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Kognitive Bias bei Depressionen im Kindes- und Jugendalter und bei Kindern depressiver Eltern

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vorgelegt von

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München, den 04.08.2024
Ort, Datum

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Inhaltsverzeichnis

Abkürzungsverzeichnis

AB	Aufmerksamkeitsbias
IB	Interpretationsbias
HR-Gruppe	high risk group bzw. Hochrisikogruppe (Kinder depressiver Eltern mit erhöhtem Risiko, selbst an Depressionen zu erkranken)
LR-Gruppe	low risk group bzw. Kontrollgruppe (gesunde Kinder und Jugendliche mit gesunden Eltern, die ein niedriges Risiko haben, selbst an Depressionen zu erkranken entsprechend der Normalbevölkerung)
MD-Gruppe	major depression group bzw. Depressiongruppe (Kinder und Jugendliche, die selbst an Depression erkrankt sind)

Publikationsliste

Originalarbeiten in dieser Dissertation

Buhl, C., Sfärlea, A., Loechner, J., Starman-Wöhrle, K., Salemink, E., Schulte-Körne, G., & Platt, B. (2023). Biased Maintenance of Attention on Sad Faces in Clinically Depressed Youth: An Eye-Tracking Study. Child Psychiatry & Human Development, 54(1), 189-201. https://doi.org/10.1007/s10578-021-01229-z

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Platt, B., Sfärlea, A., **Buhl, C.**, Loechner, J., Neumüller, J., Thomsen, L. A., Starman-Wöhrle, K., Salemink, E., & Schulte-Körne, G. (2021). An Eye-Tracking Study of Attention Biases in Children at High Familial Risk for Depression and Their Parents with Depression. Child Psychiatry & Human Development, 1-20.

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Kongressbeiträge

Poster:

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Vortrag:

Platt, B., Sfärlea, A., Löchner, J., Starman, K., **Buhl, C.,** Störmann, A., Neumüller, J., Asperud Thomsen, L., Salemink, E., Schulte-Körne, G. (2018). Prävention der Depression im Kindes- und Jugendalter. Projekte der PRODO-Forschungsgruppe der Kinder- und Jugendpsychiatrie des Klinikums der Universität München. Landespsychologentag des BDP Bayern, München.

Beitrag zu den Veröffentlichungen

Die vorliegenden Publikationen entstammen dem Forschungsprojekt „Konsequenz oder Risikofaktor? Die Rolle kognitiver Bias bei Depressionen im Kindes- und Jugendalter (KROKO)“, das auf Grundlage des übergeordneten Projektes „Die Weitergabe von Depression durch Eltern an ihre Kinder: Eine generationsübergreifende Studie zur Aufmerksamkeits- und Interpretationsprozessen (GENERAIN)“ entstand. Das Projekt wurde von Herrn Prof. Dr. med. Schulte-Körne und Frau Dr. Belinda Platt konzipiert sowie von Frau Dr. Anca Sfärlea maßgeblich mitgestaltet. Die Durchführung und Koordination der Studie sowie das Verfassen der Manuskripte wurden von Frau Dr. Belinda Platt und Frau Dr. Anca Sfärlea unterstützt und von Herrn Prof. Dr. med. Schulte-Körne supervidiert. Das Projekt wurde während seiner gesamten Laufzeit von Herrn Prof. Dr. med. Schulte-Körne supervidiert.

Es wurde gefördert durch das Förderprogramm für Forschung und Lehre (FöFoLe, Reg.-Nr. 895) der Medizinischen Fakultät der Ludwig-Maximilians-Universität München, die Hans und Klementia Langmatz Stiftung, das LMU Gender-Mentoring-Programm und die Friedrich-Baur-Stiftung. Die Open Access Finanzierung wurde ermöglicht durch das Projekt DEAL. Das Votum auf ethisch-rechtliche Unbedenklichkeit des übergeordneten Projektes „GENERAIN“ (Projektnummer 441-15) wurde am 02.09.2015 durch die Ethikkommission der Medizinischen Fakultät der Ludwig-Maximilians-Universität München erteilt. Für dieses Forschungsprojekt („KROKO“) wurde ein Änderungsantrag des übergeordneten Projektes gestellt und am 19.07.2017 bewilligt.

Die Autorin der vorliegenden Dissertation wurde im Oktober 2017 als medizinische Doktorandin in das Projekt aufgenommen. Zum Zeitpunkt des Eintretens der Autorin in das Projekt stand das Studiendesign bereits fest und die Rekrutierung der Probanden hatte vor Kurzem begonnen. Die Autorin war, unter Supervision von Frau Dr. Anca Sfärlea und Frau Dr. Belinda Platt, maßgeblich verantwortlich für die Probandenrekrutierung, die Organisation und Durchführung der Testungen, die Datenerhebung (eigenständige Durchführung von diagnostischen Interviews, Intelligenztestungen und Fragebögen sowie der experimentellen Testungen inklusive Aufzeichnung der Augenbewegungen) sowie für die Dateneingabe. Die so erhobenen Daten bildeten die Grundlage beider Veröffentlichungen. Zusätzlich wurden Teile der Daten der Kontrollgruppe und der Risikogruppe aus dem Projekt „GENERAIN“ verwendet. Bei der Rekrutierung der klinischen Gruppen wurde die Autorin von den Studienassistentinnen Frau Petra Wagenbüchner und Frau Veronika Jäger sowie von Frau Sonja Stolp, Dipl.-Psych. und ihrem Praxisteam unterstützt. Zudem arbeitete die Autorin zeitweise mit Frau Ann-Sophie Störmann (studentische Hilfskraft) zusammen, die sie gemeinsam mit der Studienkoordinatorin Frau Dr. Sfärlea einarbeitete und supervidierte und die an einem Teil der Datenerhebung und -eingabe beteiligt war.

Beitrag zu Studie I

Zusätzlich zu den o.g. Aufgaben nahm die Autorin die Aufbereitung und Verarbeitung der behavioralen und Eyetracking Daten von Studie 1, deren Auswertung sowie die Interpretation der Ergebnisse zum großen Teil eigenständig vor. Angeleitet und supervidiert wurde sie hierbei von Frau Dr. Anca Sfärlea und Frau Dr. Belinda Platt, an die sie sich jederzeit mit Fragen wenden konnte. Als Erstautorin des Papers zu Studie 1 verfasste die Doktorandin das Manuskript zum größeren Teil eigenständig, zum kleineren Teil in Zusammenarbeit mit Frau Dr. Anca Sfärlea, die als Zweitautorin wesentlich zum Methoden- und Ergebnisteil beitrug. Zuletzt arbeitete die Autorin die Rückmeldungen aller Koautoren und der Reviewer in die Publikation ein.

Beitrag zu Studie II

Zusätzlich zu den o.g. Aufgaben nahm die Autorin die Aufbereitung und Verarbeitung der behavioralen Daten gemeinsam mit Frau Dr. Sfärlea, der Erstautorin von Studie 2, vor. Als Zweitautorin unterstützte sie Frau Dr. Anca Sfärlea beim Verfassen des Manuskriptes durch Literaturrecherchen und beim Verfassen der Einleitung sowie einzelner Punkte in der Diskussion.

1. Einleitung

1.1. Hintergrund und Ausgangslage

Depressionen zählen zu den häufigsten psychischen Erkrankungen, auch im Kindes- und Jugendalter, weltweit und betreffen ca. 3,8% der Weltbevölkerung, also ca. 280 Mio. Menschen (WHO, 2023). Bis zum Ende der Adoleszenz erleben schätzungsweise bis zu 20% der Kinder und Jugendlichen mindestens eine depressive Episode (Thapar et al., 2012).

Gekennzeichnet ist diese episodisch auftretende affektive Störung typischerweise durch anhaltend gedrückte Stimmung, Anhedonie und Antriebsmangel. Weitere häufige charakteristische Beschwerden sind Schlafstörungen, verminderte Konzentration, reduziertes Selbstwertgefühl, Schuldgefühle und Suizidalität (Dilling et al., 2015). Einige Symptome von erwachsenen und pädiatrischen Patienten überschneiden sich, es gibt jedoch auch Unterschiede in Häufigkeit und Ausprägung: v.a. Kinder zeigen vermehrt Bauch- oder Kopfschmerzen, Irritabilität, Traurigkeit, Müdigkeit u.a. (Kölch et al., 2020). Bei Jugendlichen ähnelt das Bild mehr dem der „erwachsenen“ Depression, ist jedoch seltener verbunden mit Anhedonie oder Konzentrationsschwäche, dafür häufiger mit dem somatischen Syndrom (Appetitveränderungen, Erschöpfung, Schlafstörungen u.a.) (Rice et al., 2019). Auch selbstverletzendes Verhalten und Suizidalität sind im Jugendalter besonders häufig (Kölch et al., 2020). Zudem beeinträchtigen Depressionen die Entwicklung, v.a. auf sozio-emotionaler und schulischer Ebene (Essau & Chang, 2009). Dies wirkt sich noch bis ins Erwachsenenalter negativ auf Bildungsniveau, soziale Einbindung, körperliche (Fergusson & Woodward, 2002) und psychische Gesundheit (Kim-Cohen et al., 2003) aus.

Die als Goldstandard empfohlene psychotherapeutische Behandlung (Kognitive Verhaltenstherapie, Interpersonelle Therapie, Systemische Therapie sowie Psychodynamische Psychotherapie), gelegentlich unterstützt durch Psychopharmakotherapie, v.a. mittels SSRI[1] (DGKJP, 2013), zeigt bislang leider maximal moderate Effekte, die der Psychotherapieforschung zufolge nicht über 12 Monate hinaus andauern (Eckshtain et al., 2020; Ng et al., 2020; Weisz et al., 2017; Weisz et al., 2006)). Eine große Metaanalyse von Psychotherapiestudien der letzten 50 Jahre zu Depression, Angststörungen, Aktivitäts- und Aufmerksamkeitsstörungen (ADHS) und Sozialverhaltensstörungen bei Jugendlichen errechnete für die depressionsspezifischen Therapien im Vergleich sogar die geringste Effektstärke (Weisz et al., 2017). Nichtsdestotrotz belegen diese Studien, dass Psychotherapie bei Depressionen im Kindes- und Jugendalter wirksam ist (insbes. Kognitive Verhaltenstherapie, Interpersonelle Therapie und Systemische Therapie, mit geringeren Effekten auch psychodynamische Verfahren). Ihre Wirkung ist bisher nur noch nicht ausreichend und nicht

[1] In Deutschland ist für Minderjährige ab 8 Jahren bislang nur Fluoxetin zugelassen.
(Gerlach, M., Mehler-Wex, C., Walitza, S., Warnke, A., & Wewetzer, C. (2016). *Neuro-/Psychopharmaka im Kindes-und Jugendalter: Grundlagen und Therapie*. Springer-Verlag.)

langfristig genug. Über ein besseres Verständnis zentraler auslösender und aufrechterhaltender Faktoren der Erkrankung und ihr Zusammenwirken könnten bestehende Methoden effektiver und wirksamer gestaltet werden. Eine noch größere Hilfe wäre es natürlich, schon vor Ausbruch der Erkrankung entsprechende Risikogruppen identifizieren und mit einer wirksamen Prävention der Entstehung der Krankheit entgegenwirken zu können.

1.1.1. Entstehung der Depression

Zur Entstehung der Depression gibt es zahlreiche theoretische Modelle und empirische Erkenntnisse neurobiologischer, sozialer, emotionaler und kognitiver Beeinträchtigungen und Einflussfaktoren. Ausgehend vom bio-psycho-sozialen Erklärungsmodell (Engel, 1977; Schotte et al., 2006) wird ein Zusammenspiel angenommen von genetischer und neurobiologischer Vulnerabilität (s.u.) mit psychosozialen Belastungen wie schulischer Leistungsanforderung, „life events" (Umzug, Trennung der Eltern, Verlust von Bezugspersonen etc.), „adverse childhood events", d.h. belastenden Kindheitserlebnissen (z.B. Vernachlässigung, Misshandlung/Missbrauch oder Mobbing) sowie ungünstigen innerfamiliären Dynamiken (z.B. konfliktreiche innerfamiliäre Beziehungen u.a.) (Kölch et al., 2020). Zu letzteren zählt auch die psychische Erkrankung eines Elternteils: Kinder depressiver Eltern haben ein bis zu dreimal höheres Risiko für Depression, erkranken durchschnittlich früher und haben häufiger einen rezidivierenden Verlauf (Weissman et al., 2016). Das gängigste theoretische Modell zur transgenerationalen Weitergabe der erhöhten Vulnerabilität von Goodman and Gotlib (1999) identifiziert, neben genetischer Heritabilität (1) und neuroregulatorischen Dysfunktionen[2] (2), folgende psychosoziale Aspekte: (3) das Erleben maladaptiver emotionaler, kognitiver und behavioraler Bewältigungsstrategien der depressiven Eltern sowie (4) das Aufwachsen in einer von vermehrtem Stress geprägten Umgebung infolge der elterlichen Depression.

Präventive Interventionen für die Risikogruppe der Kinder depressiver Eltern zielen v.a. auf diese kognitiven, emotionalen und behavioralen Faktoren (s. (3)) ab (Loechner et al., 2020). Reviews und Metaanalysen zeigen zwar eine Reduktion (subklinischer) depressiver Symptome und der Inzidenz depressiver Episoden, allerdings halten die Effekte bisher nur 4 -12 Monate nach Intervention an bei eher geringen Effektstärken (z.B. Hetrick et al., 2016; Loechner et al., 2018). Auch die präventiven Ansätze zeigen also Wirksamkeit, bedürfen aber ebenso wie die therapeutischen Verfahren noch weiterer Verbesserung. Der Bedarf an Forschung für ein umfassenderes, differenziertes Verständnis der Mechanismen, die der Erkrankung zugrunde liegen, und ihres Zusammenspiels ist daher groß.

[2] z.B. in Form einer überschießenden Stressreaktion der HPA-Achse (hypothalamic–pituitary–adrenal axis/ Hypothalamus-Hypophysen-Nebennierenrinden-Achse) oder der Veränderungen der Konnektivität diverserer neuronaler Netzwerke u.a. (Kertz et al., 2019)

1.1.2. Kognitive Bias bei Depressionen

Ein Ansatzpunkt ist die Forschung zu negativen kognitiven Bias, die in theoretischen kognitiven Modellen als zentral gelten für die Entstehung und Aufrechterhaltung von Depressionen (z.B. Beck&Haigh, 2014; Disner et al., 2011). Es handelt sich dabei um schnelle, automatische, nicht bewusste Verzerrungen der kognitiven Verarbeitung emotionaler Informationen ins Negative. Diese werden aktiviert, gemäß dem Diathese-Stress-Modell, durch einen entsprechenden salienten Stimulus, d.h. einen zumeist synthymen, emotionalen Reiz, der wiederum eine entsprechende emotionale Reaktion hervorruft (Aaron T. Beck 2008; Scher et al., 2005). Solche kognitiven Verzerrungen finden sich bei erwachsenen Depressionspatienten auf mehreren Ebenen: der Aufmerksamkeitslenkung, der Interpretation und dem Gedächtnis. Das bedeutet, akut depressive Erwachsene richten ihre Aufmerksamkeit mehr und länger auf negative emotionale (i.d.R. synthyme, also traurige) Informationen als auf positive oder neutrale Inhalte (negativer Aufmerksamkeitsbias, AB), interpretieren emotional ambivalente oder neutrale Informationen und Situationen negativer (negativer Interpretationsbias, IB) und speichern vermehrt negativ besetzte emotionale Informationen im Gedächtnis ab (negativer Gedächtnisbias) (Everaert et al., 2017; LeMoult & Gotlib, 2019; Peckham et al., 2010). Zudem gibt es im Erwachsenenalter zunehmend Belege, dass AB und IB auch eine prädiktive Rolle spielen für gedrückte Stimmung und depressive Symptomatik (Beevers et al., 2015; Jones & Sharpe, 2017; MacLeod, 2012; Sanchez-Lopez et al., 2019).

Kognitive Bias gelten in theoretischen Modellen der Depressionsentstehung als zentraler Bestandteil für das Zusammenspiel der biologischen (s.o.), kognitiven (z.B. kognitive Steuerung, Aufmerksamkeitssteuerung) und emotionalen (z.B. Emotionsregulation) Faktoren (De Raedt & Koster, 2010; Kertz et al., 2019). So werden z.B. Aufmerksamkeitsprozesse beeinflusst durch genetische und neuroregulatorische Faktoren, wie die bei Depressionen typische Hyperaktivität der Hypothalamus-Hypophysen-Nebennierenrinden-Achse (hypothalamic–pituitary–adrenal axis / HPA-Achse)(Kertz et al., 2019). Zudem wird von einer bidirektionalen Beziehung zwischen kognitiven Bias und Emotionsregulationsprozessen ausgegangen, in der Gross (1998) den kognitiven Bias einen kausalen Effekt auf die Emotionsregulation (z.B. Rumination, also Grübeln) attestiert, während z.B. Joormann und Stanton (2016) annehmen, dass der Effekt kognitiver Bias auf die Entstehung depressiver Symptome erst über die Emotionsregulation vermittelt wird.

Der Fokus der vorliegenden Dissertation soll auf Aufmerksamkeitsbias und Interpretationsbias bei Depressionen im Kindes- und Jugendalter gerichtet sein. In dieser Altersgruppe findet rege Entwicklung und Veränderung statt auf Ebene der kognitiven Funktionen, der Emotionsregulation, aber auch der neuronalen Netzwerke, die u.a. an Aufmerksamkeitsprozessen beteiligt sind (Amso & Scerif, 2015; Blakemore & Choudhury, 2006). Daher erscheint ein direktes Übertragen der Erkenntnisse aus der „Erwachsenenforschung“ auf Kinder und Jugendliche nicht sinnvoll.

Denkmuster haben sich vermutlich noch nicht zu stabilen, individuell charakteristischen Schemata verfestigt (z.B. Lakdawalla et al., 2007), gleichzeitig geht die unabgeschlossene neuronale Ausreifung, gepaart mit hormonellen Umstellungen, vermutlich mit erhöhter emotionaler Sensitivität einher (z.B. Paus et al., 2008). Diese Entwicklungsprozesse scheinen einerseits die Vulnerabilität für psychische Erkrankungen wie Depressionen zu erhöhen, könnten diese Altersgruppe aber auch empfänglicher machen für präventive und therapeutische Interventionen (Konrad et al., 2013; Lo Iacono & Carola, 2018), sodass effektive Interventionen gerade hier essentiell wären.

Das Vorliegen, die Charakteristika und die Rolle kognitiver Bias sind in dieser Altersgruppe noch nicht so umfassend untersucht wie im Erwachsenenalter. Zwar gibt es Hinweise auf das Vorliegen von negativen AB und IB bei depressiven Kindern und Jugendlichen, aber mit teils widersprüchlichen Ergebnissen v.a. bei AB (Kertz et al., 2019; Platt et al., 2017). Während teils analog zu den Erwachsenen vermehrte Aufmerksamkeit für traurige, aber auch wütende Stimuli (Hankin et al., 2010; Sylvester et al., 2016) berichtet wird, gibt es auch Befunde reduzierter Aufmerksamkeit für negative Stimuli (Harrison & Gibb, 2015) oder gar keinen Nachweis eines AB (Neshat-Doost et al., 2000). Lediglich zwei Studien verglichen gezielt IB depressiver Jugendlicher mit einer gesunden Kontrollgruppe (Micco et al., 2014; Orchard et al., 2016) mit dem Ergebnis eines negativen IB der depressiven Gruppe sowie eines Zusammenhangs negativer IB mit der Ausprägung depressiver Symptome. Um sich der Funktion von AB und IB in der Entstehung der Depression zu nähern, werden auch Kinder depressiver Eltern als besondere Risikogruppe untersucht: sie zeigten bisher zumeist einen negativen AB für traurige (Joormann et al., 2007; Kujawa et al., 2011; Owens et al., 2015) oder wütende Stimuli (Montagner et al., 2016; Waters et al., 2015), seltener das Meiden trauriger Gesichter (Connell et al., 2013; Gibb et al., 2009).

Um kognitive Bias zu messen wurden anfänglich meist Fragebögen zur Selbstauskunft angewendet (Haley et al., 1985; Wisco & Nolen-Hoeksema, 2010). Mittlerweile werden experimentelle Methoden bevorzugt, die weniger Verzerrungen durch Response-Bias unterliegen, d.h. bewusst überlegten, sozial erwünschten und/oder an vermutete Erwartungen der Untersucher angepassten Antworten, die nicht die tatsächlichen unbewussten Prozesse widerspiegeln (Gotlib & Joormann, 2010; Hirsch et al., 2016). Häufig werden behaviorale Methoden eingesetzt, die zur Messung von **AB** Reaktionszeiten auf positive, neutrale und negative emotionale Stimuli unter Zeitdruck vergleichen, um möglichst wenig Raum für bewusste Steuerung zu lassen. Um **IB** abzubilden, werden Probanden ambivalente emotionale Informationen präsentiert und deren positive, neutrale und negative Interpretationen zur Auswahl gestellt. In den letzten Jahren werden zunehmend neurophysiologische Korrelate v.a. der Aufmerksamkeitsprozesse erhoben, da sie noch weniger dem bewussten Einfluss der Probanden unterliegen und die unbewussten, automatisch ablaufenden Prozesse noch objektiver und differenzierter abbilden (Harrison & Gibb, 2015; Lazarov et al., 2018). Diese werden erfasst z.B. mittels evozierter Potenziale im EEG (Gibb et al., 2016) oder

mittels Messung von Augenbewegungen (Eyetracking) als direktes Korrelat für visuelle Aufmerksamkeit (Platt et al., 2017). Besonders letztere ermöglichen es, zwischen den einzelnen Stadien der Aufmerksamkeit zu unterscheiden: initiale Aufmerksamkeitslenkung (d.h. initiale Blicklenkung), Halten der Aufmerksamkeit (d.h. Länge der Betrachtungsdauer) und Ablösen derselben (d.h. Häufigkeit der Rückkehr des Blicks zu einem bestimmten Stimulus) (Armstrong & Olatunji, 2012). Um kognitive Bias messbar zu machen, werden sie vor der Messung zunächst aktiviert, indem Stress bzw. ein synthymer Affekt induziert wird gemäß dem Diathese-Stress-Modell (Aaron T. Beck 2008; Scher et al., 2005). Für die Messung negativer kognitiver Bias bei Depressionen ist daher die Induktion eines traurigen Affekts bei den Probanden vor Durchführung der Messung erforderlich. Es hat sich als effektiv erwiesen, einen traurigen Ausschnitt aus dem Film „König der Löwen“ (Allers et al., 1994) zu zeigen (von Leupoldt et al., 2007).

1.2. Übergeordnetes Ziel und Ergebniszusammenfassung

Die vorliegende Dissertation soll zu einem besseren Verständnis kognitiver Bias und ihrer Rolle bei der Entstehung und Aufrechterhaltung pädiatrischer Depressionen beitragen.

Untersucht wurden Vorliegen, Art und Ausprägung von Aufmerksamkeits- und Interpretationsbias bei Kindern und Jugendlichen zwischen 9 – 14 Jahren in drei Gruppen: (1) Probanden mit Depressionen (Major-Depression-/MD-Gruppe), (2) gesunde Probanden mit depressivem Elternteil als Hochrisikogruppe (High-Risk-/HR-Gruppe) und (3) eine Kontrollgruppe gesunder Probanden mit gesunden Eltern (Low-Risk-/LR-Gruppe). Wenn negative kognitive Bias bereits in der HR-Gruppe auftreten, könnte dies ein Hinweis auf deren Rolle als möglicher Risikofaktor bei der Entstehung von Depressionen im Kindes- und Jugendalter sein, wie bereits in theoretischen kognitiven Modellen vermutet (Beck & Haigh, 2014; Disner et al., 2011) und vereinzelt empirisch untermauert (Orchard et al., 2016; Owens et al., 2015). Wenn sich zudem eine stärkere Ausprägung der Bias in der MD-Gruppe als in der HR-Gruppe zeigt, so könnte dies eine Verstärkung im Rahmen der depressiven Symptomatik widerspiegeln. In beiden Studien wurden mindestens zwei unterschiedliche Paradigmen verwendet, die jeweils unterschiedliche Aspekte der beiden Bias abbilden für ein differenzierteres Bild. Beide Studien verwenden experimentelle, behaviorale Methoden, Studie 1 zudem ein Eyetracking-Paradigma zur Erfassung von Augenbewegungen als neurophysiologischer Korrelate der Aufmerksamkeit (s.o.). Der Fokus von Studie 1 lag auf der Erfassung des AB, der Fokus von Studie 2 auf der Erfassung des IB. Dies sind die ersten Studien, die einen direkten Vergleich kognitiver Bias bei depressiven Kindern und Jugendlichen und der Hochrisiko-Gruppe der Kinder depressiver Eltern anstellen, zudem unter Verwendung verschiedener Paradigmen, um unterschiedliche Aspekte der jeweiligen Bias abzubilden.

1.2.1. Fragestellungen der einzelnen Veröffentlichungen

Studie 1 (Buhl et al., 2021) untersuchte zum einen das Vorliegen, die Art und die Ausprägung von **Aufmerksamkeitsbias (AB)** der (1) MD-Gruppe (n=32) sowie (2) in der HR-Gruppe (n=49), jeweils im Vergleich mit der LR-Gruppe (n=43). Zum anderen wurden die AB und ihre Charakteristika der MD-Gruppe und der HR-Gruppe miteinander verglichen, um Hinweise auf die Rolle von AB bei der Vulnerabilität für Depression zu erhalten.

Dafür führten die Probanden aller drei Gruppen (nach Induktion gedrückter Stimmung) zunächst zwei behaviorale Tests durch, während derer zusätzlich ihre Augenbewegungen via Eyetracking aufgezeichnet wurden. Zur besseren Vergleichbarkeit der Ergebnisse mit der bisherigen Literatur wurde die sehr häufig verwendete **Dot Probe Task** (DPT, (MacLeod et al., 1986)) eingesetzt, die allerdings geringe Reliabilitäten zeigt (Aktar et al., 2019; Schmukle, 2005; Waechter et al., 2014), und die **Visual Search Task** (VST, (De Voogd et al., 2014)) mit akzeptablen Reliabilitäten (Aktar et al., 2019; Platt et al., 2021; Van Bockstaele et al., 2020). In der DPT wurde gleichzeitig ein emotionaler und ein neutraler Stimulus gezeigt, gefolgt von einem Ziel- und einem Distraktorelement (unterschiedlich angeordnete Punkte). Eine kürzere Reaktionszeit zur Identifikation des Zielelementes, wenn es auf derselben Stelle erscheint wie zuvor der negative emotionale Stimulus (z.B. ein trauriges Gesicht), deutet auf einen negativen AB hin. In der VST soll ein Zielstimulus schnellstmöglich zwischen Distraktoren identifiziert werden. Die im Verhältnis kürzeste Reaktionsgeschwindigkeit zur Identifikation von negativen Zielstimuli deutet auf einen negativen AB hin. Zuletzt wurden die Augenbewegungen beim freien Betrachten der Stimuli mittels Eyetracking in der **Passive Viewing Task (PVT,** (Harrison & Gibb, 2015)) erfasst, um einen negativen AB abbilden und zwischen den drei Stadien der Aufmerksamkeit differenzieren zu können. Als Stimuli wurden in allen drei Paradigmen Fotografien von kindlichen und jugendlichen emotionalen Gesichtsausdrücken (Freude, Traurigkeit, Wut, Angst und ein neutraler Ausdruck) aus der Karolinska Directed Emotional Faces Datenbank (Lundqvist et al., 2022) verwendet.

Leider erwiesen sich die Reliabilitäten der behavioralen DPT und der Eyetracking-Daten der VST als so gering, dass deren Ergebnisse kaum verwertbar waren und daher nur im Supplement aufgenommen wurden. Die behavioralen Daten der **VST** ergaben bei akzeptabler Reliabilität keinerlei signifikante Unterschiede in der Aufmerksamkeitslenkung zwischen den Gruppen und damit keinen Anhalt für einen Aufmerksamkeitsbias. In der experimentellen **PVT** zeigte sich hingegen bei guter Reliabilität ein signifikant längeres Halten der Aufmerksamkeit auf traurige Gesichter in der depressiven Gruppe verglichen mit der Hochrisikogruppe, nicht jedoch im Vergleich mit der Kontrollgruppe. Zudem korrelierte die Betrachtungszeit trauriger Gesichter mit dem Ausmaß depressiver Symptome. Dies deutet auf einen negativeren AB in der Betrachtungsdauer synthymer, störungsspezifischer emotionaler Stimuli bei Depressionen im Kindes- und Jugendalter hin, wenn auch nur im Vergleich mit der Hochrisikogruppe. In einer *nicht signifikanten* Tendenz

schienen die Probanden der Hochrisikogruppe einen etwas geringer ausgeprägten negativeren AB aufzuweisen als die Kontrollgruppe. Auch wenn dies bei fehlendem Nachweis rein spekulativ bleibt, wirft es doch die Frage auf, ob diese Risikopopulation ggf. eher zur Vermeidung negativer emotionaler Informationen neigen könnte. Eine vertiefte Darstellung des Hintergrunds, des Ablaufs und der Ergebnisse der Studie sowie eine vertiefte Diskussion findet sich in der entsprechenden Publikation (Buhl et al., 2021).

Studie 2 (Sfärlea et al., 2020) untersuchte zum einen das Vorliegen, die Art und Ausprägung von **Interpretationsbias (IB)** (1) in der MD-Gruppe (n=32) und (2) in der HR-Gruppe (n=48), jeweils im Vergleich mit der LR-Gruppe (n=42). Zum anderen wurden die IB der MD-Gruppe und der HR-Gruppe verglichen, um Hinweise auf ihre Rolle bei der Vulnerabilität für Depression zu erhalten.

Hierfür führten die Probanden aller drei Gruppen (nach Induktion gedrückter Stimmung) zwei verschiedene behaviorale Paradigmen durch. In der häufig eingesetzten **Ambiguous Scenarios Task (AST,** (Mathews & Mackintosh, 2000)) lasen Probanden zunächst ambivalente Szenarien mit Bezug zu sich selbst (z.B. „Du bist mit einem Freund verabredet, den du länger nicht gesehen hast. Während du wartest, bist du sicher, er wird denken, du…“) und sollten dann, nach einer deren positive und negative Deutung anhand ihrer Ähnlichkeit mit der zuvor gelesenen Situation bewerten (z.B. „Während du wartest, bist du sicher, er wird das Treffen mit dir langweilig finden.“ u.a.). Ein IB ergab sich dann aus der Differenz zwischen Auswahl positiver und negativer Interpretationen (De Voogd et al., 2017). In der **Scrambled Sentences Task** (SST, (Wenzlaff & Bates, 1998)) waren sie aufgefordert, aus einer Auswahl an Wörtern einen Satz zu bauen, der eine Situation entweder positiv oder negativ darstellen kann (z.B. „Ich bin ein totaler Gewinner/Loser.“). Hier ergibt sich der IB aus dem Verhältnis negativer zu positiver gebildeter Sätze. Beide Paradigmen wurden bei Kindern und Jugendlichen bereits eingesetzt und zeigten akzeptable Reliabilitäten (Micco et al., 2014; Sfärlea et al., 2019).

Die Kinder und Jugendlichen der depressiven Gruppe zeigten in beiden Paradigmen deutlich stärker ausgeprägte IB im Vergleich zu beiden gesunden Gruppen (HR- und LR-Gruppe) mit großen Effektstärken. Der IB der HR-Gruppe im Vergleich zur LR-Gruppe war allerdings nur in der SST stärker ausgeprägt. Zudem korrelierten negative IB deutlich positiv mit depressiven (und Angst-) Symptomen, bei der SST in allen Gruppen, bei der AST jedoch nur in der MD-Gruppe. Diese Ergebnisse bestätigen also einerseits die Hypothese, dass IB auch bei Kindern und Jugendlichen mit Depressionen vorliegen. Andererseits deuten sie auch auf einen, wenn auch geringer ausgeprägten, IB bei Kindern und Jugendlichen mit erhöhtem Depressionsrisiko hin. Allerdings liegt dieser vermutlich eher auf einer impliziten Ebene vor, die die SST zu erfassen scheint, nicht aber die AST. Diese Annahme beruht auf dem Zeitdruck und der höheren kognitiven Loads bei der

SST, die weniger Raum für willentliche Kontrolle und bewusstes Antworten lassen, während die AST etwas mehr Zeit zum Überlegen vor der Antwort gibt und damit vermutlich eher eine bewusste, explizite Ebene der Interpretation abbildet. Darauf deuteten auch die Ergebnisse bei Kindern depressiver Eltern in der Vorläuferstudie hin (Sfärlea et al., 2019). Implizite negative IB könnten also bereits in dieser Risikopopulation vorliegen, d.h. einen Risikofaktor für Depression darstellen. Bei Ausbruch der Erkrankung könnten sie dann verstärkt und auch auf expliziter Ebene in Erscheinung treten. Eine vertiefte Darstellung des Hintergrunds, des Ablaufs und der Ergebnisse der Studie sowie eine vertiefte Diskussion findet sich in der entsprechenden Publikation (Sfärlea et al., 2020).

1.2.2. Zusammenfassende Diskussion und Ausblick

Zusammenfassend zeigte sich bei depressiven Kindern und Jugendlichen eine signifikant längere Betrachtungsdauer synthymer, störungsspezifischer emotionaler Stimuli (d.h. trauriger Gesichter)im Vergleich mit der Hochrisikogruppe (Studie 1), jedoch kein negativer Aufmerksamkeitsbias im Vergleich mit der Kontrollgruppe, sowie ein **negativer Interpretationsbias** auf expliziter und impliziter Ebene (Studie 2). In der Hochrisikogruppe ließ sich nur ein impliziter, weniger stark ausgeprägter negativer Interpretationsbias nachweisen (Studie 2), jedoch kein Aufmerksamkeitsbias (Studie 1). Beide kognitive Bias waren gruppenübergreifend umso ausgeprägter, je mehr depressive Symptome bestanden.

Die Hypothese einer negativen Verzerrung von Aufmerksamkeit und Interpretation bei pädiatrischen Depressionen und depressiver Symptomatik, analog zu erwachsenen Depressionen (Armstrong & Olatunji, 2012; Peckham et al., 2010), wird durch diese Ergebnisse in Teilen unterstützt. Hinweise für die hypothetische Rolle kognitiver Bias als Risikofaktoren für pädiatrische Depression ergeben sich nur für einen impliziten negativen Interpretationsbias.

Dass depressive Kinder und Jugendliche ihre **Aufmerksamkeit** länger auf störungsspezifische synthyme Stimuli gerichtet halten, bestätigt zwar auch die Ergebnisse behavioraler Studien (Hankin et al., 2010; Sylvester et al., 2016), widerspricht jedoch der verkürzten Betrachtungsdauer trauriger Gesichter, die Harrison und Gibb (2015) mittels Eyetracking feststellten. Dies könnte möglicherweise am geringeren Durchschnittsalter ihrer Stichprobe liegen, da die Aufmerksamkeitslenkung sich zu verändern und Aufmerksamkeitsbias zuzunehmen scheinen mit steigendem Alter bei Kindern und Jugendlichen mit z.B. Angststörungen (Dudeney et al., 2015). Der fehlende Nachweis eines vergleichbaren Aufmerksamkeitsbias in der Hochrisikogruppe steht im Kontrast zur Mehrheit der Literatur, die häufiger negative Aufmerksamkeitsbias auch bei Kindern depressiver Eltern gefunden hat (Platt et al., 2017). Vereinzelt fand sich jedoch auch das Meiden trauriger Gesichter (Connell et al., 2013; Gibb et al., 2009). Betrachtet man das zusammen mit der *nicht signifikanten* Tendenz unserer Stichprobe, traurige Gesichter zu meiden, wirft

dies die spekulative Frage auf, ob diese Risikogruppe ggf. auf eine Art Schutzmechanismus zurückgreifen könnte. Ein solcher könnte die Konfrontation mit negativen emotionalen Informationen verringern, um einen negativen Affekt zu reduzieren oder zu vermeiden. Ähnliche Überlegungen stellten auch Harrison und Gibb (2015) an, denn Aufmerksamkeitslenkung ist eine effektive Strategie zur Emotionsregulation (Gotlib & Joormann, 2010; Gross, 2014) und überschneidet sich in Teilen mit dem Konzept des Aufmerksamkeitsbias. Um dieser Frage nachzugehen und zu prüfen, ob ein solcher hypothetischer Effekt eventuell sogar den fehlenden Nachweis negativer Aufmerksamkeitsbias in unserer Risikogruppe erklären könnte, fehlte uns leider jegliche Datenbasis. Für künftige Studien zu Ansatzpunkten für Präventionsstrategien könnte die Frage nach einem potenziell schützenden Aufmerksamkeitsbias i.S. der Aufmerksamkeitslenkung in dieser Risikogruppe aber interessant sein.

Die Unterschiede zwischen depressiver und Risikogruppe bei der **Interpretation** sowie die Differenzierung zwischen explizitem und implizitem negativem Interpretationsbias unterstützen die Hypothese des negativen Interpretationsbias als möglichem Vulnerabilitätsfaktor für Depressionen, auch im Kindes- und Jugendalter und bestätigen die Ergebnisse von Dearing und Gotlib (2009). Sie passen zudem zu denen der beiden Vorläuferstudien mit der Frage nach einem Zusammenhang elterlicher und kindlicher kognitiver Bias bei elterlichen Depressionen: sowohl depressive Eltern, als auch ihre gesunden Kinder wiesen negative Interpretationsbias auf, die zusätzlich miteinander korrelierten (Sfärlea et al., 2019). Für Aufmerksamkeit ließen sich weder ein Bias bei den gesunden Kindern, noch ein Zusammenhang mit dem Bias ihrer depressiven Eltern nachweisen (Platt et al., 2022). Es ist also denkbar, dass ein impliziter negativer Interpretationsbias bereits vor Erkrankung vorliegt und z.B. das Entstehen depressionstypischer, negativer Denkmuster begünstigt (Williams et al., 2013) oder über Beeinträchtigung der Emotionsregulation, z.B. über ein Erschweren kognitiver Umbewertung ins Neutrale oder Positive (eine wichtige adaptive Emotionsregulationsstrategie) den Affekt negativ beeinflusst (Joormann & D'Avanzato, 2010; Mogg & Bradley, 2018). Ein Zusammenhang zwischen kognitiven Bias in Aufmerksamkeit und Interpretation und Emotionsregulation wurde bereits nachgewiesen bei depressiven Erwachsenen (z.B. (Duque & Vázquez, 2015; Manera et al., 2014; Strauss et al., 2016)) und bei depressiven Kindern und Jugendlichen (Hilt & Pollak, 2013; Romens & Pollak, 2012). Dies ließ sich auch an unserer Stichprobe, aufbauend auf den in dieser Dissertation vorgestellten Ergebnissen, feststellen: sowohl Aufmerksamkeits- als auch Interpretationsbias hatten einen direkten Effekt auf die depressiven Symptome, der durch maladaptive (und bei Interpretation auch durch adaptive) Emotionsregulationsstrategien vermittelt wurde (Sfärlea et al., 2021). Einen solchen Zusammenhang und die Einflüsse der einzelnen Komponenten empirisch weiter nachzuverfolgen, ist für die weitere Entwicklung theoretischer Modelle der Depression und in der Folge effektiver Therapie- und Präventionsinterventionen sicher interessant.

Die Ergebnisse dieser Dissertation legen insgesamt die Schlussfolgerung nahe, dass Interpretationsbias eine größere Rolle in der Entstehung der pädiatrischen Depression spielen könnten als Aufmerksamkeitsbias. Somit wären sie ein geeigneterer Ansatzpunkt für präventive Interventionen und z.B. für die therapeutische Rezidivprophylaxe. Dafür müsste aber zunächst ein Kausalzusammenhang nachgewiesen werden, also dass kognitive Bias, v.a. der Interpretationsbias, tatsächlich zum Entstehen einer Depression beitragen. Hierfür sind longitudinale Studien vonnöten, die einen Zusammenhang zwischen dem Vorliegen kognitiver Bias und der Entwicklung einer depressiven Episode in der Zukunft prüfen.

2. Zusammenfassung:

Depressionen sind eine der häufigsten psychischen Erkrankungen weltweit, auch im Kindes- und Jugendalter. Neben der Krankheitslast sind in diesem Alter die massiven Beeinträchtigungen der psychischen und sozioemotionalen Entwicklung ein großes Problem und ziehen soziale Nachteile und gesundheitliche Folgen bis ins Erwachsenenalter nach sich. Die bestehenden Behandlungs- und Präventionsmethoden zeigen zwar Wirkung, jedoch nur mit mäßigen, eher kurzfristigen Effekten. Ein differenziertes Verständnis der vielfältigen Mechanismen, die zur Entstehung und Aufrechterhaltung der Depression beitragen und ihres Zusammenspiels ist essenziell, um bestehende Methoden weiter zu verbessern.

Als zentrales Bindeglied zwischen neurobiologischen und psychologischen Faktoren der Depressionsentstehung und als Risikofaktor gelten negative kognitive Bias, d.h. ins Negative verzerrte kognitive Prozesse wie Aufmerksamkeit auf und Interpretation von emotionalen Informationen. Im Erwachsenenalter ist dies bereits gut untersucht, bei Kindern und Jugendlichen ist die Datenlage noch vergleichsweise dünn und eher widersprüchlich. Die vorliegende Dissertation untersucht daher das Vorliegen und die Charakteristika kognitiver Bias bei Kindern und Jugendlichen mit Depression sowie bei gesunden Gleichaltrigen mit depressivem Elternteil als Risikogruppe für Depression. Studie 1 erfasst verschiedene Aspekte der Aufmerksamkeit für emotionale Stimuli (Aufmerksamkeitsbias) auf behavioraler und neurophysiologischer Ebene, während Studie 2 verschiedene Aspekte der Interpretation potenziell mehrdeutiger emotionaler Situationen (Interpretationsbias) mittels behavioraler Methoden beleuchtet.

In Studie 1 zeigten nur depressive Kinder und Jugendliche einen negativen Aufmerksamkeitsbias (längere Aufmerksamkeit für traurige, also depressionsspezifische Stimuli) im Vergleich zur Risikogruppe, nicht jedoch im Vergleich zur Kontrollgruppe. Die Kinder depressiver Eltern zeigten keinen Aufmerksamkeitsbias. Studie 2 hingegen konnte sowohl bei depressiven Kindern und Jugendlichen als auch bei der Risikogruppe einen negativen Interpretationsbias (vermehrt negative Interpretation ambivalenter Situationen) feststellen. Bei der depressiven Gruppe lag dieser auf vermutlich impliziter und expliziter Ebene vor, bei der Risikogruppe war er geringer ausgeprägt und zeigte sich nur auf eher impliziter Ebene.

Negative Aufmerksamkeitsbias zeigten sich also nur bei depressiven Kindern und Jugendlichen, nicht bei Kindern depressiver Eltern. Negative Interpretationsbias zeigten sich dagegen in beiden Gruppen, in der Risikogruppe allerdings in abgeschwächter und eher impliziter Form. Demnach könnten Interpretationsbias in der Entstehung pädiatrischer Depressionen möglicherweise eine größere Rolle spielen als Aufmerksamkeitsbias und eventuell eher als Ziel therapeutischer und präventiver Methoden geeignet sein.

3. Abstract (English):

Major depression is one of the most common psychiatric illnesses worldwide, in adulthood as well as in childhood and adolescence. Apart from the burden of the disease itself, the impact on psychological, social and emotional development at young age is devastating and has ramifications on social and health status well into adulthood. Current therapeutic and preventive interventions do help, but show rather modest, short-term effects. A nuanced understanding of the various mechanisms underlying development and maintenance of depression as well as of their interplay is crucial to further improve existing methods.

A supposed central link between neurobiological and psychological factors of depression development and potential risk factors are cognitive biases, i.e., a shift towards the negative in cognitive processes such as attention to an interpretation of emotional information. This has been well established in adult research, whereas in childhood and adolescence, data on cognitive biases is rather scarce and inconsistent. The present dissertation aims to investigate presence and characteristics of cognitive biases in depressed children and adolescents as well as in youth at high risk for depression due to a depressed parent. Study 1 examines different aspects of attention to emotional information (attention bias) with different behavioral and neurophysiological measures. Study 2 examines different aspects of interpretation of potentially ambiguous situations (interpretation bias) using differing behavioral paradigms.

In study 1 only depressed youth showed a negative attention bias (longer maintenance of attention on sad, i.e., depression-specific stimuli) compared to at-risk youth, but not compared to the control group. At-risk youth did not exhibit any attention bias. Study 2, however, proofed depressed as well as at-risk youth to have a negative interpretation bias (i.e., interpreted ambiguous situations more negatively). In depressed youth, interpretation appeared biased on an explicit, as well as an implicit level, whereas in at-risk youth it only showed on a rather implicit level and was less pronounced.

These findings point to the presence of negative attention biases only in depressed, but not at-risk youth, whereas negative interpretation biases seem to be present in both currently depressed as well as in at-risk youth. Interpretation bias in the latter seems to differ a little from the one in currently depressed youth, since it appears to be only at an implicit level and to be less pronounced. In summary, one could assume interpretation biases might play a more important role in development of depression and therefore could be more applicable as a potential target in preventive and therapeutic interventions.

4. Studie I

Biased Maintenance of Attention on Sad Faces in Clinically Depressed Youth: An Eye-Tracking Study

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ORIGINAL ARTICLE

Biased Maintenance of Attention on Sad Faces in Clinically Depressed Youth: An Eye-Tracking Study

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Abstract
The role of negative attention biases (AB), central to cognitive models of adult depression, is yet unclear in youth depression. We investigated negative AB in depressed compared to healthy youth and tested whether AB are more pronounced in depressed than at-risk youth. Negative AB was assessed for sad and angry faces with an eye-tracking paradigm [Passive Viewing Task (PVT)] and a behavioural task [Visual Search Task (VST)], comparing three groups of 9–14-year-olds: youth with major depression (MD; n = 32), youth with depressed parents (high-risk; HR; n = 49) and youth with healthy parents (low-risk; LR; n = 42). The PVT revealed MD participants to maintain attention longer on sad faces compared to HR, but not LR participants. This AB correlated positively with depressive symptoms. The VST revealed no group differences. Our results provide preliminary evidence for a negative AB in maintenance of attention on disorder-specific emotional information in depressed compared to at-risk youth.

Keywords Attention bias · Youth depression · Risk for depression · Eye-tracking

Introduction

Major Depression (MD) is among the most common mental illnesses in children and adolescents with a prevalence of 17% up to the age of 18 years [1]. It not only has as major impact on development during childhood and adolescence but it is also associated with adverse outcomes in adulthood regarding education, social life and physical [2] as well as mental [3] health. Considerable neurobiological and cognitive development as well as high neural plasticity during childhood and adolescence may explain why youth are more vulnerable to psychopathology [4, 5]. With modest effects and high recurrence rates, however, current standard treatment does not suffice [6]. In order to refine and complement existing treatment, a more detailed understanding of mechanisms underlying development and maintenance of depression in youth is needed.

Negative Attention Biases (AB) in Depression

Cognitive models of depression consider cognitive biases a key element in development and maintenance of MD [7, 8]. Cognitive biases describe a shift in three aspects of information processing: attention to, interpretation of and memory for emotional information [9–11]. This shift promotes the filtering of incoming information according to the depressive schemas that initially activated the biases and in turn results in confirming these schemas, facilitating negative mood [8]. The shift in attention towards negative compared to positive or neutral information is referred to as negative attentional biases (AB). According to the model of vulnerability to depression by De Raedt and Koster [12], attentional processes are influenced by genetic and neuroregulatory factors [e.g. hypothalamic–pituitary–adrenal (HPA) axis functioning and impaired attentional networks] and are bi-directionally associated with emotion regulation (e.g. rumination). In this framework, negative AB would be essential in linking

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psychological and biological vulnerabilities for depression and its recurrence [12].

Importantly, attention is not a unitary process but comprises multiple consecutive components: orientation, maintenance and detachment of attention [13]. Studies on adult depression find reliable evidence for AB in the maintenance of attention on negative disorder-specific stimuli, while results regarding orientation of attention are less robust [11, 13]. Since major development occurs in cognitive and emotional functioning [14] and in attentional networks [15] during childhood and adolescence, results from adult studies cannot be directly transferred to youth. Cognitive patterns might not evolve into stable, trait-like "cognitive styles" until adulthood [16], therefore these might have less influence on cognitive vulnerability in youth than in adult depression. Alternately, brain maturation and hormonal changes associated with an enhanced emotional sensitivity [17] might make youth more susceptible to negative cues in ambiguous emotional information, resulting in more pronounced negative cognitive biases.

Negative Attention Biases (AB) in Youth Depression

There is a growing body of literature on AB in depressed youth, yet findings are heterogeneous [18]: while some studies found youth with MD to show increased attention *towards* negative disorder-specific (sad) information [19, 20], another study found them to *avoid* sad stimuli [21]. An association between negative AB towards threatening information (angry faces) and depressive symptoms in unselected youth was observed by one study [22], while no evidence for AB was discovered at all in a different study [23]. These differences could be due to moderating factors like genetic differences in e.g. hypothalamic–pituitary–adrenal (HPA) axis reactivity [24], or due to the different methods employed or different aspects of attention measured (e.g. allocation, maintenance with or without distraction) in different samples. As such, the direction of AB, i.e. whether depressed individuals prefer or avoid (i.e., show AB towards or away from) negative stimuli is unclear. Results are also unequivocal regarding specificity, i.e. whether AB apply to disorder-specific stimuli (e.g. sad faces) or threatening stimuli (e.g. angry faces) or negative information in general.

Measuring AB

To assess AB, reaction-time (RT) based behavioural measures are used regularly, with speed of response acting as indicator for AB towards or away from emotional stimuli. Investigating AB by measuring RT involves drawing indirect inferences about the focus of attention at one distinct point in time, neglecting that attention consists of different consecutive stages [13]. In addition, RT is influenced by non-attention-related processes like the speed of motor response, which may be generally delayed in MD [12]. The most frequently used paradigm, the Dot-Probe Task (DPT) [25], in which a probe appears in the location of either an emotional or a neutral stimulus, has been shown to have unacceptable psychometric properties [26–28]. The emotional Visual Search Task (VST) [29], an alternative paradigm measuring RTs to identify a target emotional stimulus among distractors, shows better reliability [30, 31].

A more direct approach to assess attention is registering overt visual attention by tracking eye movements [13]. In eye-tracking (ET) studies, free viewing paradigms like the Passive Viewing Task (PVT) [21] are used most frequently. Participants are presented with various emotional stimuli to look at without further instruction. This method is not influenced by (non-ocular) motor response and, more importantly, provides data of visual attention over a longer period of time, enabling to distinguish between the various components of visual attention (unlike RT based measures). As Högström et al. [32] elaborate, the vigilance-avoidance-hypothesis in research of AB in anxiety states that differentiating categorically between visual attention towards (vigilance) or away from (avoidance) salient stimuli might not grasp the attentional process accurately. Instead, there is evidence from eye-tracking research that individuals with anxiety show initial vigilance to disorder-related stimuli, followed by avoidance (see e.g. [32–34]). As both, initial orientation of attention as well as maintenance of attention can be assessed via the PVT, it allows to investigate if the vigilance-avoidance-hypothesis or similar more complex attentional mechanisms also apply to youth depression.

Additionally, psychometric properties of the PVT have been found acceptable in adults [27, 35] and in youth [36]. To our knowledge, only two studies have employed this paradigm to investigate bias in sustained attention in youth depression: one found AB away from sad faces in youth with MD [21], the other found AB towards sad faces in youth at risk for MD, moderated by genetical differences in HPA-axis reactivity [24].

The Current Study

The study had two main aims. The *first aim* was to investigate whether negative AB are present in youth with MD and to characterise AB by (1) direction (attention towards or avoidance of negative emotional stimuli) and (2) specificity to emotions and to particular aspects of attention. To investigate specificity to emotion, we assessed biases for disorder-specific (sad) as well as non-specific (angry) faces. To investigate different aspects of attention, we used multiple age-adapted experimental tasks: the DPT as the most commonly used AB task, the VST, an RT-based measure guiding participants' attention towards distinct emotions and

the PVT, an ET based measure in which individuals freely gaze at the emotional stimuli.

We compared 9–14-year-olds[1] with MD to two groups of non-depressed children and adolescents varying in their risk for depression: children of parents with a history of depression, known to have an increased risk for MD themselves (high-risk; HR), see e.g. [39] and children of parents with no history of any mental disorder with a low risk for depressive disorders (low risk; LR). The comparison of those three groups enabled us to pursue the study's *second aim*: to determine whether AB are more pronounced in currently depressed youth compared to youth at elevated risk for depression. HR youth have been found to show AB for negative information, although their direction and specificity has not been established yet with evidence for AB towards sad [40, 41] or angry [42] stimuli, as well as for AB away from sad stimuli [43]. Negative AB in children and adolescents at risk for depression would indicate that AB might act as a cognitive vulnerability contributing to the development of depression, as suggested by theoretical models, e.g. [7, 8]. Even more pronounced AB in currently depressed children and adolescents however would indicate that these biases might be exacerbated as a consequence of depressive symptomatology.

No study to date has directly compared AB in depressed, HR and LR youth, however, studies on interpretation [44] and memory [45] biases have found negative biases to be present in both depressed as well as high-risk youth compared to low-risk youth but to be more pronounced in currently depressed youth than in high-risk groups.

With respect to our first aim we expected to find more negative AB in currently depressed youth compared to healthy youth (both high- and low-risk), in accordance with theoretical models [8] and previous research [18]. Regarding specificity, we expected AB for sad faces (i.e. mood-congruent depression-specific stimuli) rather than angry faces (i.e. threatening anxiety-specific stimuli) in both the MD and HR groups. Due to differences in direction of AB in previous studies, we did not make predictions on direction of AB, i.e., whether MD participants would look preferably towards negative stimuli or avoid them. With respect to our second aim, we expected negative AB to be present in youth at high risk for depression compared to youth at low risk for depression (according to [40–42, 46]) but to be more pronounced in the MD versus HR group, as found for interpretation and memory biases [44, 45].

Material and Methods

Data on AB presented in this paper were collected as add-on to a study on cognitive biases in the offspring of depressed versus non-depressed parents [37]. Data from tasks comparing AB in MD, HR and LR youth are presented here. Data from interpretation bias tasks [38, 44] and tasks comparing AB in children and parents of HR and LR groups [36] are presented elsewhere. To ensure quality of our tasks and results, we determined psychometric properties of each task and parameter and only report those with acceptable reliabilities (PVT, VST). Additional tasks and results can be found in the supplement.[2]

Participants

In total, 124 children and adolescents aged 9–14 years were included in data analysis.[3] Participants formed three groups based on their current mental health state and risk of developing MD: n = 32 youth with MD (MD group), n = 49 mentally healthy youth at high familial risk for MD (HR group) and n = 43 mentally healthy youth with low risk for MD (LR group). Sample size was based on an a priori power analysis (α error probability = 0.05; power = 0.8; two-tailed) for the comparison of HR and LR groups (a smaller effect size was expected for this effect than for comparison with the MD group). Based on effect sizes (ES) from previous studies with mood induction procedures [40, 41], we expected an ES of at least d = 0.7, resulting in a required sample of n = 34 per group.

Participants with MD were recruited mainly at a University Hospital for Child and Adolescent Psychiatry in Germany, some by a cooperating licensed psychotherapist and some responded to public adverts. Data of the LR and HR groups was largely (87%) derived from a study evaluating the transgenerational transmission of cognitive biases [36, 38] in which children and adolescents participated with one of their parents. N = 29 HR participants were recruited from a previous study on a preventive intervention for this particular risk group [48], n = 12 of them had taken part in the programme by the time they were tested in the present study.

[1] As the present study was planned as add-on to a study on transgenerational transmission of cognitive biases 37, 38, it focused on the same age range. Children younger than 9 years were not included due to concerns about their ability to understand and perform the tasks. Adolescents above 14 years were not included since the incidence of MD in children of depressed parents increases substantially after that age, e.g. 39, and investigating older mentally healthy children of depressed parents might result in examining a particularly resilient, thus non-representative sample.

[2] In addition to PVT, VST and DPT, we aimed to assess AB with a computerized version of the Scrambled Sentences task (SST, 47) via ET in addition to interpretation bias (IB; see 44 for results on IB). Due to poor reliability, DPT and SST are included in the supplement.

[3] 126 children and adolescents were tested; two were excluded due to poor compliance.

Others, as well as children in the LR group, were recruited by local and online advertisements and by letters to randomly selected families with children in the corresponding age range provided by the local registry office.

Youth were included in the MD group if they currently met criteria for MD according to DSM-IV [49]. Of those 32 youths, n = 4 fulfilled criteria for a recurrent course of MD, n = 2 were in partial remission, n = 15 had at least one comorbid anxiety disorder and n = 3 were treated pharmacologically. The HR group comprised youth who did not meet criteria for any axis I disorder, current or past,[4] but at least one of their parents fulfilled diagnostic criteria for MD (n = 47; of which n = 8 fulfilled diagnostic criteria at the time of participation) or dysthymia (n = 2) during the child's lifetime. Youth were not included if their parents had a history of bipolar disorder, schizophrenia or substance abuse. Participants were included in the LR group if they did not meet criteria for any axis I disorder currently or in the past and none of their parents met criteria for any axis I disorder at any time. All participants had normal or corrected to normal vision. Exclusion criteria for participants in all three groups were an intelligence quotient (IQ) < 85,[5] assessed with the CFT-20-R [50], a pervasive developmental disorder, attention deficit and hyperactivity disorder or a history of schizophrenia or bipolar disorder.

All procedures were approved by the ethics committee of the Medical Faculty of the LMU Munich. Written informed consent was obtained from all participants and parents after a comprehensive explanation of the experimental procedures. HR and LR youth who participated with their parents in the previous study on transgenerational transmission of cognitive biases received a reimbursement of €50 while MD participants who took part without their parents only in this study received €30.

Psychopathology Assessment

Before inclusion, all participants underwent extensive diagnostic assessment. The K-DIPS ("Diagnostisches Interview bei psychischen Störungen im Kindes- und Jugendalter") [51], a standardised, semi-structured psychiatric diagnostic interview for assessment of psychiatric diagnoses in youth, was administered to participants and one of their parents. The K-DIPS is a well-established German diagnostic measure based on diagnostic criteria of axis I disorders according to DSM-IV [50] with good interrater-reliabilities [52]. Interviews were conducted and evaluated by trained interviewers. Interrater-reliability was determined for 18% of HR and LR participants and revealed an accordance rate of 100% for lifetime diagnosis of depression (pre-defined criterion). Interviews from the MD group were not re-rated, but most MD participants were receiving treatment for a clinical diagnosis of depression that was confirmed with the diagnostic interview. Psychiatric diagnoses of LR and HR participants' parents were assessed with the adult version of the interview, the Diagnostisches Interview bei psychischen Störungen (DIPS), [53], with good interrater-reliability [54]. Accordance rate for lifetime diagnosis of depression was 94% in our sample. In the HR group, the DIPS was administered only to the parent affected by depression; in the LR group the DIPS was administered at least to one parent and whenever possible to both parents.[6] The German version of the Beck Depression Inventory-II [55], obtained from both parents for 83% of LR youth, was used to measure parents' depressive symptoms. Scores differed significantly ($t_{64.5} = 6.0$, $p < 0.001$) between parents of HR (M = 9.9; SD = 8.5) and LR participants (M = 1.9; SD = 3.5).

For the assessment of the participants' depressive symptoms the German version of the Children's Depression Inventory "DIKJ" [56] was used and symptoms of anxiety were measured by the trait scale of the German version of the State Trait Anxiety Inventory for Children, STAIC [57]. For 123 of 124 included participants, a score for depressive symptoms could be determined and for 119 of 124 children an anxiety score was available. In our sample, reliability of both self-report measures was excellent (DIKJ: Cronbach's $\alpha = 0.96$; STAIC-T: Cronbach's $\alpha = 0.92$).

Stimuli

Coloured photographs of children's faces displaying sad, angry, happy and neutral expressions on black background served as stimuli in both tasks [58]. Half of the models were male, half female in each task. The stimulus set comprised photographs of 16 models with sad, angry and happy expressions in the VST and 24 models with sad, angry, happy and neutral expressions in the PVT.

[4] One HR participant had met criteria for enuresis in the past, but did not report any other symptoms of any other mental disorder, so she was included nonetheless.

[5] Two MD group participants scored just below 85. The substandard IQ did not correspond to the clinical impression and was most likely due to a lack of compliance and inability to concentrate in the context of their MD. Therefore, they were still included.

[6] This was possible for 79% of LR participants. For the other 21% the second parent was not available for the interview, for example because participants grew up in a single parent household with little or no contact to the second parent. We still included those children and adolescents as excluding them would have decreased representativeness of the sample.

Fig. 1 Example of an emotional trial of the Visual Search Task (VST; [29])

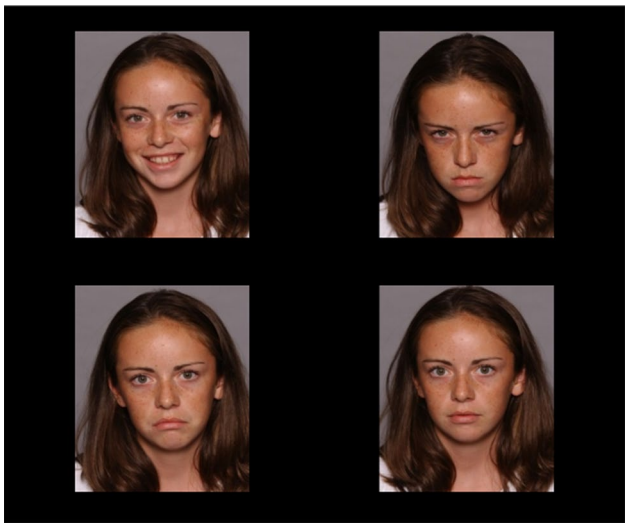

Fig. 2 Example stimulus display from the Passive Viewing Task (PVT; [20])

Visual Search Task (VST)

An emotional VST, adapted from [29] was used to assess AB in an RT-based task with explicit instructions to attend to specific emotions. The task was administered during ET, but due to poor reliability of the ET indices, ET results are reported in the supplement.

Each trial started with a drift correction (small white circle in the screen's centre). Upon fixation of the circle, the trial was initiated. A fixation cross was then presented for 500 ms in the screen's centre. Subsequently, the stimuli were presented in a 4 × 4 grid containing 15 distractors and one target (see Fig. 1). Each stimulus display contained all 16 models randomly allocated to the 16 grid positions. The participants' task was to identify the face showing a certain emotion (i.e., the target) as quickly as possible and click on it with the mouse. Time to identify the target was unlimited. The experiment consisted of four blocks: Two blocks with happy targets and negative (either sad or angry) distractors and two with negative targets and happy distractors. Each block comprised 32 trials with the target appearing twice in each position and being twice each model. Blocks as well as trials within the blocks appeared in random order. Before each block, participants completed three practice trials.

Data Processing and Outcome Variables

Trials with incorrect responses or RTs shorter than 200 ms or longer than 2 SDs above each participant's mean were excluded, in line with previous studies, e.g. [24]. Participants with poor accuracy (a correct and valid trial rate of 2 SDs below mean rate) were identified as outliers in terms of accuracy and excluded (n = 1 MD; n = 2 HR; n = 1 LR). In the remaining sample of 120 children, on average 119.6 correct and valid trials per participant (SD = 1.9; 93% of 128 trials; no group differences, Fs < 1, ps > 0.1) were available for analysis of the behavioural data.

A bias score (AB_{VST}) was calculated by subtracting the mean RT in blocks with negative targets and positive distractors from the mean RT in blocks with positive targets and negative distractors [29, 59]. Hence, positive bias scores indicate more distraction by negative information (i.e. negative AB) and negative bias scores indicate more distraction by positive information (i.e. positive AB). AB_{VST} scores for sad and angry faces were computed separately.

Reliability

To investigate internal consistency for the VST, split-half reliability was assessed by correlating bias scores based on odd versus even trials [60]. Reliability of the behavioural bias score was acceptable for both emotions (sad: r = 0.83, p < 0.01, Spearman-Brown corrected: 0.91; angry: r = 75, p < 0.01, Spearman–Brown corrected: 0.86).

Passive Viewing Task (PVT)

As a purely ET-based measure of AB, enabling participants to freely gaze at the emotional stimuli, a PVT was administered [21]. Each trial began with a drift correction (see above). A fixation cross followed for 1000 ms. Then the 2 × 2 stimulus array was presented for 15000 ms. The task consisted of 16 emotional trials, corresponding to the minimum trial number suggested for ET research [61] and eight neutral trials (not analysed), presented in random order. In the emotional trials, each array consisted of four photographs of the same model displaying a sad, angry, happy and neutral facial expression (see Fig. 2). The position of each emotional facial expression was randomly assigned to one of the quadrants with each emotion being presented four times in each quadrant. The neutral trials comprised four photographs of the same model with a neutral facial expression. Stimuli were sized approximately 9.5 cm × 7.5 cm and were presented with a distance of approximately 6.5 cm horizontally and 1 cm vertically between. Participants were instructed to fixate the white circle and fixation cross and then freely view the stimuli, required only to keep their attention focussed on the screen.

Eye-Tracker

Eye movements were registered with an EyeLink 1000 Plus Desktop mounted eye-tracker (SR Research). Participants were seated in front of a 15-inch monitor (1024 × 768 pixel resolution) on which the experiments were presented using Experiment Builder 1.10 (SR Research Ltd., 2013). Viewing was binocular while eye movements were registered from the dominant eye via infrared video-based tracking technology with a sampling rate of 1000 Hz. A forehead and chin rest minimized head movements and kept the viewing distance constant at 65 cm. Lighting of the room was kept constant for all participants. Before each task, a 9-point calibration and validation procedure was conducted and calibration was accepted if the average error was less than 0.5° of visual angle and the maximum error was less than 1° of visual angle.

Eye movement events were detected using a velocity and acceleration-based saccade detection method with saccades defined, in line with other studies [e.g., 28, 62], as events with a velocity above the threshold of 30°/s or an acceleration above the threshold of 8000°/s2. Gaze positions that were stable within 1° of visual angle for at least 100 ms were defined as fixations (in line with other studies [e.g., 63].

To ensure data quality, trials with a total dwell time of less than 75% of the presentation time were excluded due to excessive blinks or missing data [62] and ET data of each participant was inspected for systematic calibration errors. Subsequently, participants with less than 70% valid trials [64] and systematic calibration errors were excluded from the analyses of the eye-tracking data (n = 3 MD, n = 3 HR and n = 1 LR).[7]

Data Processing and Outcome Variables

After exclusion, a remaining sample of 115 children with on average 15.3 trials (SD = 1.1; 95.6% of 16 trials) per participant were available. This did not differ between groups ($F \leq 1.8$; $ps > 0.1$).

As an indicator of initial orientation of attention, percentages of location of the first fixation on each emotion were assessed. As this parameter showed poor reliability, results are reported only in Supplement 2. As indicator of maintenance of attention, percentages of dwell time (defined as summation of all fixations) on each of the four emotions were assessed. For appraising the course of attention over time, trials were divided into five time windows (each 3000 ms).

Reliability

To assess reliability of the PVT, Cronbach's alpha was calculated for percentage of dwell time on all four emotions (as for this task no AB scores were computed). Reliabilities for percentage of dwell time ranged from acceptable to good (angry: $\alpha = 0.69$, happy: $\alpha = 0.86$, neutral: $\alpha = 0.83$, sad: $\alpha = 0.86$).

Procedure

The course of the experimental session corresponds to [38]. Tasks were presented in random order and a mood induction procedure was administered twice during the experimental session. Participants watched a 2 min scene from the movie The Lion King [64] that had successfully induced unpleasant mood in children and adolescents before [65]. In our study, participants in both healthy groups reported a significantly worse mood, assessed using the valence dimension of the 9-point Self-Assessment Mannequin scale [66] after watching the movie scene compared to baseline ($Fs \leq 43.22$; $ps < 0.001$). Mood did not change significantly, however, in the MD group ($F2.4 = 1.15$; $p = 0.33$). Details are presented in Supplement 5.

Data Analysis

Statistical data analysis was conducted with SPSS25. Significance level was set to $p = 0.05$ (two-tailed).

[7] PVT: Data of 1 MD and 1 HR participant were unavailable due to technical difficulties.

Table 1 Demographic and clinical characteristics

	MD	HR	LR	ANOVA	Post hoc tests	
	$n=32$	$n=49$	$n=43$			
Gender m/f	6/26	19/30	18/25	$\chi^2=4.9$	n.s	
Age; M (SD)	13.4 (1.4)	11.8 (1.7)	12.1 (1.7)	$F_{2,121}=9.8$	$p<.001$	MD > HR = LR
IQ; M (SD)	105.2 (13.6)	108.8 (11.5)	111.8 (10.2)	$F_{2,121}=2.9$	n.s	
Depressive symptoms; M (SD)	31.5 (8.9)	7.9 (5.7)	6.6 (5.2)	$F_{2,120}=163.5$	$p<.001$	MD > HR = LR
Anxiety; M (SD)	45.1 (8.8)	30.0 (6.4)	28.1 (6.2)	$F_{2,116}=56.6$	$p<.001$	MD > HR = LR

Depressive symptoms were assessed with DIKJ (raw values presented), anxiety with STAIC-T. All post-hoc tests were significant ($p<.001$)

MD major depression group, *HR* high-risk group, *LR* low-risk group, *M* Mean, *SD* Standard Deviation

Table 2 AB scores from the Visual Search Task

AB_{VST}	MD	HR	LR
	$n=31$	$n=47$	$n=42$
AB_{VST} for sad faces M (SD)	−47.0 (1040.1)	−259.2 (1098.6)	−323.8 (832.6)
AB_{VST} for angry faces M (SD)	−11.0 (882.2)	227.4 (1227.9)	89.2 (884.6)

AB_{VST} attention bias score from the Visual Search Task, *MD* major depression group, *HR* high-risk group, *LR* low-risk group, *M* Mean, *SD* Standard Deviation

For the VST, one-way analyses of variance (ANOVAs) were conducted to assess group differences in AB_{VST} scores. To assess relationships between psychopathology and AB, correlations were calculated of AB_{VST} score with depression and anxiety scores.

For the PVT, a repeated-measures ANOVA with within-subject factors Time Window (5: time windows 1–5) and Emotion (4: angry, happy, neutral, sad) and the between-subjects factor Group (3: MD, HR, LR) were performed for percentages of dwell time. Degrees of freedom were adjusted via Greenhouse–Geisser correction when necessary. As this study's main focus was a group comparison, only significant effects involving the factor Group were followed up using post-hoc ANOVAs and t-tests. To assess relationships with psychopathology, correlations of dwell time on each emotion (averaged across time windows) with depression and anxiety symptoms were computed.

All analyses were repeated excluding participants with psychopharmacological treatment (n = 3), as this has been found to reduce negative cognitive biases [67] and enhance attention toward positive stimuli [68]. The pattern of results in our sample remained the same, so findings are reported based on the whole sample. We did not include age as a covariate in our analyses as this is not appropriate when the between-groups factor (group) and covariate (age) are non-independent [69]. However, we performed additional analyses to investigate if age may have accounted for our results (see below).

Results

Sample Characteristics

Sample characteristics are presented in Table 1. Groups did not differ in gender ratio or IQ but in age: participants in the MD group were significantly older than participants of the HR and LR groups. As expected, the groups also differed in psychopathology: the MD group reported higher depression and anxiety symptoms than the healthy groups, which did not differ from each other, indicating that the HR group was as psychiatrically healthy as the LR group.

Visual Search Task

One-way ANOVAs on AB_{VST} scores revealed no significant differences between MD, HR and LR youth ($Fs<1$; $ps>0.1$) regarding sad or angry faces. The AB_{VST} for sad faces was significantly <0 in the LR group ($t_{41}=2.5$, $p=0.016$), indicating a positive AB for sad faces (i.e. away from sad faces/towards happy faces), but bias scores for sad faces in the other groups as well as for angry faces were not significantly different from 0 ($ts\leq1.6$, $ps>0.1$). Bias scores are presented in Table 2. The correlational analyses revealed no relationship between AB_{VST} scores for sad or angry faces with depressive or anxiety symptoms ($r\leq0.17$; $p\geq0.072$).[8]

[8] As reaction times were not normally distributed, we repeated our analyses with bias scores calculated from median instead of mean reaction times as well as bias scores based on square root transformed reaction times. The pattern of results did not change.

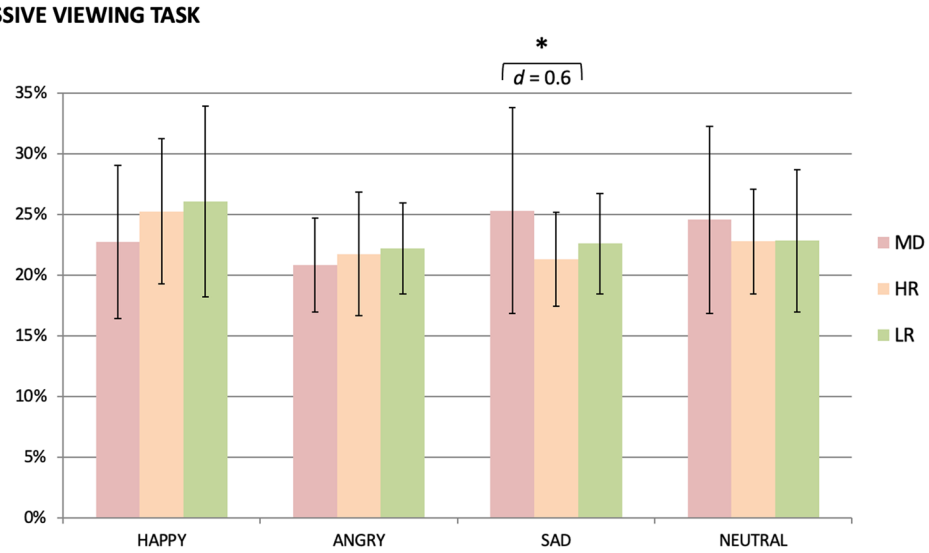

Fig. 3 Percentage of dwell time on emotional faces among groups. *MD* major depression group, *HR* high-risk group, *LR* low-risk group. * MD and LR group differ significantly in their dwell times on sad faces. Error bars represent standard deviations

Passive Viewing Task

The TimeWindow × Emotion × Group ANOVA revealed a significant main effect of TimeWindow ($F_{1.9,207.3} = 24.3$, $p < 0.001$, $\eta_p^2 = 0.18$) and Emotion ($F_{2.6,295.1} = 4.5$, $p = 0.006$, $\eta_p^2 = 0.04$). Significant TimeWindow × Emotion ($F_{9.6,1076.0} = 1.9$, $p = 0.040$, $\eta_p^2 = 0.02$) and Emotion × Group ($F_{5.3,295.1} = 2.5$, $p = 0.027$, $\eta_p^2 = 0.04$) interactions emerged. All other main effects and interactions were non-significant ($Fs \leq 2.3$; $ps \geq 0.1$). To follow up the Emotion × Group interaction, ANOVAs with the factor Group were calculated separately for each emotion on percentage of dwell time averaged across time windows: a significant effect emerged of Group for sad faces ($F_{2,112} = 4.7$, $p = 0.011$, $\eta_p^2 = 0.08$), but no other emotion ($Fs \leq 2.5$, $ps \geq 0.08$). Post-hoc t-tests revealed a significant difference in percentage of dwell time on sad faces between the MD and HR groups ($t_{36.2} = 2.3$, $p = 0.027$, $d = 0.6$) with the MD group dwelling more on sad faces than the HR group. Differences between MD vs. LR groups ($t_{33.4} = 1.5$, $p = 0.145$, $d = 0.4$) and between HR and LR groups ($t_{85} = 1.7$, $p = 0.090$, $d = 0.4$) were non-significant, with a trend for HR participants dwelling less on sad faces than LR participants. Percentages of dwell time are presented in Fig. 3. Furthermore, positive correlations of dwell time on sad faces with depressive ($r = 0.29$, $p = 0.002$) and anxiety symptoms ($r = 0.38$, $p < 0.001$) and a small negative correlation between dwell time on happy faces and depressive symptoms ($r = -0.21$ $p = 0.023$) were found among all participants.[9]

Additional Analyses

As groups differed in age, we performed additional analyses to investigate if this may have accounted for the group differences in dwell times on sad faces. Pearson's correlations between age and dwell time on sad faces were computed separately within each group (to rule out that correlations were artifacts of group differences): no significant correlations emerged ($rs \leq 0.23$, $ps > 0.1$).

Discussion

The overarching goal of the present study was to investigate the nature of negative AB in depressed youth. With two different experimental approaches, a passive viewing ET paradigm and an RT-based task externally guiding attention, we evaluated AB in three groups of 9–14-year-olds: currently depressed youth (MD group), mentally healthy youth with a high familial risk for depression (HR group) and with a low familial risk for depression (LR group). While the behavioural paradigm revealed no evidence of AB in any group, the eye-tracking paradigm revealed a more negative bias towards disorder-specific stimuli in depressed compared to high-risk youth in maintenance of attention. This measure correlated with depressive symptoms across groups.

Our *first aim* was to characterise AB in depressed youth regarding presence, direction, specificity to disorder-related information and specificity to particular attentional

[9] As groups differed in psychopathology scores and dwell time, correlational analyses were repeated within each group: correlations between dwell time on sad faces and depressive symptoms as well as anxiety scores were non-significant ($rs \leq .28$, $ps \geq .083$).

components. Our *second aim* was to determine to which extent AB are more pronounced in currently depressed youth compared to at-risk youth.

We found a significant group difference in dwell time on sad faces in the PVT between youth with MD and at-risk youth: as expected, youth with MD dwelled longer on sad faces compared to youth at risk for depression. Contrary to our expectations, the LR group's dwell time on sad faces was in between: they dwelled less on sad faces than the MD group but more than HR youth (although these differences were non-significant). No differences were found for the other emotions. These results partially support our hypotheses: they suggest that youth with MD might show more negative AB in maintenance of attention on disorder-specific negative stimuli in comparison to healthy children. However, according to our results, this would appear to be the case only for healthy children with a familial risk of depression.

Youth with MD preferentially attending to disorder-specific negative information is in line with several studies [19, 20], nevertheless, the only study that used a similar passive viewing ET paradigm [21] found that youth with MD looked less at sad faces, i.e. avoided them. These contradicting results might be explained by the age of the investigated samples: while the mean age of the depressed groups in the studies by Hankin et al. [19], Sylvester et al. [20] and ours was above 13 years, Harrison and Gibb [21] examined a considerably younger sample with a mean age of 11.2 years which might have captured youth before a "maladaptive shift" in their emotion regulation starting approximately from age 12 [70, 71]. Harrison and Gibb [21] argue that children may use avoidance of sad faces to regulate negative emotion and that this ability may diminish with age. Thus, it would be lost in older adolescents and adults with depression, leaving them to preferentially attend to negative information. A similar idea of a change in attention bias with age is found in research on AB for threatening stimuli in youth with anxiety disorders: as Dudeney et al. [33] showed in their meta-analysis, differences in AB to threat between children with anxiety diagnosis and control groups are found to increase with age. This change might be due to a general tendency in children to be more immediately reactive to external stimuli, which would normally decrease over time as their ability to inhibit attention and information processing develops. Children and adolescents who develop an anxiety disorder might instead maintain this heightened attention towards threat [34]. If this reactivity would not only apply to threatening stimuli, but also to other salient stimuli, the same development might potentially occur regarding AB towards sad stimuli.

Although not statistically significant, our HR group showed a slightly *less* pronounced negative AB compared to the LR group. This pattern of results was somewhat surprising as AB in high-risk youth are proposed to act as a risk factor for depression [46] and to be exacerbated during an episode of depression (as memory and interpretation biases [44, 45]) and are therefore expected to have the same direction as AB in currently depressed youth. As attentional deployment is an effective emotion regulation strategy (see e.g. [9, 72]), AB away from negative information might act as a protective mechanism against development of depression. Our sample of children of depressed parents tended to show AB away from sad faces, as described for mentally healthy youth [19, 73]. It is conceivable, albeit rather speculative, that they might have acquired this mechanism as a protective response to their parents' disorder. This might add to their resilience, helping to explain why they are still psychiatrically healthy despite their heightened risk for MD.[10] Maybe at-risk youth who do not apply this protective mechanism would be more vulnerable to depression and may have already developed a depressive disorder [74]. In line with this assumption, participants in our MD group did not show this protective mechanism—either because their ability to avoid negative information was already less pronounced before, adding to their vulnerability, or because their ability to regulate their emotions this way diminished as a consequence of depressive symptomatology [75]. Due to the cross-sectional design of our study, we cannot make conclusions about time course or causality, i.e. whether the more negative AB in the MD group compared to the HR group is a consequence of depression, present before disorder onset, or if the use of avoidance of negative stimuli as an emotion regulation strategy decreases with age as suggested by Harrison and Gibb [21]. However, these deliberations are highly speculative since differences between HR vs. LR and MD vs. LR did not reach significance, the difference between HR and MD groups would not have been significant if a correction for multiple testing had been applied and effect sizes for differences between groups were smaller than expected.

Other indices of attention we investigated yielded either non-interpretable results due to poor reliability (e.g., location of the first fixation in the PVT as index of initial attention allocation; see Supplement 2) or did not reveal any group differences despite acceptable reliability (e.g., the behavioural AB_{VST} parameter). In the VST, the LR group was found to show a small positive AB regarding sad faces, but no significant biases emerged for HR or MD groups as well as no group differences. Since the VST was originally designed to modify AB and measure within-subject differences in a Cognitive Bias Modification Training [29, 76], it

[10] Note that in our HR group, only children of depressed parents who did *not* meet criteria for any axis I disorder (current or past) were included, i.e. only the still mentally healthy. Therefore, this sample of HR children is not representative of unselected children of depressed parents, expected to show more pronounced psychopathology on average.

might not be sensitive to between-group differences. Moreover, the VST is based on distinct instructions which emotion to attend to, i.e. attention is guided externally, whereas in the PVT, participants can deliberately choose where to turn their attention. In our study, evidence for AB in depressed youth was found only with the PVT, not the VST, suggesting that depressed and high-risk youth differ only in an internally controlled and at least to some extent conscious aspect of attention. This is in line with Teachman et al. [77] who found evidence for a more conscious, intentional bias in attention. Importantly, the measure revealing group differences—percentage of dwell time on sad faces in the PVT—not only showed good reliability but was also related to depressive symptoms across groups, suggesting it is a valid indicator of "depressive" processing.[11] Of note, dwell time as a measure of AB cannot be easily attributed a certain component of attention. Longer dwell times, i.e., longer maintenance of attention on certain stimuli, may result from participants more frequently looking at them, having difficulties disengaging their attention from them, or deliberately maintaining their attention on them. Future studies may try to tease apart those mechanisms in order to identify which is or are responsible for our results.

Strengths

To our knowledge, this is the first study directly comparing AB in currently depressed, high-and low-risk youth. It contributes to a more detailed understanding of AB in youth depression and their role in development and maintenance of MD. Another strength is our use of a standardised, semi-structured diagnostic interview with all participants, conducted by trained personnel to ensure diagnostic accuracy. Moreover, parental psychopathology was also assessed via a psychiatric interview in the HR and LR groups rather than relying on self-report measures. In addition, we used multiple measures of AB, assessing attention in deliberate vs. externally guided circumstances. We evaluated reliabilities of our measures, a practice often omitted in AB research [36], and only interpreted the results of those measures with at least acceptable reliability. This led to differing results, contributing to a more nuanced understanding of AB in youth depression.

Limitations

With most MD participants recruited at a Department of Child and Adolescent Psychiatry or through outpatient psychotherapists, most had received psychotherapy at the time they participated. Unfortunately, we did not systematically assess treatment type or duration. As psychotherapy is expected to reduce AB (e.g. in anxiety disorders; see e.g. [78–80]) effect sizes might be underestimated in our study. Furthermore, we recruited the HR group partly from a study evaluating a prevention program for at-risk youth [49] some had already participated in. This Cognitive Behavioural Therapy based group intervention conveyed distraction as a coping strategy, among others, which might have influenced participants' volitional attention maintenance and added to our HR group's resilience, rendering them not entirely representative for children of depressed parents. Another limitation results from comorbid anxiety disorders in nearly half of the participants in the MD group, known to be associated with AB, as well [80]. However, anxious youth are found to show AB for threatening stimuli [80–82] while depressed individuals are commonly found to show AB for sad stimuli [13]. Since we found AB for sad faces only, it is more likely that the AB we captured were related to participants' depression rather than the comorbid anxiety disorders. In addition, our three groups differed significantly in age with the MD group being the oldest. As the incidence of MD increases with puberty [83] this does not come as a surprise. However, since the detected AB did not correlate with age, it is unlikely that this difference accounted for our results. Furthermore, it has to be emphasized that although our sample size is larger than previous studies' (e.g., [21]: $n = 19$ in the MD group; [23]: $n = 19$ in the MD group; [73]: $n = 10$ in the high-risk group), the sample size was only powered to detect medium ES and may have prevented us from finding smaller effects. At the same time, it is possible that the significant effect we found is not a real group difference but a false positive result since we did not correct for multiple testing (in line with, e.g. [21]). Replication in larger samples of children and adolescents is therefore crucial to rule out that our result is a chance finding and to be able to draw firmer conclusions.

Finally, even though we determined and reported reliabilities of our measures and the correlation of the PVT maintenance score with depressive symptoms indicates that it could be a valid indicator of depressive processing, we cannot provide a full description of the psychometric properties of our tasks. The appropriateness of measures that have often been used to assess AB in the past, like the DPT, has repeatedly been called into question [26–28], while at the same time no alternative measure has yet become the widely accepted norm. Therefore, future studies should further examine reliability and validity of tasks assessing ABs, refine existing tasks and develop new ones that can measure AB with less error. As this should reduce the variability of results, it would truly move the field forward.

[11] It has to be noted that dwell time on sad faces was not specifically related to depressive symptoms but also to anxiety scores.

Summary

In summary, our study provides preliminary evidence for a more negative AB in depressed youth compared to healthy youth at risk for depression. Our sample of youth with MD preferentially attended to sad faces, i.e., their AB was directed towards negative information. This AB was found only regarding sad, not angry faces, suggesting AB in youth depression may be specific to disorder-related negative emotional information. In addition, the more negative AB in depressed youth was found only for maintenance of attention in a task where attention was allocated deliberately, suggesting this AB might be specific to an internally controlled and at least to some extent conscious aspect of attention. Our results suggest that depressed and at-risk youth might show AB in opposite directions with AB towards negative information in depressed youth and AB away from negative information in at-risk youth, potentially acting as a protective mechanism in this group. However, this interpretation remains highly speculative and replication in larger samples is essential. Longitudinal research is necessary to address the temporal course of AB in youth, i.e. if youth with AB away from negative information are less likely to develop a depressive disorder than those with negative AB towards or if negative AB arises with depressive symptomatology. This will help shed more light on the role negative AB play in the development and maintenance of depressive symptoms. We think that despite the speculative nature of our interpretations they provide an interesting incentive for the elaboration of theoretical frameworks and starting points for future investigations.

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Declarations

Conflict of interest All authors declare that they have no conflicts of interest.

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5. Studie II

“I Am a Total...Loser” – The Role of Interpretation Biases in Youth Depression

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"I Am a Total…Loser" – The Role of Interpretation Biases in Youth Depression

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Abstract

Negative interpretation biases have been found to characterize adults with depression and to be involved in the development and maintenance of the disorder. However, less is known about their role in youth depression. The present study investigated i) whether negative interpretation biases characterize children and adolescents with depression and ii) to what extent these biases are more pronounced in currently depressed youth compared to youth at risk for depression (as some negative interpretation biases have been found already in high-risk youth before disorder onset). After a negative mood induction interpretation biases were assessed with two experimental tasks: Ambiguous Scenarios Task (AST) and Scrambled Sentences Task (SST) in three groups of 9–14-year-olds: children and adolescents with a diagnosis of major depression ($n = 32$), children and adolescents with a high risk for depression (children of depressed parents; $n = 48$), as well as low-risk children and adolescents ($n = 42$). Depressed youth exhibited substantially more negative interpretation biases than both high-risk and low-risk groups (as assessed with both tasks), while the high-risk group showed more negative interpretation biases than the low-risk group only as assessed via the SST. The results indicate that the negative interpretation biases that are to some extent already present in high-risk populations before disorder onset are strongly amplified in currently depressed youth. The different findings for the two tasks suggest that more implicit interpretation biases (assessed with the SST) might represent cognitive vulnerabilities for depression whereas more explicit interpretation biases (assessed with the AST) may arise as a consequence of depressive symptomatology.

Keywords Interpretation bias · Major depression · Children and adolescents · Familial risk for depression · Ambiguous scenarios task · Scrambled sentences task

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Introduction

Depression is one of the most common psychiatric disorders in childhood and adolescence (Costello et al. 2003; Lewinsohn et al. 1993) with up to 20% of young people having experienced at least one episode of major depression (MD) by the end of adolescence (Thapar et al. 2012). Early-onset MD is associated with adverse outcomes later in life such as educational underachievement (Fergusson and Woodward 2002), impairments in psychosocial functioning (Hammen et al. 2008), and reduced life satisfaction (Lewinsohn et al. 2003). In addition, early-onset MD often follows a recurrent course (e.g., Lewinsohn et al. 1999; Weissman et al. 1999), which further contributes to the negative consequences of the disorder (Wilson et al. 2015; Hammen et al. 2008).

Cognitive theories of depression propose that cognitive vulnerabilities such as cognitive biases play a crucial role in the development and maintenance of depressive disorders (e.g., A. T. Beck and Haigh 2014; Disner et al. 2011). Negative cognitive biases are tendencies to preferentially process negative compared to positive or neutral information and can be found on various levels of information processing, including attention, interpretation, and memory (Everaert et al. 2012; LeMoult and Gotlib 2019). Negative interpretation biases, in particular, refer to tendencies to create more negative and fewer positive meanings to explain ambiguous emotional information (Everaert et al. 2017). For example, a situation in which one is giving a speech in front of a group and people are laughing could be interpreted negatively in terms of people laughing at one or positively in terms of people appreciating one's jokes. In adults, the association between negative interpretation biases and depression has received particularly substantial empirical support (see Everaert et al. 2017, for a comprehensive meta-analysis).

However, results obtained from studies on adults with MD cannot be directly transferred onto depressed youth (Lakdawalla et al. 2007), as major cognitive and affective development is ongoing during childhood and adolescence (Blakemore and Choudhury 2006; Steinberg 2005). Therefore, cognitive vulnerabilities might either play a smaller role in youth than adult depression as cognitive patterns might not have evolved into stable, trait-like "cognitive styles" yet at this younger age (e.g., Lakdawalla et al. 2007). Alternatively, young people might be particularly susceptible to negative cues in ambiguous emotional information due to brain maturation and hormonal changes associated with an enhanced emotional sensitivity (see e.g., Paus et al. 2008), resulting in more pronounced negative cognitive biases. Considering the particularly detrimental consequences of early-onset MD, understanding the mechanisms that are involved in the development and maintenance of the disorder at this early age is crucial in order to improve prevention and early intervention (Loechner et al. 2018; Weisz et al. 2006).

Still, research on the association of interpretation biases and depression in children and adolescents is rather scarce (Platt et al. 2017). Some studies have reported correlations between interpretation bias scores and depressive symptoms in unselected adolescent samples (e.g., Klein et al. 2018; Orchard et al. 2016a; Smith et al. 2018) as well as samples with elevated symptoms of depression (de Voogd et al. 2017), but only two studies have compared interpretation biases in clinically depressed versus healthy youth. As part of a validity check in their study of an intervention for clinically depressed adolescents and young adults (14–21 years old), Micco et al. (2014) compared the depressed group's baseline interpretation bias (assessed with the experimental Ambiguous Scenarios Task, AST; Mathews and Mackintosh 2000) with that of a healthy control group and found the depressed adolescents and young adults to show a more negative interpretation bias. However, as the comparison of depressed and non-depressed groups was not the main aim of the study, this result is presented only briefly and its importance is not discussed. Orchard et al. (2016b) on the other hand, used the Ambiguous Scenarios Test for Depression in Adolescents, a questionnaire measure they had previously adapted and validated (Orchard et al. 2016a), to investigate interpretation biases in 12–18-year-old adolescents. They found a more negative interpretation bias in adolescents with a diagnosis of MD not only compared to healthy adolescents from the community but also to clinically-referred non-depressed youth and adolescents from the community with elevated depressive symptoms.

To date, no study has focused on comparing interpretation biases in depressed and non-depressed youth using experimental tasks. These do not rely on participants' awareness of their depressive cognitions and are less prone to distortions due to demand characteristics (i.e., participants matching their responses to the experimenter's presumed expectation), response biases (i.e., participants endorsing negative responses irrespective of the content corresponding to their interpretation or not), and deliberate response strategies (i.e., participants generating their responses based on a voluntary strategy instead of their immediate reaction to the ambiguous information) that are typical for self-report measures (e.g., Gotlib and Joormann 2010; Hirsch et al. 2016). Thus, experimental tasks enable a more objective assessment of cognitive processes and allow more automatic and unconscious processes that operate outside a person's awareness to be captured. Therefore, the first aim of the present study was to investigate interpretation biases in youth depression using age-adapted experimental approaches to assess interpretation biases in children and adolescents with MD.

We administered the AST (Mathews and Mackintosh 2000) in which participants read several self-referent ambiguous scenarios and are then presented with different interpretations of each scenario. Interpretation bias is indexed by the

difference between the endorsement of negative and positive interpretations (de Voogd et al. 2017). In addition, the Scrambled Sentences Task (SST; Wenzlaff and Bates 1998), which was specifically developed to assess interpretation biases in depressive disorders, was applied. In this task, participants form sentences out of arrays of words which can be either positive or negative. The proportion of negatively resolved sentences indicates the interpretation bias. Applying two experimental measures of interpretation bias allows the examination of different aspects of interpretation, with the AST presumably measuring a more conscious and explicit aspect and the SST capturing a more automatic and implicit aspect (Sfärlea et al. 2019). Both tasks have already been used in adolescent samples (e.g., de Voogd et al. 2017; Burnett Heyes et al. 2017) where they demonstrated at least acceptable reliability (Micco et al. 2014; Sfärlea et al. 2019).

Children and adolescents with MD were compared to two groups of non-depressed children and adolescents that varied in their risk for depression: children of parents with a history of depression, who are known to have an increased risk for MD themselves (e.g., Weissman et al. 2006) and children of parents with no history of depression or any other mental disorder, who have a low risk for depressive disorders. This allowed us to pursue the second aim of our study: to determine the extent to which interpretation biases are more pronounced in currently depressed youth compared to at-risk youth (that have been found to be characterized by more negative interpretation biases than youth at low risk for depression; Dearing and Gotlib 2009; Sfärlea et al. 2019). While negative interpretation biases in children and adolescents at high risk for depression indicate that these biases might be cognitive vulnerabilities or risk factors contributing to the development of depression (as suggested by theoretical models, e.g., Disner et al. 2011), even more pronounced interpretation biases in currently depressed children and adolescents indicate that these biases might be exacerbated as a consequence of depressive symptomatology. No study to date has directly compared interpretation biases in depressed, high-, and low-risk youth. One study that investigated memory biases in children and adolescents with MD, children and adolescents whose mothers were affected by MD, and children and adolescents without familial history of MD (Fattahi Asl et al. 2015) found negative memory biases in both depressed as well as at-risk youth compared to low-risk youth. However, the negative memory biases were more pronounced in currently depressed children and adolescents than in the at-risk group.

In order to be able to compare currently depressed youth to at-risk youth we focused on children and adolescents aged 9–14 years. Children younger than 9 years were not included due to concerns about their ability to understand and perform the tasks. Adolescents older than 14 years were not included since the incidence of depression in children of parents with a history of depression increases substantially after that age (e.g., Weissman et al. 2006), and investigating older children of depressed parents that had not yet suffered from an episode of MD might result in examining a particularly resilient and therefore non-representative high-risk sample.

With respect to the first aim of the study, we expected to find more negative interpretation biases in children and adolescents with MD in comparison to healthy children and adolescents (both high- and low-risk youth), based on theoretical predictions (e.g., Disner et al. 2011) and previous findings (Orchard et al. 2016b; Micco et al. 2014). Regarding the second aim, we expected negative interpretation biases to be to some extent present in youth at high risk for depression compared to youth at low risk for depression (corresponding to our previous results, Sfärlea et al. 2019; as well as Dearing and Gotlib 2009; Goodman and Gotlib 1999), but to be more pronounced in depressed versus high-risk youth (as found for memory biases; Fattahi Asl et al. 2015).

Methods

The present data on interpretation biases were collected within a broader project on cognitive biases in depressed as well as high- and low-risk youth. It was planned as an add-on to a study on cognitive biases in the offspring of depressed versus non-depressed parents (Platt 2017; Sfärlea et al. 2019). Data from interpretation bias tasks[1] are presented here while data from attention bias tasks are presented elsewhere (Buhl et al. in preparation; Platt et al. submitted).

Participants

A total of 122 children and adolescents aged 9–14 years were included in the data analysis.[2] The sample consisted of $n = 32$ children and adolescents with MD, $n = 48$ children and adolescents at high familial risk for depression (HR group), and $n = 42$ children and adolescents at low familial risk for depression (LR group). The data from 87% of the HR and LR children was collected within a study investigating the transgenerational transmission of cognitive biases (Platt 2017; Sfärlea et al. 2019), in which they participated with one of their parents. Of the HR children, 28 were recruited through a study evaluating an intervention to prevent the development of depression in

[1] In addition to the AST and the SST that are presented here, a short, picture-based task (resembling that used by Haller et al. 2016) was piloted. However, the validity of this task was limited in our study (see Supplement 1).

[2] Altogether, 126 children and adolescents were tested. Two participants were excluded due to bad compliance and two because of severe reading difficulties (as both interpretation bias tasks are based on reading). The sample size was based on an a priori power analysis (α error probability = .05, power = .8, one-tailed) for the comparison of HR and LR groups (as a smaller effect size was expected for this effect than for the comparisons with the MD group). An effect size around $d = 0.6$ (corresponding to Dearing and Gotlib 2009) was expected, therefore a sample of at least $n = 36$ per group was aimed for.

children of parents with a history of depression (Platt et al. 2014). Eleven of those had already received the prevention program by the time they took part in the present study while the others took part before receiving the intervention. Other HR as well as the LR families were recruited via local advertisements, previous studies, and mailings to randomly-selected families with children in the corresponding age range provided by the local registry office. Youth with MD were mostly in- or outpatients from a Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy of the University Hospital of the LMU Munich, $n = 2$ were recruited through licensed outpatient psychotherapists, and $n = 3$ were respondents to our mailings.

Exclusion criteria for all participants were intelligence quotient (IQ) < 85[3] (assessed with the CFT 20-R; Weiß 2006), pervasive developmental disorders, attention deficit and hyperactivity disorder, and a history of schizophrenia or bipolar disorder. Children and adolescents were included in the MD group if they currently met criteria for MD according to DSM-IV[4] (American Psychiatric Association 2000) as assessed with a standardized psychiatric interview (see below). Of the 32 participants in this group, $n = 4$ had recurrent episodes of MD, $n = 2$ were partially remitted (analyses excluding these participants revealed the same pattern of results), $n = 15$ fulfilled criteria for at least one comorbid anxiety disorder, and $n = 3$ (9.4%) were receiving psychotropic medication (selective serotonin reuptake inhibitors). Children and adolescents were included in the HR group if they did not meet criteria for any current or past axis I disorder[5] but at least one of their parents met criteria for MD ($n = 46$) or dysthymia ($n = 2$; analyses excluding these participants revealed the same pattern of results) during the child's lifetime. Children of parents with a history of bipolar disorder, schizophrenia, or substance abuse were not included. Children and adolescents were included in the LR group if they did not meet criteria for any current or past axis I disorder and none of their parents met criteria for any past or current axis I disorder.

All procedures were approved by the ethics committee of the Medical Faculty of the LMU Munich (Project 441–15). Written informed consent was obtained from all participants and their parents after a comprehensive explanation of the study procedures. HR and LR participants who participated together with their parents in the study on transgenerational transmission of cognitive biases received a reimbursement of 50 € per family while participants taking part only in this study received a reimbursement of 30 €.

[3] Two of the participants in the MD group scored just below 85. However, the substandard IQ did not correspond to the clinical impression and was most likely due to a lack of compliance and inability to concentrate on that particular day so those participants were still included.

[4] DSM-IV criteria were used as the diagnostic interviews for DSM-V were not available in German by the beginning of data collection.

[5] One girl met criteria for enuresis in the past. However, as she did not report symptoms of any other mental disorder she was included nonetheless.

Psychopathology Assessment

All participants underwent extensive diagnostic assessment before inclusion in the study. A standardized, semi-structured psychiatric interview (K-DIPS; Schneider et al. 2009) was conducted with both participants and one of their parents to assess psychiatric diagnoses in children and adolescents. The K-DIPS is a well-established German diagnostic interview that allows diagnosis of a wide range of psychiatric axis I disorders according to DSM-IV (American Psychiatric Association 2000) with good interrater-reliability (accordance rates of at least 97% were reported for all diagnoses; Neuschwander et al. 2013). The interviews were conducted and evaluated by trained interviewers. Interrater-reliability was determined for 18% of the participants of the HR and LR groups by an independent researcher re-rating audio recordings of the diagnostic interviews and found the accordance rate for lifetime diagnosis of depression (pre-defined criterion) to be 100%. Interviews from the MD group were not audiotaped, but the participants in this group were referred to our study because they had a clinical diagnosis of depression which was confirmed with the diagnostic interview.

The adult version of the interview (DIPS; Schneider and Margraf 2011) was used to assess psychiatric diagnoses in the parents of the HR and LR participants (for HR participants it was applied to the parent affected by depression; for LR participants it was applied to both parents whenever possible, i.e., for 79% of participants). Interrater-reliability of the DIPS has been found to be good (with accordance rates of at least 87% reported for all diagnoses; Suppiger et al. 2008) and the accordance rate for lifetime diagnosis of depression was 94% in our sample. In addition, depressive symptoms of the parents were assessed with the German version of the Beck Depression Inventory-II (BDI-II; Hautzinger et al. 2006, obtained from both parents for 81% of HR and LR participants) and differed significantly (ts = 3.2, p-s ≤ .002) between parents of HR (parent with a history of MD: $M = 9.9$, $SD = 8.5$; other parent: $M = 4.2$, $SD = 4.5$) and LR participants ($M = 1.6$, $SD = 3.2$).

Depressive symptoms of the participants were assessed with the German version of the Children's Depression Inventory (DIKJ; Stiensmeier-Pelster et al. 2014) and anxiety symptoms were measured by the trait scale of the German version of the State Trait Anxiety Inventory for Children (STAIC; Unnewehr et al. 1992). A score for depressive symptoms was available for 121 and a score for anxiety symptoms for 117 of the 122 participants. Reliability of both self-report measures was excellent in our sample (DIKJ: Cronbach's $\alpha = .96$; STAIC-T: Cronbach's $\alpha = .93$).

Ambiguous Scenarios Task

A computerized version of the AST (Mathews and Mackintosh 2000; adapted from Belli and Lau 2014) was used to assess the tendency to interpret ambiguous situations as positive or negative.

Stimuli Stimuli consisted of ten ambiguous scenarios, i.e., descriptions of self-referent situations that could be interpreted either positively or negatively. Stimuli were based on the original stimulus set by Mathews and Mackintosh (2000) which was developed to assess interpretation biases in relation to anxiety. The set was translated and adapted to be age-appropriate (by creating situations related to school, sports, or friends to which the studied age group could relate; Belli and Lau 2014; Klein et al. 2018; Lothmann et al. 2011) and more depression-specific (by including not only social situations that might lead to rejection but also situations targeting low self-esteem and the tendency to overgeneralize/catastrophize potentially negative events, which are typical of depressive thinking). Separate versions for girls and boys were generated (differing mainly in using female or male words when referring to, e.g., friends or classmates). See Fig. 1 for an example scenario (and Sfärlea et al. 2019, Supplement 3, for an English translation of all scenarios).

Task Procedure The trial procedure is depicted in Fig. 1. The experiment was presented using E-Prime 2.0 (Psychology Software Tools Inc 2013). In the first part of the task, each trial started with the title and the description of a situation with one word missing at the end. Participants were instructed to read the description carefully and to imagine they were in that situation. After reading the description, participants pressed the spacebar to reveal a fragment of the missing word. They completed the word by typing in the missing letter. Subsequently, a comprehension question that had to be answered by pressing "J" for Yes and "N" for No was presented, followed by feedback. The word completion and comprehension question were included to ensure that participants read the scenarios carefully.

After the first part, the task continued with a second part in which the title of each scenario was presented with four probe statements. Participants had to rate the similarity of the statements to the original scenario from 1 ("not similar at all") to 4 ("very similar"). The statements consisted of one valid negative and one valid positive interpretation (targets), as well as one negative statement and one positive statement that were not directly related to the scenario (foils). For each scenario, the four probe statements were presented consecutively in random order.

The ten scenarios were presented in random order in both parts and were preceded by one neutral scenario to familiarize participants with the task.

Outcome Variables An interpretation bias score (IB_{AST}) was calculated by subtracting the mean positive target score from

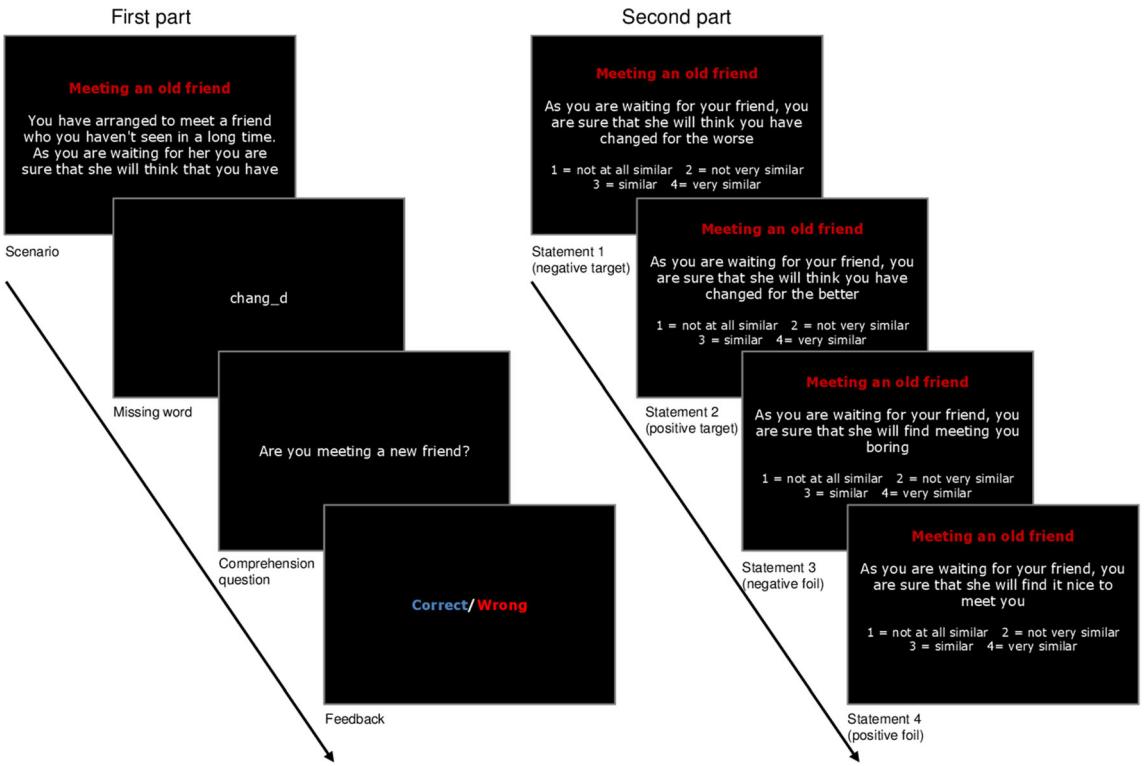

Fig. 1 Example scenario from the Ambiguous Scenarios Task (AST; Mathews and Mackintosh 2000)

the mean negative target score (e.g., de Voogd et al. 2017) so that scores > 0 indicated a negative interpretation bias and scores < 0 indicated a positive interpretation bias. A foil ratio was similarly calculated. Comparing the interpretation bias score and the foil ratio allows analyzing the endorsement of negative versus positive interpretations of ambiguous scenarios (i.e., an interpretation bias, represented by the IB_{AST} score) compared to the tendency to simply endorse non-specific negative versus positive statements (i.e., a negative response bias, represented by the foil ratio; Belli and Lau 2014).

Reliability Split-half reliability of the task was assessed by correlating bias scores based on odd versus even trials (see e.g., Van Bockstaele et al. 2017) and was good ($r = .66$, $p < .001$, Spearman-Brown-corrected reliability: .80).

Scrambled Sentences Task

A computerized version of the SST (Wenzlaff and Bates 1998; adapted by Everaert et al. 2014) was used to assess the tendency to form negative or positive statements out of ambiguous verbal information. The task was administered during eye-tracking in order to simultaneously assess attention biases (Everaert et al. 2014), but these data are reported elsewhere (Buhl et al. in preparation).

Stimuli The stimuli consisted of 50 scrambled sentences: 30 emotional sentences (e.g., "total I winner a loser am") and 20 neutral sentences (e.g., "like watching funny I exciting movies"). The emotional sentences were based on the original stimulus set developed by Wenzlaff and Bates (1998) and included, e.g., sentences targeting low mood, low self-worth, and negative thoughts about oneself and the future, which are typical cognitions in depression. The sentences were translated into German (Rohrbacher 2016), extended, and adapted to be easily understandable and relevant to children and adolescents (see Supplement 4 of Sfärlea et al. 2019, for an English translation of the stimuli). All sentences contained six words and had two possible solutions. In emotional trials, one solution was positive (e.g., "I am a total winner") whereas the other was negative (e.g., "I am a total loser"). In neutral trials both solutions were emotionally neutral. Across the stimulus set, target words (the words in each sentence that accounted for the positive or negative solution) were matched for length and frequency in the German language.[6] In line with Everaert et al. (2014), word position within each sentence was randomized, with target words not allowed next to each other or in the first or last position and counterbalanced whether the positive or negative target word was presented first.

Task Procedure The trial procedure is depicted in Fig. 2. The experiment was presented using Experiment Builder 1.10 (SR Research Ltd 2013). Each trial started with a fixation cross presented for 500 ms on the left side of the screen. After that, the stimulus display appeared, consisting of six words in scrambled order presented at the center of the screen on a single line. Participants were instructed to read the words, mentally form a grammatically correct five-word sentence as quickly as possible, and click on the mouse button as soon as they did so to continue to the response part of the trial. The scrambled sentence was presented for a maximum of 8000 ms; if no mouse click occurred during that time the response part was omitted and the next trial began. In the response part, five boxes appeared below the scrambled sentence and participants were required to build the sentence they had mentally formed by ordering the words into the five boxes via mouse click.

Trials were randomly divided into five blocks of ten, each containing six emotional and four neutral trials presented in random order. Before the first block participants completed five practice trials to familiarize themselves with the task.

Similarly to earlier studies (e.g., Everaert et al. 2014; Burnett Heyes et al. 2017) a cognitive load procedure was included to prevent deliberate response strategies. Before each block, a 4-digit number was presented for 5000 ms which had to be memorized and recalled at the end of the block.

Data Processing and Outcome Variables Participants' responses were rated as correct or incorrect. Trials in which no grammatically correct sentence was built (time-out or incorrect sentence) were excluded from the analysis. Participants with a correct sentence rate of three standard-deviations (*SD*) below the mean were identified as outliers in terms of accuracy and excluded (2 HR children), resulting in a sample of 119 children (as data from only 121 of 122 participants were available for the SST due to technical problems) for analysis of the SST data. In that remaining sample, on average 44.2 correct trials ($SD = 4.1$; 88% of 50 trials) per participant were available (not different between groups, $p > .1$).

The correctly unscrambled emotional sentences were categorized as either positive or negative. An interpretation bias score (IB_{SST}) was calculated as the proportion of negatively resolved sentences from the total number of correctly resolved emotional sentences (Everaert et al. 2014).

Reliability Split-half reliability of the SST was calculated analogous to the AST and was excellent ($r = .89$, $p < .001$, Spearman-Brown-corrected reliability: .94).

[6] Positive target words: Word length $M = 7.3$ ($SD = 2.6$) characters, word frequency (category according to http://wortschatz.uni-leipzig.de/de) $M = 10.3$ ($SD = 2.9$); Negative target words: word length $M = 7.4$ ($SD = 2.6$) characters, word frequency $M = 10.3$ ($SD = 4.0$); $ts < 1$ in paired *t*-tests.

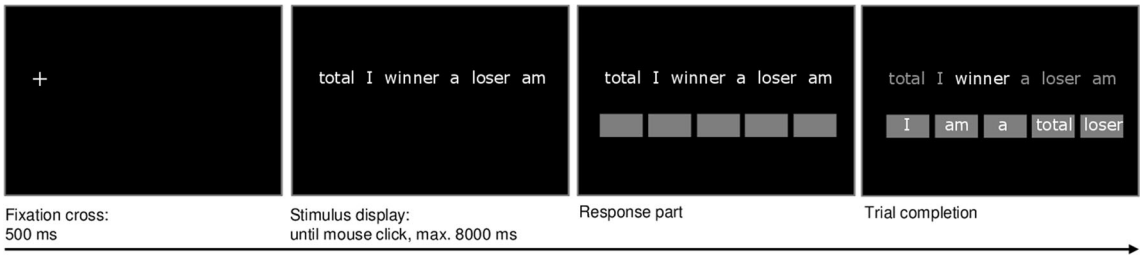

Fig. 2 Example of an emotional trial of the Scrambled Sentences Task (SST; Everaert et al. 2014; Wenzlaff and Bates 1998)

Experiment Procedure

Tasks were administered in random order. The course of the experimental session was the same as in Sfärlea et al. (2019; see Supplement 5).

As cognitive models of depression suggest that cognitive vulnerabilities such as negative biases are activated by stressful life events or negative mood (e.g., Disner et al. 2011; Scher et al. 2005), a negative mood induction procedure was administered twice during the experimental session: Participants watched a 2 min scene from the movie *The Lion King* (Hahn et al. 1994) that had successfully induced negative mood in children in earlier studies (von Leupoldt et al. 2007). In our study participants also reported significantly worse mood (assessed using the valence dimension of the 9-point Self-Assessment Mannequin scale; Lang 1980) after watching the movie scene compared to baseline ($ts \geq 7.9$, $ps < .001$). Details are presented in Supplement 2.

Data Analysis

Statistical data analysis was conducted with SPSS 25. To assess group differences in demographic and clinical characteristics, interpretation bias scores (IB_{AST} and IB_{SST}),[7] as well as the AST foil ratio, one-way analyses of variance (ANOVAs) and follow-up *t*-tests (Bonferroni-Holm corrected; Holm 1979) were conducted. Correlations were calculated between bias scores and depression and anxiety symptoms to assess relationships between psychopathology and interpretation bias. Furthermore, in order to examine if interpretation bias scores from the two tasks were related, a correlation between IB_{AST} and IB_{SST} scores was computed.

All analyses were repeated excluding the participants that were taking psychotropic medication, as this might influence cognitive biases (e.g., Wells et al. 2014). As the overall pattern of results remained the same, the findings based on the whole sample are reported.

[7] Relative bias score were used since significantly larger effect sizes were reported for studies computing relative bias scores compared to studies computing absolute positive or negative bias scores (Everaert et al. 2017). In addition, relative bias scores allow to examine if bias scores from different tasks are related to each other. An alternative analysis of the AST with absolute positive and negative values can be found in Supplement 3.

Results

Sample Characteristics

Sample characteristics are presented in Table 1. Groups did not differ significantly in gender ratio or IQ but in terms of age: participants in the MD group were significantly older than participants in the HR and LR groups. To examine whether interpretation bias scores were related to age, Pearson's correlations between age and IB_{AST} as well as IB_{SST} scores were calculated separately for each group: no significant correlations emerged ($rs \leq .29$, $ps > .1$). As expected, groups also differed in psychopathology with the MD group reporting significantly more symptoms of depression and anxiety than the groups of healthy children (which did not differ from each other, further indicating that the HR group was indeed as psychiatrically healthy as the LR group yet).

Ambiguous Scenarios Task

The one-way ANOVA revealed a significant effect of group ($F_{2,119} = 13.0$, $p < .001$, $\eta^2 = .18$) that was followed up by *t*-tests: the MD group's IB_{AST} score was significantly more negative than that of the HR group ($t_{48.0} = 4.1$, $p < .001$, $d = 1.0$) and the LR group ($t_{44.8} = 3.3$, $p = .002$, $d = 0.8$), while the HR and LR groups did not differ from each other ($t_{88} = 1.5$, $p > .1$). The IB_{AST} score was significantly > 0 in the MD group ($M = 0.4$, $SD = 1.0$; $t_{31} = 2.2$, $p = .034$), indicating a negative interpretation bias, and significantly < 0 in the HR and LR groups (HR: $M = -0.4$, $SD = 0.6$; LR: $M = -0.2$, $SD = 0.5$; $ts \geq 2.9$, $ps \leq .006$), indicating a positive interpretation bias.

The one-way ANOVA on foil ratios also yielded a significant effect of group ($F_{2,119} = 8.0$, $p = .001$, $\eta^2 = .12$) with similar results in the post-hoc *t*-tests but smaller effect sizes (MD vs. HR: $t_{78} = 3.6$, $p = .001$, $d = 0.8$; MD vs. LR: $t_{47.9} = 2.6$, $p = .013$, $d = 0.6$; HR vs. LR: $t_{88} = 1.3$, $p > .1$). *T*-tests against zero revealed that while foil ratios in the HR ($M = -0.4$, $SD = 0.6$) and LR groups ($M = -0.3$, $SD = 0.5$) were significantly < 0 ($ts \geq 3.3$, $ps \leq .002$), the foil ratio of the MD group ($M = 0.2$, $SD = 0.9$) was not significantly different from zero ($t_{31} = 1.2$, $p > .1$). IB_{AST} scores and foil ratios are presented in Fig. 3.

Furthermore, positive correlations between IB_{AST} scores and depression ($r = .44$, $p < .001$) as well as anxiety symptoms

Table 1 Demographic and clinical characteristics of the sample

	MD $n = 32$	HR $n = 48$	LR $n = 42$			Post-hoc tests
Gender m/f	6/26	19/29	17/25	$\chi^2 = 4.7$	n.s.	
Age; *M (SD)*	13.4 (1.4)	11.8 (1.7)	12.2 (1.7)	$F_{2,119} = 9.3$	$p < .001$	MD > HR = LR
IQ; *M (SD)*	105.2 (13.6)	109.1 (11.5)	111.7 (10.3)	$F_{2,119} = 2.8$	n.s.	
Depression symptoms; *M (SD)*	31.5 (8.9)	7.8 (5.8)	6.6 (5.3)	$F_{2,118} = 161.0$	$p < .001$	MD > HR = LR
Anxiety symptoms; *M (SD)*	45.1 (8.8)	30.1 (6.4)	28.0 (6.2)	$F_{2,114} = 56.3$	$p < .001$	MD > HR = LR

MD Major depression, *HR* high-risk, *LR* low-risk

Depressive symptoms were assessed with the DIKJ (raw values presented) and anxiety was assessed with the STAIC-T. Post-hoc *t*-tests were all significant with $p \leq .001$

($r = .41$, $p < .001$) were found. These two correlations did not differ in size ($z = 0.4$, $p > .1$; Lee and Preacher 2013). As the groups differed in both, psychopathology scores as well as IB_{AST} scores, the correlational analyses were repeated within the groups. In the MD group, significant correlations between IB_{AST} scores and depression ($r = .39$, $p = .026$) as well as anxiety symptoms ($r = .39$, $p = .047$) emerged, while in the HR and LR groups no such correlations were apparent ($rs \leq .22$, $ps > .1$).

Scrambled Sentences Task

The one-way ANOVA on IB_{SST} scores revealed a significant effect of group ($F_{2,116} = 129.0$, $p < .001$, $\eta^2 = .69$) that was followed up by *t*-tests: the MD group ($M = .65$, $SD = .26$) had a significantly more negative bias than the HR ($M = .14$, $SD = .12$; $t_{40.7} = 10.4$, $p < .001$, $d = 2.5$) and LR ($M = .08$, $SD = .09$; $t_{37.3} = 11.8$, $p < .001$, $d = 2.9$) groups, and the HR group had a more negative interpretation bias than the LR group ($t_{82.5} = 2.5$, $p = .014$, $d = 0.6$). Results are presented in Fig. 4.

Strong positive correlations of IB_{SST} scores with symptoms of both depression ($r = .89$, $p < .001$) as well as anxiety ($r = .72$, $p < .001$) were found, although the relationship with depressive symptoms was significantly stronger than with anxiety ($z = 5.7$, $p < .001$; Lee and Preacher 2013). When recalculated within groups, correlations of IB_{SST} scores with depressive symptoms were evident in each group (MD: $r = .70$, $p < .001$; HR: $r = .56$, $p < .001$; LR: $r = .43$, $p = .005$) and correlations with anxiety symptoms became apparent in the MD ($r = .39$, $p = .046$) and HR groups ($r = .48$, $p = .001$; LR: $r = .22$, $p > .1$).

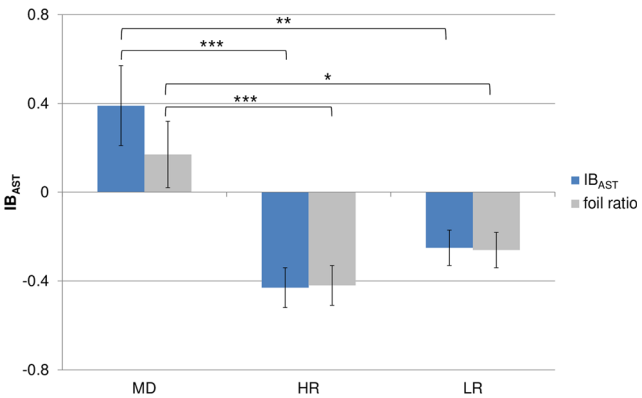

Fig. 3 IB_{AST} scores and foil ratios for the three groups. Error bars represent standard errors. Significant group differences are indicated: *** $p < .001$, ** $p < .01$, * $p < .05$

Relationship between AST and SST

A significant positive correlation between IB_{AST} and IB_{SST} scores emerged across groups ($r = .53$, $p < .001$) but within groups this relationship was only found in the MD group ($r = .56$, $p = .001$; HR and LR: $rs \leq .18$, $ps > .1$).

Discussion

The present study investigated the role of interpretation biases in youth depression. Two experimental tasks capturing different aspects of interpretation were used to assess interpretation

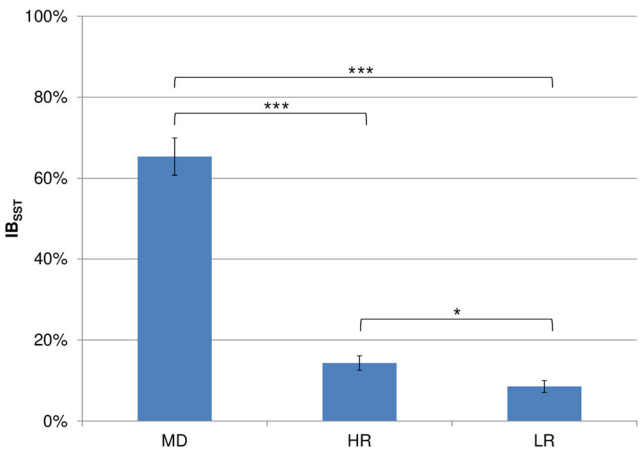

Fig. 4 IB_{SST} scores for the three groups. Error bars represent standard errors. Significant group differences are indicated: *** $p < .001$, * $p < .05$

biases in three groups of children and adolescents: currently depressed children and adolescents (MD group), children and adolescents at high risk for depression due to having a parent with a history of depression (HR group), and children and adolescents with a low risk for depression (LR group). Both tasks revealed a more negative interpretation bias in children and adolescents with MD compared to both groups of healthy youth and strong correlations between bias scores and depression and anxiety symptoms (collapsed across groups), while only one task (SST) revealed a more negative interpretation bias in youth at risk for depression compared to low-risk youth (see also Sfärlea et al. 2019).

The first aim of the present study was to test the assumption that children and adolescents with MD show more negative interpretation biases compared to healthy youth. As expected, we found the MD group to draw more negative interpretations of ambiguous scenarios (AST) as well as sentences (SST), i.e., to show more negative interpretation biases, than the two groups of healthy children and adolescents. The effect sizes of the group differences were large, especially for the SST, and comparable to those found with questionnaire measures of interpretation bias (Orchard et al. 2016b). Of note, as we calculated relative bias scores, our results do not elucidate if the more negative interpretation biases in depressed children and adolescents were due to a lack of positive interpretations or an excess of negative interpretations. However, an additional analysis of the AST data with absolute positive and negative scores instead of a relative bias score indicated that group differences in the AST were mainly driven by the MD group being more likely to endorse *negative* interpretations compared to HR and LR groups while no differences were found for positive interpretations (results of this analysis are presented in Supplement 3). It also has to be acknowledged that the foil ratio of the AST was also more negative in the MD group than in the HR and LR groups (although with smaller effect sizes: $d = 0.6–0.8$ vs. $d = 0.8–2.9$). As the foil ratio represents the tendency to endorse non-specific negative statements this suggests that the more negative interpretation bias in the MD group may partly be explained by a more general negative response bias. Our study is the first to focus on comparing interpretation biases in depressed versus non-depressed youth using multiple experimental measures. The results extend those of prior studies that have investigated interpretation biases in depressed adolescents (aged 12–18; Orchard et al. 2016b; and 14–21 years; Micco et al. 2014) to a younger age group. The presence of negative interpretation biases in depressed children and adolescents corroborates the assumption that negative interpretation biases are a characteristic of individuals with depression not only in adults and adolescents but also in 9–14 year old youth and provides empirical support that cognitive theories of depression (e.g., Disner et al. 2011) apply to this group as well. However, as it remains unclear how interpretation biases emerge across childhood and adolescence, future studies may compare interpretation biases between different age groups, e.g., children vs. adolescents, or investigate interpretation biases longitudinally across childhood and adolescence.

The bias score was strongly positively related to depressive symptoms in the full sample, replicating previous results in youth with depression (Micco et al. 2014) or elevated symptoms of depression (de Voogd et al. 2017) as well as unselected samples of adolescents (e.g., Klein et al. 2018; Orchard et al. 2016a). However, when correlations were calculated separately within each group, consistent correlations with depressive symptoms were found only for interpretation bias as assessed with the SST, while the interpretation bias assessed with the AST only correlated with depressive symptoms within the MD group, probably due to lower values and/or less variance of depression, anxiety, and IB_{AST} scores in the HR and LR groups. Similar relationships were found for anxiety symptoms, which is not surprising considering the well-established association of anxiety and interpretation biases in children and adolescents (Stuijfzand et al. 2018). However, a comparison of the correlation coefficients indicated that for the interpretation bias score as assessed with the SST, the association with depressive symptoms was significantly stronger than the association with anxiety symptoms, suggesting at least partial specificity. For the interpretation bias score as assessed with the AST, on the other hand, correlations with symptom scores did not differ.

The second aim of the study was to determine the extent to which interpretation biases are more pronounced in currently depressed youth compared to at-risk youth. In line with our expectations and previous studies (Dearing and Gotlib 2009), children and adolescents at high risk for depression showed a more negative interpretation bias compared to children and adolescents at low risk for depression (see also Sfärlea et al. 2019). However, only the interpretation bias as assessed with the SST (not the AST) was more negative in the HR group than in the LR group and it was much less pronounced than in the MD group. This is the first time interpretation biases are compared between currently depressed children and adolescents and children and adolescents with a high or low risk for depression. The results indicate that while being to some extent already present in at-risk populations,[8] negative interpretation biases are strongly exacerbated in currently depressed children and adolescents.

The two tasks assessing interpretation biases yielded divergent results: the AST differentiated only between depressed and non-depressed children and adolescents and was related to depressive symptoms only within the MD group, while the SST also differentiated between high- and low-risk youth

[8] Note that parental history of depression is not the only risk factor for depression. Psychosocial factors like exposure to stressful life events (e.g., bereavement) or chronic adversity (e.g., maltreatment, bullying) also put children and adolescents at risk for developing depression (Thapar et al. 2012). It remains unclear if our results are specific for children of depressed parents or apply to other risk groups as well.

and was associated to depressive symptoms within all groups. Moreover, interpretation bias scores from the two tasks were only related within the MD group. Based also on our previous results (Sfärlea et al. 2019), we suppose that the AST and the SST capture different aspects of interpretation (an issue which Everaert et al. 2017, pointed out as especially important to investigate): the SST is more cognitively demanding due to the time constraint and the cognitive load procedure, so less resources are left for volitional control and deliberate response strategies. Therefore, the SST may capture a more automatic (in terms of quick and effortless processing that occurs unintentionally and uncontrollably; cf. Beevers 2005; Teachman et al. 2012) and implicit aspect of interpretation. The AST, on the other hand, allows more reflection on one's answers and might therefore be more susceptible to distorted responding, similarly to self-report measures (e.g., Gotlib and Joormann 2010). Hence, the AST presumably measures a more conscious and explicit aspect of interpretation (see Sfärlea et al. 2019, for more details). According to this assumption, our results suggest that an implicit interpretation bias can already be found in at-risk youth before onset of a depressive disorder and thus might act as a cognitive vulnerability or risk factor contributing to the development of depression (as suggested by theoretical models; e.g., Disner et al. 2011). The explicit interpretation bias, on the other hand, was only found in the currently depressed group, indicating that this type of bias may arise as a consequence of depressive symptomatology. The finding that these two aspects of interpretation operate differently with respect to the question of being present already in youth at risk for depression or only in currently depressed children and adolescents contributes to a more comprehensive and differentiated understanding of interpretation biases in youth depression. However, the cross-sectional design of the study does not allow any conclusions about time course or causality: we cannot determine the predictive value of interpretation biases for prospectively predicting the onset of an episode of MD, i.e., whether the more negative interpretation bias in the HR group compared to the LR group indeed acts as a risk factor for the development of MD. Likewise, we cannot conclude if the more negative interpretation biases we found in the MD group compared to the HR group are consequences of the depressive disorder or had already characterized those individuals that developed MD before disorder onset. Longitudinal research is needed to address these important questions as well as to investigate what role negative interpretation biases play in the maintenance of depressive symptoms.

Clinical Implications

We found strong negative interpretation biases in children and adolescents with MD on explicit as well as implicit levels. This suggests that therapeutic attempts to modify these biases in depressed youth might be more efficient if they address interpretation biases not only explicitly via Cognitive Behavioral Therapy (e.g., J. S. Beck 2011) but also implicitly, for example via Cognitive Bias Modification interventions that have been shown to successfully modify interpretation biases not only in healthy (Lothmann et al. 2011) but also in depressed adolescents (LeMoult et al. 2018; Micco et al. 2014).

The presence of negative implicit interpretation biases also in youth at high risk for depression, on the other hand, indicates that this kind of interpretation bias might also be a target for preventive approaches trying to reduce the impact of cognitive vulnerabilities in children of depressed parents. Modifying cognitive processes using implicit methods might enhance the efficacy of prevention programs in this high-risk group, whose effects are rather small and short-term (Loechner et al. 2018). However, as some studies implementing Cognitive Bias Modification interventions for interpretation bias reported that those lacked transfer effects (e.g., LeMoult et al. 2018; Yiend et al. 2014), these interventions clearly need to be refined and improved before representing useful therapeutic tools for treatment and prevention of depressive disorders. Moreover, as any intervention intended for younger age groups, Cognitive Bias Modification interventions for children and adolescents need to be age-adapted, e.g., by using picture-based instead of text-based stimuli for younger children.

Furthermore, as the two measures of interpretation bias presumably capture different aspects of interpretation, the AST and the SST could be useful tools for assessing the extent to which existing interventions are able to change interpretation biases in children and adolescents with MD separately on conscious as well as automatic levels.

Strengths

The present study makes a significant contribution to our knowledge of the role of interpretation biases in youth depression holding several methodological strengths.

Two different tasks were administered to experimentally assess interpretation biases. The reliability of the tasks was determined and turned out to be at least good for both measures (corresponding to e.g., Micco et al. 2014; Novović et al. 2014). Furthermore, the correlations between bias scores and depressive symptoms underline the construct validity of the measures as indicators of depressive processing.

Moreover, not only did all participants included in the study undergo extensive diagnostic assessment, psychopathology was also carefully assessed in one (HR group) or both (LR group) of their parents via a diagnostic interview instead of relying on self-report of mental disorder history only.

Limitations

One limitation of the present study is that the three groups investigated differed in age with participants in the MD group

being significantly older than participants in the HR and LR groups. This probably results from the prevalence of depression being rather low in childhood and rising substantially with puberty (Thapar et al. 2012) and therefore the majority of the participants in the MD group being 12 to 14 years old. However, as age was not related to bias scores, it is unlikely that the age difference accounts for the group differences we found.

Another limitation results from nearly half of the participants in the MD group having a comorbid anxiety disorder. Also, not only depressive but also anxiety symptoms were related to interpretation biases, which was to be expected considering that the stimuli used in the tasks – even though adapted to our study population – were not entirely depression-specific due to the symptom overlap between depression and particular anxiety disorders like social anxiety disorder or generalized anxiety disorder. Therefore, it cannot be ruled out that comorbid psychopathology contributed to our results. However, the association with depressive symptoms was stronger than the association with anxiety symptoms (for the SST, which is the more depression-specific measure), suggesting at least partial specificity.

Furthermore, it remains unknown if group differences in interpretation bias, particularly the difference between HR and LR groups in the SST, can also be observed during baseline mood and without the cognitive load, as interpretation biases were only assessed following a negative mood induction and the SST was not applied without the cognitive load procedure. These possibilities should be addressed by future studies as they have important implications for cognitive models of depression.

Finally, since most participants in the MD group were recruited at a Department of Child and Adolescent Psychiatry or through licensed outpatient psychotherapists, it is likely that most of them were receiving some form of psychotherapy at the time of their participation (unfortunately, this was not assessed systematically). Since psychotherapy, particularly Cognitive Behavioral Therapy, targets negative interpretation biases, our effect sizes might be underestimates of the effect sizes in untreated youth depression. Furthermore, since a considerable proportion of the participants in the HR group were recruited through a study evaluating a family-based prevention program for children of parents with a history of depression (Platt et al. 2014), our HR participants might have been less vulnerable to depression than the average offspring of depressed parents (see Sfärlea et al. 2019, for a more detailed discussion).[9] In summary, our MD and HR samples might not be entirely representative and group differences might be underestimated in our study.

[9] Analyses excluding the 11 children and adolescents that had already participated in the prevention program before taking part in the present study indeed yielded a larger effect size ($d = 0.7$) for the difference between HR and LR children in the SST.

Conclusion

The present study provides evidence for the presence of explicit as well as implicit negative interpretation biases in children and adolescents with MD and implicit interpretation biases in children and adolescents at risk for depression. Pending replication in longitudinal studies, this suggests that implicit interpretation biases might represent cognitive vulnerabilities for depression while explicit interpretation biases seem to arise as a consequence of depression. The results have important clinical implications for the improvement of interventions to prevent and treat youth depression.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Approval All procedures were approved by the ethics committee of the Medical Faculty of the LMU Munich (Project 441–15) and were in accordance with the latest version of the Declaration of Helsinki.

Informed Consent Written informed consent was obtained from all participants and their parents after a comprehensive explanation of the study procedures.

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Anhang A: Supplement zu Studie I

Supplement 1: Visual Search Task eye-tracking results

An emotional Visual Search Task (VST; adapted from [1]) was administered during Eye-Tracking (ET) to assess overt visual attention to the different emotional stimuli during the task in addition to the reaction time (RT) based measure of attention bias (AB). RT results are reported in the manuscript, while ET results are reported here.

Task procedure. The task procedure is described in the manuscript.

ET data processing and outcome variables. In addition to excluding trials with incorrect responses or RTs shorter than 200ms or longer than 2 SDs above each participant's mean, (trials with poor data quality (see data processing of the Passive Viewing Task ET data in the manuscript for criteria) and participants with insufficient trials available (n=1 MD) were excluded. 118.1 correct and valid trials per participant were available for the ET analysis in VST (SD = 4.0; 92.3% of 128 trials). This did not differ between groups ($F \leq 1.8$; $ps > .1$).

An ET based AB score ($AB_{VST\text{-}ET}$) was calculated by subtracting the mean percentage of dwell time on positive distractors from the mean percentage of dwell time on negative distractors. Hence, positive values indicate more attention towards positive information (i.e. a positive bias) and negative values indicate more attention towards negative information (i.e. a negative bias). $AB_{VST\text{-}ET}$ scores for sad and angry faces were computed separately.

Reliability. Split-half reliability was assessed by correlating bias scores based on odd versus even trials (see e.g. [2]). The reliabilities of the $AB_{VST\text{-}ET}$ scores were poor for both emotions (angry: $r = .13$, $p = .378$, Spearman-Brown corrected: .23; sad: $r = .37$ $p = .011$, Spearman-Brown corrected: .54).

Data analysis. One-way analyses of variance (ANOVAs) were conducted to assess group differences in $AB_{VST\text{-}ET}$ scores. To assess relationships between psychopathology and AB, correlations were calculated between $AB_{VST\text{-}ET}$ scores and depression as well as anxiety scores.

We found results on reaction times in the VST were inconsistent with a gaussian distribution using Kolmogorov-Smirnov (: $\leq .15$, $ps \leq .001$) and Shapiro-Wilk tests ($\leq .96$, $ps \leq .001$). The histogram showed them to be mildly right-skewed instead.

We therefore determined the median RT instead of the mean RT and proceeded to calculate bias scores using the median of reaction times instead of their mean.

Results. The one-way ANOVA on $AB_{VST\text{-}ET}$ revealed no significant group differences between MD, HR and LR groups ($Fs < 1$, $ps > .1$) for either sad or for angry faces. No correlations between dwell time and depression or anxiety scores emerged ($|rs| \leq .18$; $ps > .05$).

One-way ANOVAs on AB_{VST} scores (calculated with median) revealed no significant differences between MD, HR and LR youth ($Fs < 1.2$; $ps > .3$) regarding sad or angry faces. The correlational analyses revealed no relationship between AB_{VST} scores for sad or angry faces with depressive or anxiety symptoms ($r \leq .17$; $p \geq .07$).

In addition, we performed a transformation of the mean RTs using the square root to achieve gaussian distribution. With the transformed data, we then calculated AB bias scores in the same manner as in the original manuscript. One-way ANOVAs on AB_{VST} scores revealed no significant differences between MD, HR and LR youth ($Fs < .71$; $ps > .49$) regarding sad or angry faces.

Supplementary table 1. Eye-tracking AB scores for negative emotional faces (sad; angry) among all 3 groups in VST.

	MD	**HR**	**LR**
	n = 30	*n* = 47	*n* = 42
$AB_{VST\text{-}ET}$ for sad faces; *M (SD)*	-1.5% (6.7%)	-1.8% (6.1%)	-1.3% (5.4%)
$AB_{VST\text{-}ET}$ for angry faces; *M (SD)*	-1.2% (4.8%)	0.4% (6.2%)	-0.6% (5.2%)

Note: $AB_{VST\text{-}ET}$ = eye-tracking attention bias score from the Visual Search Task; MD = major depression group; HR = high-risk group; LR = low-risk group; M = Mean; SD = Standard Deviation.

Interpretation of results. The results show no evidence for group differences in AB between the groups. However, due to the poor reliability of the task the interpretation is limited. As reaction times were not normally distributed, we repeated our analyses with bias scores calculated from median instead of mean reaction times as well as bias scores based on square root transformed reaction times. The pattern of results did not change.

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Supplement 2: Passive Viewing Task

Initial orientation of attention. A Passive Viewing task (PVT) as a purely ET based measure of attention bias (AB) that allows investigation of different components of attention was administered [1]. Percentages of dwell time on each of the four different emotions were assessed as an indicator of maintenance of attention while percentage of location of the first fixation after trial onset were assessed as an indicator of initial orientation of attention. However, as the latter parameter showed poor reliability, results are reported only in this supplement.

Task procedure. The task procedure is described in the manuscript.

Data Processing. Data processing is described in the manuscript.

Reliability. To assess reliability, split-half reliability was calculated for percentage of location of the first fixation on all four emotions: it ranged from r = -.09 (Spearman-Brown corrected: .16) to -.03 (Spearman-Brown corrected: .06); all p > .32.

Data analysis. In order to compare first fixations, ANOVAs with within-subject factor EMOTION (4: angry, happy, neutral, sad) and between-subjects factor GROUP (3: MD, HR, LR) were calculated. Degrees of freedom were adjusted via the Greenhouse-Geisser correction when necessary. As the main focus of the study was to compare MD, HR and LR groups, only significant effects involving the factor GROUP were followed up using post-hoc ANOVAs and t-tests. To assess relationships with psychopathology, correlations between percentage of first fixation on each of the emotions and depression and anxiety symptoms were computed.

Results. Descriptive data for ET indices is presented in Supplementary table 2. The EMOTION × GROUP ANOVA revealed no significant effects (Fs ≤ 1.6, ps > .1). No significant correlations between percentage of first fixations on neither sad faces nor any of the other emotions (|rs|≤ .04, ps ≥ .59) and depressive symptoms as well as anxiety scores (|rs|≤ .06, ps ≥ .1) were found.

Supplementary table 2. Percentages of First Fixations on each of the 4 emotional faces among all 3 groups.

	MD	**HR**	**LR**
Percentages of First Fixations (%)	*n* = 28	*n* = 45	*n* = 42
Sad faces *M (SD)*	22.9 (9.5)	25.5 (11.8)	23.5 (9.4)
Angry faces *M (SD)*	26.3 (10.1)	23.3 (10.8)	21.7 (10.9)
Happy faces *M (SD)*	25.1 (11.3)	25.6 (10.7)	28.7 (10.1)
Neutral faces *M (SD)*	25.5 (11.8)	25.7 (12.1)	26.1 (12.7)

Note: MD = major depression group; HR = high-risk group; LR = low-risk group; M = Mean; SD = Standard Deviation.

Interpretation of results. These results show no evidence for group differences in initial orientation of attention between the groups. However, due to the poor reliability of the parameter the interpretation is limited. The good reliability of the maintenance of attention index and poor reliability of the initial orientation index is in line with e.g. [2] who found that the reliability of ET measures is higher for indices measured over longer (versus shorter) periods of time.

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Supplement 3: Dot Probe Task

A modified version of the Dot Probe Task (DPT; [1, 2, 3]) was used to assess ABs for sad as well as angry faces via reaction times (RT). Due to concerns about the task's reliability that have been raised previously [4, 5] (Schmukle, 2005; Waechter et al., 2014) (Schmukle, 2005; Waechter et al., 2014) (Schmukle, 2005; Waechter et al., 2014) (Schmukle, 2005; Waechter et al., 2014) (Schmukle, 2005; Waechter et al., 2014) (Schmukle, 2005; Waechter et al., 2014) and the poor reliability we found in our previous study on AB in depressed parents and their offspring ($|r| < .1$; [6]), we decided not to include this task in the manuscript.

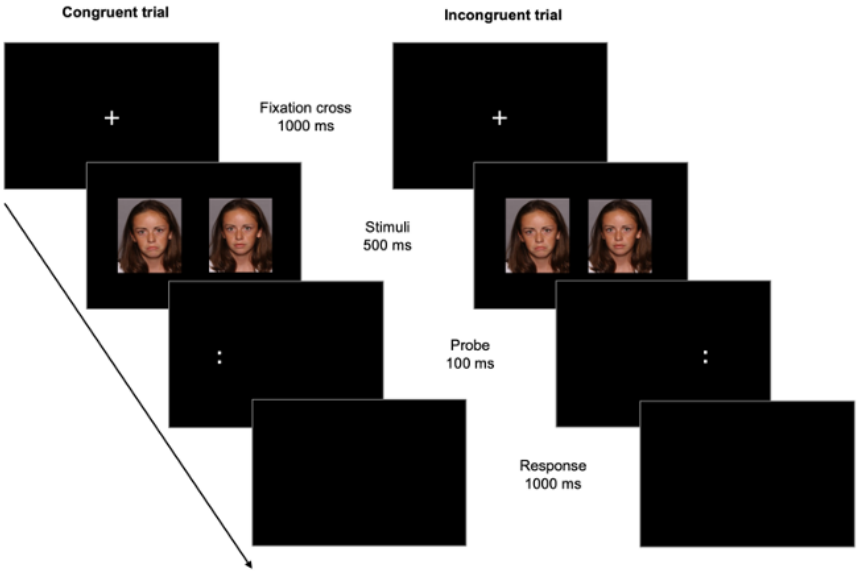
Stimuli. Stimuli were coloured photographs of faces displaying angry, sad, and neutral emotional expressions. Stimuli were age-matched, i.e. children viewed pictures of child models from the NIMH Child Emotional Faces Picture Set (NIMH-ChEFS; [7]). Five female and five male models were selected and images (13.5 × 10.5cm) were presented on a black background.

Task Procedure. The trial procedure is depicted in Supplementary Figure 1. Participants were seated in front of a 24-in. computer screen at a viewing distance of approximately 65cm. The experiment was presented using E-Prime 2.0 (Psychology Software Tools, 2013). Each trial started with a fixation cross that was presented for 1000ms at the centre of the screen. Then the face stimuli were presented for 500ms. Two pictures of the same actor were presented side-by-side: either an emotional (sad or angry) expression paired with a neutral expression (emotional trials) or two neutral expressions (neutral trials). The faces were followed by the probe which appeared in the location of one of the faces for 100ms, a timespan chosen to prevent elaborating on the previous stimulus and facilitate capturing the automatic rather than a reflective attention process [3]. The probe was two dots presented either vertically (":"; in 50% of trials) or horizontally (".."; 50% of trials) and participants were required to react as quickly and accurately as possible to the probe orientation by pressing the "Y" key for vertical or the "M" key for horizontal orientation. The probe was followed by a blank screen presented for 1000 ms during which responses were recorded (within 1100ms after probe onset).

The task comprised four blocks in random order: two measuring AB for angry faces and two measuring AB for sad faces. Each block consisted of 20 congruent trials (i.e., emotional trials in which the probe appeared in the location of the emotional face), 20 incongruent trials (i.e., emotional trials in which the probe appeared in the location of the neutral face), and 10 neutral trials, summing up to a total of 40 congruent and 40 incongruent trials per emotion across the whole task. Within each block, trials were presented in random order with emotional faces as well as the probe presented equally often on each side. Before the first block, participants completed

two practice blocks, each consisting of six trials in which they received feedback, in order to familiarize themselves with the task.

Supplementary Figure 1. Trial procedure of the modified Dot Probe Task (DPT; [1])



Data Processing and outcome variables. In line with previous studies (e.g. [3]), trials with incorrect responses or reaction times (RT) shorter than 200 ms or longer than 2 SDs above each participant's mean were excluded. Participants with less than 2 SD below the mean sum of correct trials of all participants were identified as outliers (in terms of response accuracy) and as such excluded from analysis (n = 2 MD children, n = 4 HR children, n = 1 LR child), resulting in a sample of 117 children for analysis of the DPT data. In the remaining sample, on average 164 correct and valid trials per participant were available for the children (SD = 17.5; 82% of 200 trials). This did not differ between groups ($F < 1$).

An AB score (AB_{DPT}) was calculated by subtracting the mean RT in congruent trials from the mean RT in incongruent trials so that positive values indicate an AB towards negative information (see e.g. [3, 8]) while negative values indicate an AB away from negative information. AB_{DPT} scores for sad and angry faces were computed separately.

Reliability. Split-half reliability of the task was assessed by correlating bias scores based on odd versus even trials (see e.g., Van Bockstaele et al., 2017); it was poor for both emotions (angry: $r = .01$, $p > .1$; sad: $r = .06$, $p > .1$).

Data analysis. One-way analyses of variance (ANOVAs) were conducted to assess group differences in AB_{DPT} scores. To assess relationships between psychopathology and AB, correlations were calculated between AB_{DPT} scores and depression as well as anxiety scores.

Results. Bias scores were rather small for both angry and sad stimuli (see Supplementary table 3). The ANOVA revealed a significant effect of GROUP ($F_2 = 3.88$; $p = .023$) in AB_{DPT} scores for angry faces, whereas no significant effect of GROUP ($F_2 = .53$; $p > .5$) could be found regarding sad faces. For angry faces, there was a significant difference between HR and LR participants ($t_{82.8} = 2.53$; $p = .014$) with moderate effect size ($d = 0.54$), but not between HR and MD participants ($ts \leq 0.2$; $ps > .1$) or LR and MD participants ($ts \leq 2.4$; $ps > .7$). No significant correlations between AB_{DPT} scores and depression or anxiety scores were found ($rs \leq .13$; $ps > .1$).

Supplementary table 3. AB_{DPT} scores for negative emotional faces (sad; angry) among all 3 groups.

	MD	**HR**	**LR**
	n = 30	*n* = 45	*n* = 42
AB_{DPT} for sad faces; *M (SD)*	8.0 ms (26.1)	1.4 ms (30.9)	2.3 ms (27.1)
AB_{DPT} for angry faces; *M (SD)*	0.6 ms (23.4)	2.0 ms (30.4)	12.8 ms (24.1)

Note: AB_{DPT} = behavioural attention bias score from the Dot Probe Task; MD = major depression group; HR = high-risk group; LR = low-risk group; M = Mean; SD = Standard Deviation.

Interpretation of results. The results indicate an AB towards angry faces in LR compared to HR youth but no group differences regarding AB for sad faces. However, due to the poor reliability of the outcome-parameters the interpretation is limited.

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Supplement 4: Scrambled Sentences Task

A computerized version of the Scrambled Sentences Task (SST; [1, 2]) was administered during eye-tracking (ET) in order to simultaneously assess attention biases (AB) to negative vs. positive words and interpretation biases, i.e. the tendency to form negative or positive statements out of ambiguous verbal information [1]. Interpretation bias results are reported elsewhere [3]. Due to the poor reliability we found in our previous study on AB in depressed parents and their offspring [4], we decided not to include this task in the manuscript.

Stimuli. The stimuli consisted of 50 scrambled sentences, of which 30 were emotional sentences (e.g., "total I winner a loser am") and 20 were neutral sentences (e.g., "like watching funny I exciting movies"). The emotional sentences were based on the original stimulus set developed by Wenzlaff and Bates [2] which was translated into German [5] adapted and extended. All sentences contained six words and had two possible solutions. In emotional trials, one solution was positive (e.g., "I am a total winner") whereas the other was negative (e.g., "I am a total loser"). In neutral trials both solutions were emotionally neutral. Across the stimulus set, target words (the words in each sentence that accounted for the positive or negative solution) were matched for length and frequency in the German language.[1] In line with Everaert and colleagues [1], word position within each sentence was randomised, with target words not allowed next to each other or in the first or last position and counterbalanced whether the positive or negative target word was presented first.

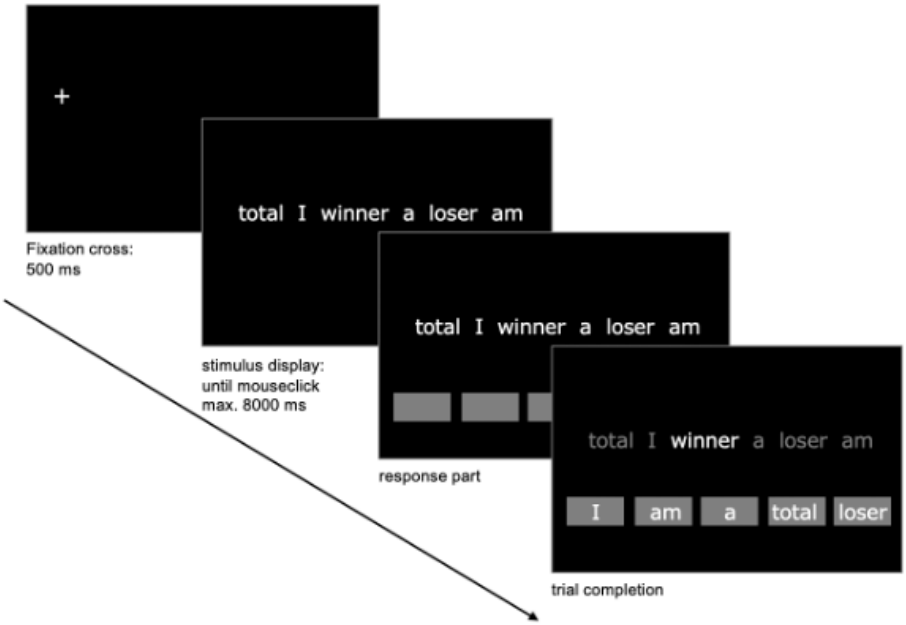
Task Procedure. Supplementary figure 2 depicts the trial procedure. Each trial began with a drift correction (small white circle on the left side of the screen) to direct the attention to that initial position. On fixation of the circle, the experimenter initiated the trial. A fixation cross followed for 500ms on the left side of the screen, preceding the stimulus display consisting of six words in a scrambled order presented at the centre of the screen on a single line. Participants were instructed to read the words and mentally form a grammatically correct five-word sentence as quickly as possible and to click on the mouse button as soon as they did so to continue to the response part of the trial. A scrambled sentence was presented for a maximum of 8000ms, if no mouse click occurred during that time, the response part was omitted, and the next trial began. In the response part five boxes appeared below the scrambled sentence and participants were

[1] Positive target words: Word length $M = 7.2$ ($SD = 2.5$) characters, word frequency (category according to http://wortschatz.uni-leipzig.de/de) $M = 9.8$ ($SD = 2.9$); Negative target words: word length $M = 7.2$ ($SD = 2.7$) characters, word frequency $M = 9.9$ ($SD = 4.1$); *t*s <1 in paired t-tests.

required to build the sentence they had mentally formed by clicking on the words in corresponding order. Time to allocate the words to boxes was not limited.

Trials were randomly divided into five blocks of ten (each containing six emotional and four neutral trials presented in random order). Before the first block participants completed five practice trials (five randomly selected neutral sentences) to familiarize themselves with the task. Similar to earlier studies (e.g., [1, 6]) we added a cognitive load procedure to prevent deliberate report strategies. Before each block, a 6-digit number was presented to the parents and a 4-digit number was presented to the children for 5000ms. Participants were instructed to memorize the number in order to recall it at the end of the block.

Supplementary figure 2. Trial procedure of the Scrambled Sentences Task (SST; [1, 2])



Data Processing and outcome variables. Participants' responses were rated as correct or incorrect. Trials in which no grammatically correct sentence was built (time-out or incorrect sentence) were excluded from the analysis. Participants with a correct sentence rate of two standard-deviations below the mean were identified as outliers in terms of accuracy and excluded (n=3 MD; n=8 HR; n=6 LR children). For the analyses of ET data we additionally excluded trials with poor data quality (see data processing of the Passive Viewing Task ET data in the manuscript for criteria) and participants with insufficient trials available due to data quality (MD: n = 23; HR: n = 37; LR: n = 34). In the remaining sample (94 children), on average 25.4 (SD = 2.68; 50.8% of 50 trials) trials per participant were available. This did not differ between groups ($F_{2,91}$ = .29; p = .75; η^2 = .01). To assess AB, we calculated an AB_{SST} score by dividing the percentage of dwell time on negative target words by the sum of

percentages of dwell times on negative and positive target words, with higher values indicating a more negative AB [1].

Reliability. Split-half reliability was assessed by correlating bias scores based on odd versus even trials (see e.g., [7]). Reliability was poor ($r = -.17$; $p = .05$).

Data analysis. A one-way analysis of variance (ANOVAs) was conducted to assess group differences in AB_{SST} scores. To assess relationships between psychopathology and AB, correlations were calculated between AB_{SST} scores and depression as well as anxiety scores.

Results. The one-way ANOVA revealed that AB_{SST} scores (MD: M (SD) = .51 (.04); HR: M (SD) = .49 (.04); LR: M (SD) = .50 (.06)) did not differ significantly between groups ($F_{2,91} = 1.42$; $p = .25$; $\eta^2 = .03$). No significant correlations emerged between AB_{SST} scores and depression or anxiety scores ($rs < .1$; $ps > .35$).

Interpretation of results. The results show no evidence for group differences in AB between the groups. However, due to the poor reliability of the outcome-measure the interpretation is limited.

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Supplement 5: Mood induction

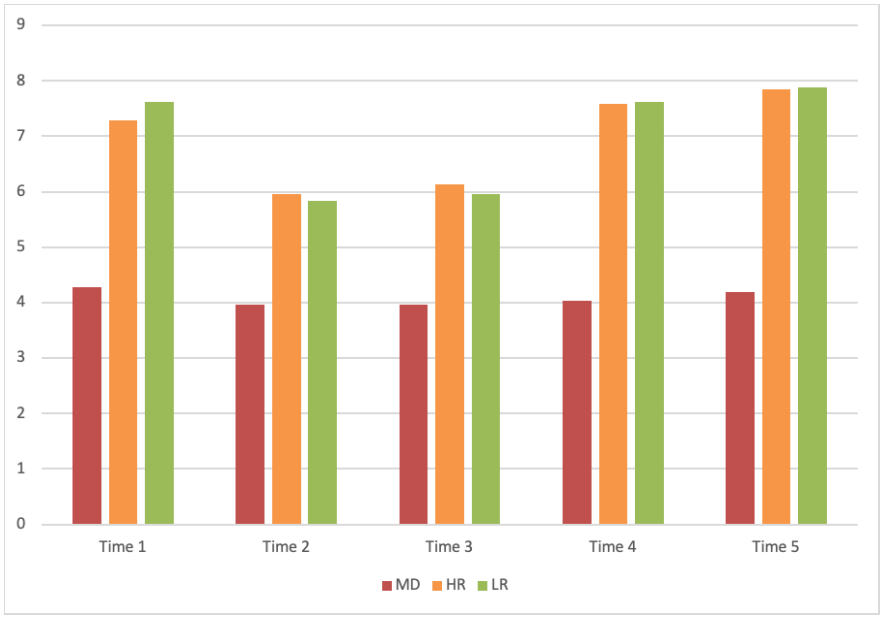
Mood was assessed five times during the experimental session (see [1]) using the valence dimension of the 9-point Self-Assessment Mannequin scale [2] and analysed with a TIME (5) × GROUP (3) ANOVA and subsequent t-tests.

Results

The ANOVA yielded significant main effects of TIME ($F_{2.1} = 54.57$; $p < .001$) and GROUP ($F_2 = 60.20$; $p < .001$), resulting from the MD group reporting more negative mood than the HR ($t_{47.3} = 8.3$, $p < .001$) and LR groups ($t_{44.6} = 8.5$, $p < .001$), as well as a significant interaction of TIME × GROUP ($F_{4.2} = 8.89$; $p < .001$). A post-hoc t-test comparing the baseline mood (mood before first mood induction: Time 1) with the other mood assessments revealed that participants rated their mood worse after watching the sad movie scene (Time 2 and Time 3; $ts \geq 7.82$; $ps < .001$) and better after watching the pleasant movie scene (Time 5; $t_{122} = 3.06$; $p = .003$) compared to baseline. Since TIME and GROUP interacted significantly, we conducted follow-up ANOVAs with the factor TIME within all groups: in both healthy control groups, the effects of mood induction were significant ($Fs < 43.22$; $p < .001$), but not in the depressed group ($F_{2.4} = 1.15$; $p = .33$). This indicated that the mood induction only influenced the mood of the non-depressed participants but had no effect on the mood of participants with MD, since their mood was more negative beforehand and remained so throughout the experimental session (see Supplementary Figure 3).

We further conducted post-hoc t-tests comparing baseline mood (mood before first mood induction: Time 1) with the other mood assessments in the HR and LR groups. These analyses revealed that both HR as well as LR participants rated their mood as worse after watching the sad movie scene (Time 2 and Time 3; $ts \geq 5.3$; $ps < .001$) and as better after watching the pleasant movie scene (Time 5; $ts \geq 2.1$; $ps \leq .044$) compared to baseline.

Supplementary Figure 3. Mean mood ratings of all children among groups in all 5 mood assessments



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Anhang B: Supplement zu Studie II

Supplement 1: Picture-based task Method

An explorative, picture-based task (PBT) resembling that used in the study of Haller, Raeder, Scerif, Kadosh, and Lau (2016) was additionally applied to assess interpretation bias.

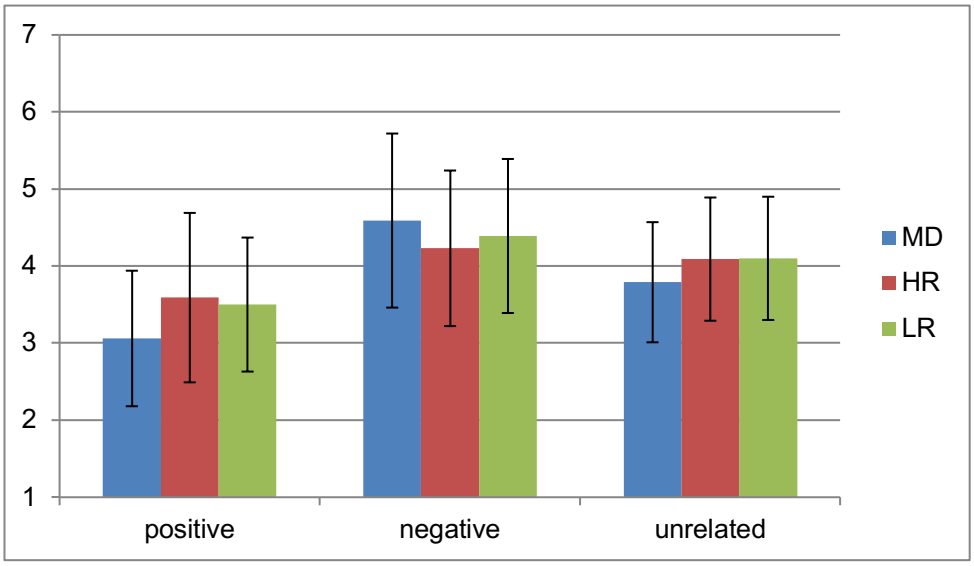
Ten pictures of social scenes (similar to those used by Haller et al, 2016; Haller, Doherty, Duta, Kadosh, Lau, & Scerif, 2017) associated with possible peer evaluation served as stimuli. In each picture a person (female in eight and male in two of the pictures) was depicted from behind. Participants were instructed to imagine they were that person and were in that situation. Pictures were presented in random order for five seconds, each followed by three statements. The statements consisted of a positive self-related interpretation of the situation (e.g., "They want me to take a picture with them"), one negative self-related interpretation (e.g., "They do not want me to be in the picture") and one interpretation unrelated to one's presence (e.g., "They are having fun taking pictures"). The three statements were presented consecutively and participants were asked to rate on a Likert scale from 1 ("very unlikely") to 7 ("very likely") how likely they would be to think that way if they were in that situation. After that, all three statements were presented simultaneously and participants were asked to select which statement represented the picture the best. The task was presented using E-Prime 2.0 software (Psychology Software Tools, Inc., 2013) and took approximately five minutes to complete.

In accordance with Haller et al. (2016), the mean likelihood rating was calculated for each interpretation type and subjected to a repeated-measures analysis of variance (ANOVA) with within-subjects factor InterpretationType (3: positive, negative, unrelated) and between-subjects factor Group (3: MD, HR, LR).

In addition, an interpretation bias score (IBPBT) was calculated by subtracting the mean likelihood rating for positive interpretations from the mean likelihood rating for negative interpretations so that scores > 0 indicate a negative interpretation bias and scores < 0 indicate a positive interpretation bias (analogous to the IBAST score). A one-way ANOVA was calculated to assess group differences the IBPBT and correlations between IBPBT and depression as well as anxiety scores were computed.

Results

The ANOVA yielded a significant main effect of InterpretationType ($F1.4,165.7 = 32.3$, $p < .001$, $\eta p^2 = .22$) resulting from positive interpretations being rated as less likely to occur than negative and unrelated interpretations (see Supplementary Figure 1). The main effect of Group ($F2,118 = 1.5$, $p > .1$) as well as InterpretationType × Group ($F1.4,165.7 = 2.2$, $p = .091$) were non-significant.



Supplementary Figure 1: Mean likelihood ratings for the three interpretation types. Error bars represent standard deviations.

IB_{PBT} scores were significantly > 0 (MD: $M = 1.5$, $SD = 1.7$; HR: $M = 0.6$, $SD = 1.9$; LR: $M = 0.9$, $SD = 1.6$; ts ≥ 2.4, ps ≤ .021), indicating a negative bias in all groups. The ANOVA on IB_{PBT} scores revealed no significant effect of GROUP ($F_{2,118} = 2.6$, $p = .076$). Positive correlations between IB_{PBT} score and depressive symptoms ($r = .29$, $p = .002$) as well as anxiety symptoms ($r = .23$, $p = .013$) were found. Exploratively, the correlations were recalculated within the groups, revealing a significant correlation only between IB_{PBT} and depressive symptoms within the MD group ($r = .40$, $p = .023$), while all other correlations were non-significant ($|r$s$| \leq .26$, ps $> .1$).

Differences between our task and that of Haller et al. (2016):

Our task differed from that of Haller et al. (2016) in some important aspects which leads to the assumption that the task is a less valid measure of interpretation bias in our study. First and most importantly, the age range of participants differed: while Haller et al. (2016) studied adolescents aged 14-17 years, our sample was 9-14 years old. Therefore it is likely that the stimuli were not age-appropriate for our younger sample. Second, Haller et al. (2016) superimposed a picture of the participant onto the pictures (so that the person depicted from behind was the participant him- or herself) to create the illusion of the participant being an active partaker within the scene.

This might render the pictures more self-relevant. Third, a mental imagery task was carried out before the completion of the PBT in the study of Haller et al. (2016), again possibly rendering the pictures more self-relevant. Forth, the task was designed to study the impact of social anxiety on the interpretation of social situations; it might be less suitable to assess interpretation biases related to depression.

References

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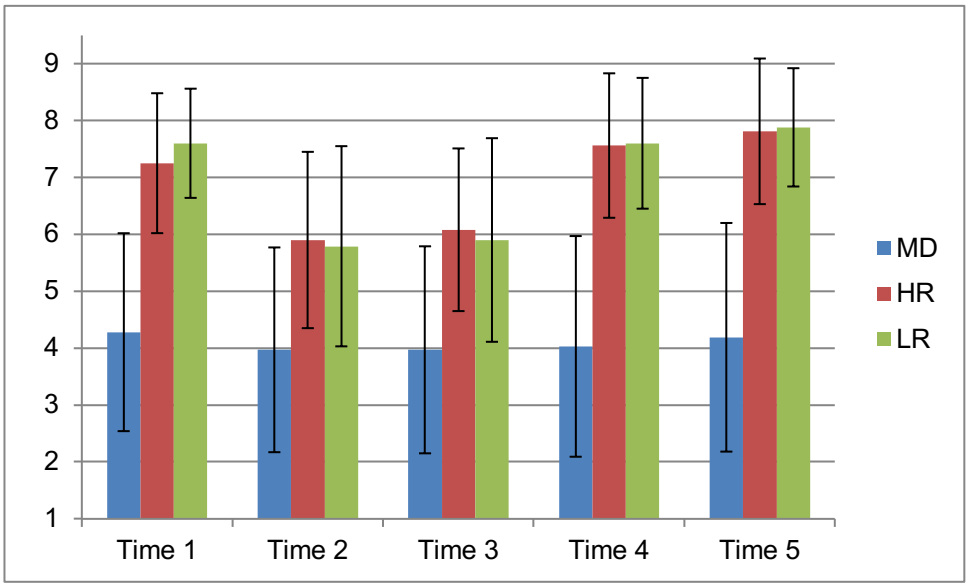
Supplement 2: Results of the mood induction

Mood was assessed five times during the experimental session (see Sfärlea et al., 2019, Supplement 5) using the valence dimension of the 9-point Self-Assessment Mannequin scale (Lang, 1980). In addition to calculating *t*-tests comparing the baseline mood (mood before first mood induction: Time 1) with mood after the mood inductions (Time 2 and Time 3) across groups (results presented in the main text), we also analysed mood using a TIME (5) × GROUP (3) ANOVA to investigate if the mood induction procedure had the same impact on mood in all three groups.

The ANOVA yielded a significant main effect of TIME ($F_{2.1,251.3} = 56.1$, $p < .001$, $\eta_p^2 = .32$), a significant main effect of GROUP ($F_{2,118} = 59.1$, $p < .001$, $\eta_p^2 = .50$), resulting from the MD group reporting more negative mood than the HR ($t_{46.9} = 8.2$, $p < .001$) and LR groups ($t_{44.8} = 8.4$, $p < .001$), as well as a TIME × GROUP interaction ($F_{2.1,251.3} = 9.3$, $p < .001$, $\eta_p^2 = .14$). To follow-up the interaction, one-way ANOVAs with the factor TIME were performed within each group resulting in significant effects within the HR and LR groups (HR: $F_{2.6,121.7} = 44.0$, $p < .001$, $\eta_p^2 = .48$; LR: $F_{1.6,64.5} = 33.8$, $p < .001$, $\eta_p^2 = .45$) but not the MD group ($F_{2.4,70.7} = 1.2$, $p > .1$). This indicated that, in fact, the mood induction only influenced the mood of the non-depressed participants while the mood of participants with MD was more negative before the mood induction and remained so throughout the experimental session (see Supplementary Figure 2).



Supplementary Figure 2: Mean mood ratings in each of the five mood assessments. Error bars represent standard deviations.

We further conducted post-hoc *t*-tests comparing baseline mood (mood before first mood induction: Time 1) with the other mood assessments in the HR and LR groups. These analyses revealed that both HR as well as LR participants rated their mood as worse after watching the sad movie scene (Time 2 and Time 3; ts $\geq$ 5.4; ps < .001) but only HR participants rated their mood better after watching the pleasant movie scene (Time 5; t_{47} = 3.5; p = .001) compared to baseline.

References

Hahn, D. (Producer), Allers, R., & Minkoff, R. (Directors). (1994). *The Lion King* [Motion Picture]. USA: Walt Disney.

Lang, P. J. (1980). Behavioral treatment and bio-behavioral assessment: Computer applications. In J. B. Sidowski, J. H. Johnson & T. A. Williams (Eds.), *Technology in Mental Health Care Delivery Systems* (pp. 119-137). Norwood: Ablex.

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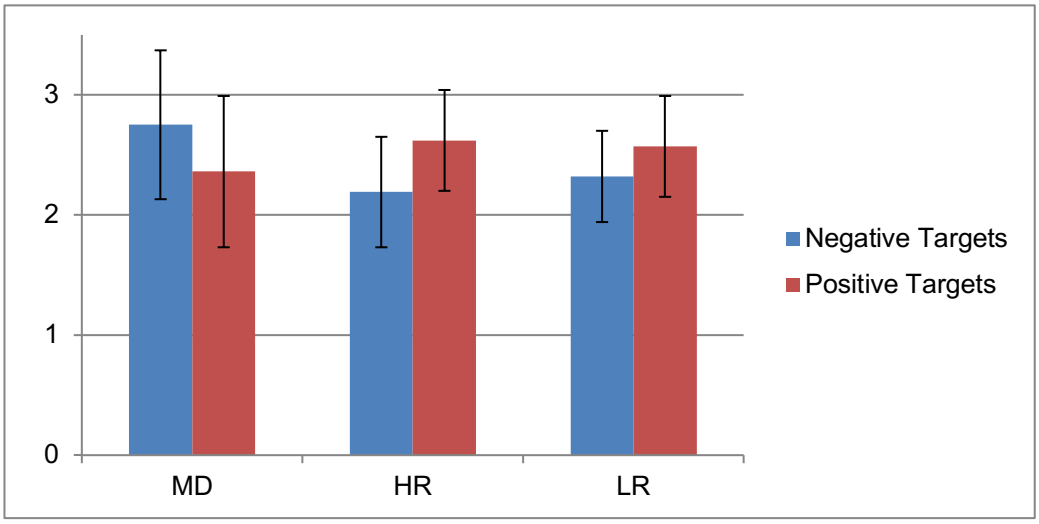
Supplement 3: Alternative analysis of the AST

An alternative way to analyse the AST with absolute positive and negative scores instead of relative scores is to calculate a 2-way ANOVA with the within-subjects factor VALENCE (2: mean negative vs. positive target scores) and the between-subjects factor GROUP (3) and corresponding post-hoc tests.

This ANOVA yielded no main effects of VALENCE ($F_{1,119} = 2.0$, $p > .1$, $\eta_p^2 = .02$) or GROUP ($F_{2,119} = 2.1$, $p > .1$, $\eta_p^2 = .03$) but a significant VALENCE × GROUP interaction ($F_{2,119} = 13.0$, $p < .001$, $\eta_p^2 = .18$). To follow up this interaction, one-way ANOVAs with the between-subjects factor GROUP were performed separately for mean negative and positive target scores. For negative target scores, this analysis yielded a significant effect of GROUP ($F_{2,119} = 13.3$, $p < .001$, $\eta^2 = .18$) with post-hoc *t*-tests indicating that the MD group was more likely to endorse negative interpretations than the HR ($t_{53.5} = 4.4$, $p < .001$, $d = 1.0$) and LR groups ($t_{48.2} = 3.4$, $p = .001$, $d = 0.8$) while the HR and LR groups did not differ from each other ($t_{88} = 1.5$, $p > .1$, $d = 0.3$). For positive bias scores, the effect of GROUP was non-significant ($F_{2,119} = 3.1$, $p = .050$, $\eta^2 = .05$). Supplementary Figure 3 illustrates the absolute values for endorsement of negative and positive targets.



Supplementary Figure 3: Mean absolute values for the endorsement of negative and positive targets. Error bars represent standard deviations.

These results indicate that the group differences in the AST were mainly driven by difference in the endorsement of *negative* interpretations, which the MD group was more likely to endorse than the HR and LR groups. Descriptively, the MD group was also less likely to endorse positive interpretations than the HR and LR groups, but differences for positive interpretations were not significant.

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