potential TED-CON, even in patients with minimal-to-no worsening of the BCVA.

We concluded that the FT classification is easy to understand and applicable in daily clinical life. Similar to FT, we observed in our data the inferior defects to be the most common ones in TED-CON patients, and thus, confirmed the precision of the classification for detecting this particular pattern.

2.5 Evaluation of medical and surgical decompression in patients with dysthyroid optic neuropathy.

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Treatment decisions in Graves orbitopathy (GO) are based on clinical activity, severity, and duration. It is known that anti-inflammatory and/or immunosuppressive treatment is significantly less effective after 18 months of disease duration. [16] Graves orbitopathy can be classified as mild, moderate to severe or sight threatening (see Figure 2). [5,16] According to the Consensus Statement of the European Group on Graves' Orbitopathy (EUGOGO), sight-threatening GO is described as dysthyroid optic neuropathy (DON) and/or corneal breakdown requiring immediate intervention to preserve vision. [5] The first line of treatment in DON involves steroid-pulse treatment, also known as medical decompression. Severe cases of DON, however, which do not respond to this initial therapy, are often treated with surgical orbital decompression. Our goal was to evaluate the effectiveness of surgical decompression among patients that were resistant to the first line of therapy.

Figure 2. Classification of severity of Graves' Orbitopathy (GO)

Classification	Features
Mild GO	Patients whose features of GO have only a minor impact on daily life insufficient to justify immunomodulation or surgical treatment. They usually have one or more of the following: • minor lid retraction (<2 mm) • mild soft-tissue involvement • exophthalmos • <3 mm above normal for race and gender • no or intermittent diplopia and corneal exposure responsive to lubricants
Moderate-to-Severe GO	Patients without sight-threatening GO whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive). They usually have two or more of the following: • lid retraction ≥2 mm • moderate or severe soft-tissue involvement • exophthalmos ≥3 mm above normal for race and gender • inconstant or constant diplopia
Sight threatening (very severe) GO	Patients with dysthyroid optic neuropathy and/or corneal breakdown

Source: The 2021 European Group on Graves' Orbitopathy (EUGOGO) Clinical Practice Guidelines for the medical management of Graves' Orbitopathy [16]

In this retrospective, observational study, patients were divided into two groups: The first group (medical decompression only) consisted of patients with a steroid-pulse treatment alone (7 patients, 16 eyes). The second group consisted of patients who received steroid treatment as a first line treatment but needed a surgical decompression after/during the steroid treatment due to worsening of symptoms or clinical findings (18 patients, 30 eyes). All patients with DON were treated with intravenous (i.v.) pulses of 500mg prednisolon (Solu Decortin: prednisolone 21-hydrogensuccinat) twice/week for 4 consecutive weeks, prednisolone was then reduced to 250mg twice/week for the following 2 weeks (a treatment strategy known as medical decompression). The duration of the medical treatment was 6 weeks, and the cumulative dose of prednisolone was 5 grams.

In DON, treatment aims to reduce the pressure on the optic nerve by lessening the volume of the orbital content, and thereby decreasing the ongoing inflammation. At present, there is no standardized, evidence-based treatment algorithm for DON. The oldest therapy involves Glucocorticoids (GCs), which can be applied locally (retrobulbar or subconjunctival), orally or i.v. [17] In light of recent studies, we can conclude that, owing to the rare side effects and statistically better results, the i.v. GC is more beneficial than oral prednisolone.[18] This finding is important, but still not sufficient for us to address DON completely.

Our results showed that both treatments (medical decompression and surgical decompression) yielded improvements in BCVA in their respective patient groups. Specifically, for 30 out of 46 eyes, medical decompression did not lead to sufficient recovery, and surgical decompression was used. Eight patients in this group were treated with high doses of i.v. steroids (1000 mg prednisolone for 3 days) prior to the 6-week scheme (500 mg twice/week for 4 weeks and 250 mg twice/week for 2 weeks) owing to the potential visual loss. These patients all needed surgery despite having received the maximum medical treatment (steroid-pulse treatment and the 1000 mg of prednisolone for 3 days additionally). These findings highlight two points: first, mild cases of DON with a better initial visual acuity (in our case series, median: 0.3 ogMAR) seem to respond well to steroid treatment, sparing patients surgery; second, therapy resistant cases with a worse initial BCVA (in our case series, median: 0.6 logMAR) still need surgery to preserve the optic nerve function. But thankfully, those cases respond well to the surgery, and despite having a worse initial condition of BCVA, end up with a statistically significant higher value of BCVA post-operation ($p < 0.0001$ visit 2 vs visit 4), which they did not show immediately after the medical treatment.

In conclusion, this retrospective study confirms the effectiveness of medical decompression in mild cases of DON as well as the effectiveness of surgical decompression in therapy-refractory cases.

3. Summary:

In summary, the present work has investigated the value of different examination methods for early diagnosis of the optic nerve compression in patients with Thyroid eye disease. We also had the great opportunity to evaluate the treatment methods.

Recent years have witnessed a number of important publications on the diagnosis, monitoring, and treatment of TED-CON. Thanks to continuously developing diagnostic tools, we now know that best-corrected visual acuity does not always reflect the disease and the diagnostic tools such as visual field examination and color vision enable us to detect those patients in early phases so that the disease can be treated before the visual acuity worsens. In the past, visual evoked potentials was thought to be an objective and reliable method to examine the optic nerve compression. However, according to our data, VEP seems to have a limited potential especially in patients with a best-corrected visual acuity described as BCVA ≤ 0.2 LogMAR for detecting the optic nerve compression.

When it comes to treatment of TED-CON, mild cases with better initial visual acuity (in our case series mean: 0.3 logMAR) seem to respond well to steroid treatment. However, therapy-resistant cases with an impaired initial BCVA (in our case series, mean: 0.6 logMAR) seem to need the surgery to preserve the optic nerve function.

We hope, all the work summarized in this thesis, help clinicians on diagnosing the disease and finding the best treatment method for our patients.

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European Journal of Endocrinology 2021; 185:4, 43–G67

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5. Abbreviations:

TED-CON:	Thyroid Eye-Disease-Compressive Optic Neuropathy
BCVA:	Best-corrected Visual Acuity
VF:	Visual Field
GO:	Graves' orbitopathy
DON:	Dysthyroid optic neuropathy
DIJOA:	Juvenile Optic Atrophy
VEP:	Visual Evoked Potentials
p-VEP:	Pattern-VEP
f-VEP:	Flash-VEP
FT:	Freitag and Tanking
GCs:	Glucocorticoids

6. List of Publications:

6.1 Original work as first or last Author:

1. **Garip Kübler A,** Priglinger S, Reznicek L.

Micropulse Cyclophotocoagulaton versus Selective Laser Trabeculoplasty: Effects on Corneal Endothelial Cells and Intraocular Pressure.

Journal of Current Glaucoma Practice 2023, accepted 13.1.23
Impact factor: 0,96 (2022)

2. **Garip Kuebler A**, Halfter K, Klingenstein A, Neuhann L, Enders C,

Priglinger S, Hintschich C.

Optikuskompression bei Endokriner Orbitopathie.

Die Ophthalmologie, accepted 21.2.23
Impact factor: 1.059 (2022)

3. **Garip Kübler A**, Halfter K, Reznicek L, Klingenstein A, Priglinger S, Rudolph G, Hintschich C.

Evaluation of visual evoked potentials in dysthyroid optic neuropathy.
Orbit. 2022; :1-6. doi: 10.1080/01676830.2022.2123929
Impact factor: 1,21 (2022)

4. **Garip-Kuebler A,** Halfter K, Reznicek L, Klingenstein A, Priglinger S, Hintschich C.

Subclinical dysthyroid optic neuropathy: tritan deficiency as an early sign of dysthyroid optic neuropathy.

British Journal of Ophthalmology 2021;105:1019-1023.
doi:10.1136/bjophthalmol-2020-316433

Impact factor: 3,97 (2020)

5. **Garip Kuebler A**, Wiecha C, Reznicek L, Klingenstein A, Halfter K, Priglinger S, Hintschich C.

Evaluation of medical and surgical decompression in patients with dysthyroid optic neuropathy.

Eye (Lond) 2020; 34:1702–09.

Impact factor: 3,78 (2020)

6. **Garip Kübler A**, Halfter K, Reznicek L, Klingenstein A, Priglinger S, Rudolph G, Hintschich C.

Evaluating the interreader agreement and intrareader reproducibility of Visual Field Defects in Thyroid Eye Disease–Compressive Optic Neuropathy

Eye 2021; doi:10.1038/s41433-021-01683.

Impact factor: 4,456

7. **Garip Kübler A**, Halfter K, Reznicek L, Klingenstein A, Priglinger S, Rudolph G, Hintschich C.

A pathological indicator for dysthyroid optic neuropathy: tritan color vision deficiency

Graefe's Archives for Clinical and Experimental Ophthalmology 2021; 259:3421-3426. doi:10.1007/s00417-021-05227-8

Impact factor: 3,535 (2021)

8. **Garip Kuebler A**, Wiecha C, Reznicek L, Klingenstein A, Halfter K, Priglinger S, Hintschich C.

Comparison of different devices to measure the intraocular pressure in thyroid-associated orbitopathy.
Graefe's Archives for Clinical and Experimental Ophthalmology 2019;257(9):2025-2032

Impact factor: 2,4 (2019)

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Evaluation of a short-term topical interferon alpha-2b treatment for histologically proven melanoma and primary acquired melanosis with atypia.

Orbit 2016; 35(1):29-34

Impact factor: 0,96 (2016)

6.2 Original work as Co-Author

1. Klingenstein A, Samel C, **Garip-Kübler A**, Hintschich C, Müller-Lisse U.

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https://doi.org/10.1038/s41598-022-16131-4

Impact Factor: 4,996 (2022)

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Impact factor: 2.029 (2022)

3. Enders C, Vogel D, **Garip-Kübler A,** Dreyhaupt J, Wolf W, Hall J, Neuhann L, Werner J.

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https://doi.org/10.1007/s00417-022-05844-x

Impact factor: 3,535 (2022)

4. Klingenstein A, **Garip-Kuebler A**, Priglinger S, Hintschich C, Mueller-Lisse U.

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Impact factor: 2,192 (2021)

5. Klingenstein A, Samel C, Messmer EM, **Garip-Kuebler A**, Priglinger S, Hintschich C.

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6. Klingenstein A, Samel C, **Garip Kuebler A,** Miller C, Liegl RG, Priglinger S, Foerster P.

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Acta Ophthalmologica 2020;98(3):381-7
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Impact factor: 2,082 (2014)

12. Klopstock T, Yu-Wai-Man P, Dimitriadis K, Rouleau J, Heck S, Bailie M, Atawan A, Chattopadhyay S, Schubert M, **Garip A,** Kernt M, Petraki D, Rummey C, Leinonen M, Metz G, Griffiths G, Meier T, Chinnery P.

A randomized placebo-controlled trial of idebenone in Leber's hereditary optic neuropathy.

Brain 2011;134:2677-86.
Impact factor: 15,255

6.3 Other Publications

Standardabläufe in der Augenheilkunde
Kapitel 13 Medikamente in der Schwangerschaft

Hirneiß, Mackert, Messmer, Priglinger (Herausgeber)
Verlag: Thieme; Auflage: 1 (2. September 2020) Sprache: Deutsch
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