Fachbereich Erziehungswissenschaft und Psychologie der Freien Universität Berlin

# Attentional Bias in Military Personnel with Posttraumatic Stress Disorder and its Modifiability after an Internet-Based Cognitive Behavioral Intervention

Aufmerksamkeitsverzerrungen in militärischen Einsatzkräften mit posttraumatischer Belastungsstörung und deren Veränderlichkeit nach Bereitstellung einer internet-basierten kognitiv-behavioralen Intervention



Dissertation zur Erlangung des akademischen Grades Doktorin der Philosophie (Dr.<sup>in</sup> phil.)

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## After all, when a stone is dropped into a pond,

## the water continues quivering even after the stone has sunk to the bottom

(Arthur Golden, Memoirs of a Geisha)

## Energy flows where the attention goes

(Milton Erickson)

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V

#### ABSTRACT

Posttraumatic stress disorder (PTSD) is a prevalent and highly disturbing mental health condition that occurs in response to extremely distressing events during the lifetime. First, military personnel represent a high-risk population for the development of posttraumatic stress symptoms (PTSS) or the full-diagnostic spectrum of the disorder due to deployment- and combat-related stressors during their military career. Despite the existence of well-established and efficacious psychotherapy treatments for PTSD, access to trauma-focused psychotherapy is limited and veterans in particular experience high barriers to accessing help from the mental health care system. A substantial proportion of affected veterans receive no or inadequate treatment, increasing the risk of secondary adverse mental and somatic health outcomes, reduced social and occupational functioning, and of the condition becoming chronic. Second, internet-based interventions (IBI), particularly internet-based cognitive behavioral therapies (iCBT), have been shown to be efficacious and widely accepted for the treatment of a range of psychiatric disorders, including PTSD. IBI can already be seen as playing a potentially important role in supplementing the landscape and provision of psychotherapeutic interventions, and this is set to grow further in the future. Indeed, IBI should be particularly beneficial for patients in rural areas with a restricted psychotherapy infrastructure, for patients with restricted mobility, and for patients who desire greater anonymity and more independence regarding the time and location of psychotherapy access. Third, the systematic and reliable assessment of objective indicators of symptom expression and symptom change is of increasing interest and relevance for psychotherapy research.

This dissertation thesis aims at incorporating these three pillars in four studies: First, a diagnostic identification of PTSD in veterans of the German Armed Forces (GAF) according to the main diagnostic manuals the International Classification of Diseases and Related Health Problems (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM); second,

a meta-analytical evaluation of the efficacy of IBI in PTSD; third, an assessment of patterns of visual attentional bias in (traumatized) veterans (with PTSS); and fourth, an exploration of the modifiability of attentional bias in veterans after receiving iCBT.

**STUDY 1** investigated the concordance of PTSD prevalence rates when transiting between the diagnostic criteria of the DSM-IV, DSM-5, ICD-10, and proposed ICD-11 in a sample of service members of the GAF. High levels of agreement emerged between the DSM-IV and the DSM-5, and between the DSM-5 and the proposed ICD-11. Prevalence rates were significantly higher according to the proposed ICD-11 compared to the ICD-10, mainly due to the deletion of the time criterion. STUDY 1 provides support for the identification of six 'core' PTSD symptoms according to the proposed ICD-11, presenting a high agreement rate with the set of twenty qualifiers according to the DSM-5.

**STUDY 2** provided meta-analytical evidence for the efficacy of IBI for the treatment of PTSD. Twenty randomized controlled trials (RCT) encompassing 21 comparisons were included, evaluating either iCBT or internet-based expressive writing (iEW) with passive or active control conditions. The results revealed that iCBT was more efficacious than passive control conditions at post-treatment assessment ( $0.66 \le g \le 0.83$ ). No superiority of either iCBT or iEW was found in contrast to active control conditions. Subgroup analyses revealed no significant moderators of iCBT efficacy. More research is needed to prove the efficacy of IBI in contrast to active control treatments and further explore the impact of moderators on treatment efficacy.

**STUDY 3** measured patterns of attentional bias in GAF veterans with PTSS, traumatized veterans without PTSS, and unexposed healthy veterans. In a free-viewing task, participants were presented with pairs of combat-related and neutral pictures, of more general threat-related and neutral pictures, and of emotional and neutral faces, while their eye gazes

were tracked. Further, the internal consistency of attentional bias indicators was calculated. The findings provide support for the maintenance hypothesis in PTSS. There was no robust evidence to support the hypothesis of hypervigilant behavior in PTSS. Findings on attentional bias variability remain unclear. Internal consistency varied across attentional bias indicators, highlighting the need for future research in this regard.

**STUDY 4** investigated the modifiability of attentional bias in veterans with PTSS through the provision of iCBT. In a free-viewing task, participants were presented with combat-related, general threat-related, and neutral pictures, and with faces with negative emotional valence and neutral facial expressions while their eye gazes were tracked. Attentional bias was examined pre- and post-intervention and at a three-month follow-up. No modifications in attentional bias were observable over time. Future investigations are warranted to systematically investigate objective measures of symptom expression and symptom change together with subjective symptom reporting and symptom change in response to psychotherapeutic treatment options.

In summary, this dissertation thesis provides a threefold contribution to the current landscape of psychotherapy research: First, it supports the concordance between the DSM-5 and the ICD-11 diagnostic criteria for PTSD. Second, it proves the efficacy of IBI for PTSD. In view of the growing relevance of IBI as a supplement to psychotherapeutic care, future research needs to examine its long-term efficacy, whether it shows equal or superior efficacy compared to other active (control) treatments, potential side effects, and whether it may lead to a deterioration of symptoms. Moreover, studies should focus on tailoring IBI to the specific needs of different patient populations to ensure patients' safety and satisfaction with IBI. Third, the present thesis underlines the need for systematic and reliable assessments of objective indicators of symptom presentation and of symptom change, in addition to subjective reports. Moreover, methodological approaches need to be extended to measure diverse dimensions of symptom presentation and symptom change and gain a better understanding of their interplay. A multidimensional diagnostic approach and treatment evaluation will be of key relevance for future intervention research and evidence-based practice.

#### KURZZUSAMMENFASSUNG

Die posttraumatische Belastungsstörung (PTBS) ist eine häufige und äußerst einschränkende psychische Störung, die in Reaktion auf belastende Lebensereignisse auftreten kann. Erstens, Soldat\*innen stellen eine Hochrisikopopulation für die Entwicklung von posttraumatischen Stresssymptomen (PTSS) als auch für die Entwicklung des diagnostischen Vollbildes der Störung dar, basierend auf der erhöhten Wahrscheinlichkeit des Erlebens potenziell traumatischer Ereignisse, denen die Einsatzkräfte während der Auslandseinsätze und Kampfhandlungen und im Laufe ihrer Berufszeit ausgesetzt sein können. Obwohl wirksame psychotherapeutische Behandlungsmethoden für die PTBS existieren und etabliert sind, zeigt sich der Zugang zu Trauma fokussierter Psychotherapie als begrenzt und insbesondere Soldat\*innen erleben hohe Hürden bezüglich der Inanspruchnahme psychologischpsychiatrischer Gesundheitsdienste und Behandler\*innen. Ein substanzieller Anteil betroffener Einsatzkräfte erhält keine oder keine angemessene psychotherapeutische Behandlung, was zu einer Erhöhung des Risikos einer Chronifizierung der PTBS führen kann, das Auftreten weiterer körperlicher und mentaler Beschwerden wahrscheinlicher macht und auch eine reduzierte soziale und berufliche Leistungsfähigkeit nach sich ziehen kann. Zweitens, internetbasierte Interventionen (IBI), insbesondere internet-basierte kognitive Verhaltenstherapie (i-KVT), erweisen sich als wirksam und akzeptabel zur Behandlung unterschiedlicher psychischer Störungen, darunter auch zur Behandlung der PTBS. IBI können bereits heute und noch mehr in künftigen Zeiten eine wichtige Rolle für die Erweiterung der psychotherapeutischen Landschaft und für die Versorgung von Patient\*innen spielen. Dies kann sich für die Versorgung von ländlichen Gebieten mit mangelnder Psychotherapie-Infrastruktur zeigen, sowie für Patient\*innen mit eingeschränkter Mobilität und für Patient\*innen, die mehr Anonymität und Unabhängigkeit von zeitlichen und örtlichen Zugangsmöglichkeiten zu Therapieangeboten wünschen. Drittens, die systematische und zuverlässige Messung von objektiven Symptomindikatoren sowie von objektiven Indikatoren zur Symptomveränderung findet zunehmendes Interesse und Relevanz in der Psychotherapieforschung.

Diese Dissertation verfolgt die Integration dieser drei Grundpfeiler anhand von vier Studien: Zuerst erfolgt ein Abgleich des diagnostischen Status zur Diagnose der PTBS in einer Stichprobe von Einsatzkräften der deutschen Bundeswehr, wenn die verschiedenen Versionen der diagnostischen Manuale der Internationalen Statistischen Klassifikation der Krankheiten und verwandter Gesundheitsprobleme (ICD) und des Diagnostischen und Statistischen Manuals Psychischer Störungen (DSM) angewendet werden; Zweitens findet eine meta-analytische Einschätzung der Wirksamkeit von IBI zur Behandlung der PTBS statt; Drittens werden Muster verzerrter visueller Aufmerksamkeitsprozesse in (traumatisierten) Einsatzkräften (mit PTSS) gemessen; Viertens wird die Veränderbarkeit jener Muster gestörter Aufmerksamkeitsprozesse durch die Gabe einer i-KVT exploriert.

**STUDIE 1** überprüfte die Übereinstimmung der PTBS Prävalenzraten in einer Stichprobe von Einsatzkräften der deutschen Bundeswehr unter der Anwendung der diagnostischen Kriterien, die dem DSM-IV, DSM-5, ICD-10 und ICD-11 Entwurf folgen. Hohe Übereinstimmungsraten wurden zwischen dem DSM-IV und dem DSM-5 sowie zwischen dem DSM-5 und dem ICD-11 Entwurf gefunden. Die PTBS Prävalenz war unter der Anwendung des ICD-11 Entwurfs gegenüber dem ICD-10 signifikant erhöht, hauptsächlich zurückführbar auf die Löschung des Zeitkriteriums im ICD-11 Entwurf. STUDIE 1 stützt die Identifikation von sechs "Kernsymptomen" der PTBS, wie durch den ICD-11 Entwurf vorgeschlagen. Dabei finden sich hohe Übereinstimmungsquoten zu dem Set der zwanzig qualifizierenden Symptome basierend auf dem DSM-5.

**STUDIE 2** bot eine meta-analytische Evaluation der Wirksamkeit von IBI zur Behandlung der PTBS. Zwanzig randomisiert-kontrollierte Studien mit 21 Vergleichen waren

inkludiert, die entweder Programme der i-KVT oder Programme des internet-basierten expressiven Schreibens (i-ES) im Vergleich zu passiven oder aktiven Kontrollbedingungen untersuchten. Die meta-analytischen Ergebnisse zeigten, dass i-KVT gegenüber passiven Kontrollbedingungen direkt nach Interventionsabschluss überlegen war ( $0.66 \le g \le 0.83$ ). Es fand sich keine Überlegenheit der i-KVT oder der i-ES gegenüber aktiven Kontrollbedingungen. Subgruppen-Analysen identifizierten keine bedeutsamen Moderatoren der Wirksamkeit der i-KVT Programme. Mehr Forschungsvorhaben werden gebraucht, um die Wirksamkeit von IBI gegenüber aktiven Kontrollbedingungen zu überprüfen, sowie um die Bedeutsamkeit möglicher Moderatoren der Wirksamkeit weiter zu erforschen.

STUDIE 3 erfasste Muster verzerrter visueller Aufmerksamkeitsprozesse in einer Stichprobe von Einsatzkräften der deutschen Bundeswehr mit PTSS, traumatisierten Einsatzkräften ohne PTSS und nicht-traumatisierten gesunden Einsatzkräften. Die Teilnehmer wurden mit Bildpaaren mit Einsatzbezug und neutralem Inhalt, allgemeinerem Gefahrenbezug und neutralem Inhalt sowie negativ-emotionalen Gesichtern und neutralen Gesichtern konfrontiert und die Blickbewegungen wurden während einer Aufgabe zur freien Betrachtung des Gezeigten mittels Eye Tracking aufgezeichnet. Darüber hinaus wurde die interne Konsistenz der Indikatoren der Aufmerksamkeitsverzerrung berechnet. Die Ergebnisse stützen die Hypothese der verlängerten Aufmerksamkeit bei der PTBS. Keine validen Hinweise zeigten sich zur Hypothese der Hypervigilanz bei der PTBS. Befunde zur Variabilität der Aufmerksamkeitsverzerrungen bleiben uneindeutig. Die interne Konsistenz variiert je nach Indikator, was die Notwendigkeit zukünftiger Forschung unterstreicht.

**STUDIE 4** untersuchte in Einsatzkräften mit PTSS die Veränderbarkeit bestehender Muster von Aufmerksamkeitsverzerrungen durch die Gabe einer i-KVT. Den Teilnehmern wurden Bilder mit Einsatzbezug, allgemeinerem Gefahrenbezug und neutralem Inhalt sowie negativ-emotionale Gesichter und neutrale Gesichter präsentiert und ihre Blickbewegungen wurden während einer Aufgabe zur freien Betrachtung des Gezeigten mittels Eye Tracking aufgezeichnet. Die Messungen erfolgten vor der Gabe der i-KVT, direkt nach deren Beendigung sowie drei Monate später. Über die Zeit hinweg zeigten sich keine Veränderungen der Aufmerksamkeitsverzerrungen. Weitere Untersuchungen sind notwendig, um objektive Symptomindikatoren und objektive Indikatoren von Symptomveränderungen zusammen mit subjektiven Berichten zum Symptomerleben und -veränderungen in Reaktion auf psychotherapeutische Interventionen zu untersuchen.

Zusammenfassend trägt diese Dissertation in dreifacher Art zur gegenwärtigen Literatur der Psychotherapieforschung bei: Zuerst stützt sie die angemessene Übereinstimmung der DSM-5 und ICD-11 Kriterien der PTBS. Zweitens belegt sie die Wirksamkeit von IBI zur Behandlung der PTBS. In Angesicht der zunehmenden Relevanz von IBI als Ergänzung zur psychotherapeutischen Versorgung wird die Notwendigkeit zukünftiger Forschung betont, die die Langzeitwirksamkeit der IBI, deren Gleichwertigkeit oder Überlegenheit zu anderen Behandlungsangeboten, als auch mögliche Nebenwirkungen oder Symptomverschlechterungen im Kontext der Anwendung von IBI untersucht. Das "Maßschneidern" von IBI sei betont, um Bedarfe verschiedener Patient\*innengruppen besser begegnen und so die Sicherheit und Zufriedenheit der Patient\*innen während der Nutzung von IBI sicherstellen zu können. Drittens, die Notwendigkeit systematischer und zuverlässiger Erhebungen von objektiven Symptom- und Veränderungsindikatoren zusätzlich zur Erhebung subjektiver Symptom- und Veränderungsoperatoren wird hervorgehoben. Es werden zukünftige Forschungsvorhaben benötigt, die bestehende methodische Ansätze erweitern, um verschiedene Dimensionen der Symptompräsentation und -veränderung zu messen, als auch um deren Zusammenspiel besser verstehen zu können. Die multidimensionale Diagnostik und Evaluation von Interventionen wird in kommenden Zeiten von bedeutender Relevanz für die Psychotherapieforschung als auch für die evidenzbasierte psychotherapeutische Praxis sein.

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## **CHAPTER 1 – Introduction and theoretical background**

Experiencing, witnessing, or being confronted with an extraordinarily stressful and potentially traumatizing event can lead to subsequent posttraumatic stress symptoms (PTSS) and ultimately to the presentation of posttraumatic stress disorder (PTSD), in line with the criteria of the 5<sup>th</sup> version of the Diagnostic and Statistical Manual of Mental Disorders, the DSM-5 (American Psychiatric Association, 2013) and the 11<sup>th</sup> revision of the International Classification of Diseases for Mortality and Morbidity Statistics, the ICD-11 (World Health Organization, 2018). Illuminating this risk, for example, a Detroit firefighter wrote in his online blog, after 32 years of service, that '*I wish my head could forget the things my eyes have seen*'<sup>1</sup>. Similarly, an American military veteran described in his biography that '*I feel no emotional connection to these outwardly human gestures. I am not there, because I never left Afghanistan*' (Wood, 2013). According to Van der Kolk and McFarlane (1996), in contrast to other psychiatric disorders, the core issue in stress and trauma disorders is *reality*.

SECTION 1.1 of this dissertation provides the reader with a brief overview of the evolution of the diagnosis of PTSD according to the DSM and the ICD. In brief, the literature on the prevalence of PTSD, its epidemiology, and comorbidities are summarized. SECTION 1.2 deals with the high-risk population of military personnel, focusing on certain characteristics of this population and their associated needs, as well as barriers to psychotherapy uptake in this population. SECTION 1.3 presents a concise overview of well-established evidence-based treatments for PTSD, with reference to cognitive-behavioral therapy (CBT). Moreover, the reader is introduced to internet-based intervention (IBI) programs for PTSD, and research findings on the efficacy of such programs are summarized. SECTION 1.4 provides a brief introduction to processes of visual attention and the technology of eye-tracking. Theories on attentional bias in PTSD are presented, along with relevant eye-tracking-based findings on

<sup>&</sup>lt;sup>1</sup> http://www.jamesgeering.com/blog/2016/11/27/i-wish-my-head-could-forget-the-things-my-eyes-have-seen (Date of access: 01/01/22)

attentional bias reported to date. SECTION 1.5 introduces and embeds the four core studies of this thesis into its overarching research project.

SECTION 2 through SECTION 5 present STUDY 1, STUDY 2, STUDY 3, and STUDY 4 of this dissertation thesis. STUDY 1 compares PTSD prevalence rates in a sample of German Armed Forces (GAF) veterans when diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders version 4 (DSM-IV; American Psychiatric Association, 1994) and version 5 (DSM-5; American Psychiatric Association, 2013), the International Classification of Diseases and Related Health Problems version 10 (ICD-10; World Health Organization, 1992), and the proposed 11<sup>th</sup> revision of the ICD (ICD-11) (Maercker, Brewin, Bryant, Cloitre, van Ommeren, et al., 2013). STUDY 2 provides a meta-analysis of the efficacy of IBI in the treatment of PTSD or PTSS. STUDY 3 describes a cross-sectional eye-trackingbased analysis of group differences between traumatized GAF veterans with PTSS versus traumatized GAF veterans without PTSS versus non-exposed healthy GAF veterans regarding patterns of attentional bias. STUDY 4 investigates the modifiability of patterns of attentional bias in veterans with PTSS who received iCBT.

SECTION 6 discusses the main findings of STUDY 1 (SECTION 6.1), STUDY 2 (SECTION 6.2), STUDY 3 (SECTION 6.3), and STUDY 4 (SECTION 6.4) in the light of recent research. Concurrently, the specific limitations of each study are critically considered. Future directions and implications for clinical research and practice are derived for each of the four main studies of this dissertation thesis. Finally, SECTION 6.5 provides a brief conclusion for STUDY 1, STUDY 2, STUDY 3, and STUDY 4.

The Appendix provides the reader with the supplementary materials of STUDY 1 through STUDY 4.

2

#### 1.1. The evolution of posttraumatic stress disorder and its diagnostic criteria

#### 1.1.1. A brief review of the evolution of 'traumatic stress responses' in the literature

Although humankind has been confronted with potentially traumatizing events since the beginning of time, stress responses and the recognition of psychiatric disorders in the aftermath of stress and trauma are relatively new to the empirical literature (Ray, 2008). After World War I, the literature coined the term 'shell shock' to describe (de-)compression of the brain caused by nearby explosions during battle activities, thus referring to a physiological alteration of the brain (Mott, 1916). Selye (1956) emphasized the role of physiological stress reactions in pioneering works on the hypothalamic-pituitary-adrenal (HPA) axis. Freud acknowledged external stressors and internal vulnerabilities of patients and introduced the term 'traumatic neurosis', which he described as presenting as 'intrusive imagery', 'physiological hyperactivity', and 'active re-living' in his traumatized patients (Freud, 1963). Following World War II, the Veterans Administration of the United States called for the establishment of a standardization, categorization, and international guidelines to diagnose and handle psychiatric disorders (Andreasen, 2010).

#### 1.1.2. PTSD in the Diagnostic and Statistical Manual of Mental Disorders

In response to this call from the Veterans Administration after World War II, the American Psychiatric Association (APA) published the Diagnostic and Statistical Manual of Mental Disorders (DSM), with the aim of creating a classification of diseases that enables practitioners and researchers to diagnose mental health conditions under a uniform procedure and referring to a standardized catalogue of diagnostic criteria (Andreasen, 2010). Today, the DSM is of extraordinary international relevance, particularly for empirical research. The first version of the DSM (DSM-I; American Psychiatric Association, 1952) included a category 'Gross stress reaction' in a section on 'Transient situational personality disorders' (Friedman,

Keane, & Resick, 2007). It was conceptualized as 'a stress syndrome or stress response to severe physical demands or extreme emotional stress such as in combat or in civilian catastrophe [...] in normal persons who have experienced intolerable stress' (American Psychiatric Association, 1952), and was declared as a transient disturbance that was expected to fade after days or weeks (Andreasen, 2010; North, Surís, Smith, & King, 2016). This category was removed from the DSM-II (American Psychiatric Association, 1968). In response to the returning Vietnam War veterans, who reported an array of excessive trauma symptoms and showed a high demand for (psychological) support, a transitory description of 'post-Vietnam syndrome' was created (DiMauro, Carter, Folk, & Kashdan, 2014). Finally, the DSM-III (American Psychiatric Association, 1980) introduced the category 'Posttraumatic stress disorder', which officially acknowledged PTSD as a psychiatric diagnosis requiring psychiatric care. PTSD was categorized as an anxiety disorder up to and including the DSM-IV-TR and was finally allocated to a newly invented class with the publication of the DSM-5: Trauma- and stressrelated disorders. Although the *necessity* of experiencing a potentially traumatizing event for a diagnosis was sustained throughout the evolution of the DSM, the definition of trauma and the trauma survivor's response to it were modified over time (Andreasen, 2010; North et al., 2016). Over the years, multiple alterations have been made to the number of symptom clusters, to the wording of symptoms, to the criteria of symptom onset and chronicity, to the criteria of distress or impairment, and to the specification of dissociative symptoms (Hunsley & Mash, 2018). Table 1 presents an overview of the diagnostic criteria of PTSD based on the DSM-III (American Psychiatric Association, 1980), DSM-III-TR (American Psychiatric Association, 1987), DSM-IV (American Psychiatric Association, 1994) and the DSM-IV-TR (American Psychiatric Association, 2000), as well as the current DSM-5 (American Psychiatric Association, 2013).

Criterion/ Manual	DSM-III	DSM-III-TR	DSM-IV/ DSM-IV-TR	DSM-5
Trauma Criterion	A recognizable stressor that would evoke significant symptoms of distress in almost everyone	The person has experienced an event that is outside the range of usual human experience and that would be markedly distressing to almost anyone, including a serious threat to one's life or physical integrity; usually experienced with intense fear, terror, and helplessness - direct personal exposure - witnessing another person's exposure to trauma - indirect exposure, learning of the exposure of one's children, spouse, or other close relatives and friends	<ul> <li>A1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of others</li> <li>AND</li> <li>A2. The person's response involved intense fear, helplessness, or horror</li> <li>direct personal exposure</li> <li>witnessing another person's exposure to trauma</li> <li>indirect exposure, learning of the exposure of family member or another close associate/friend</li> </ul>	<ul> <li>Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:</li> <li>directly experiencing</li> <li>witnessing, in person, the event(s) as it occurred to others</li> <li>learning that the event(s) occurred to a close family member or friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental</li> <li>experiencing repeated or extreme exposure to aversive details of the event(s)</li> </ul>
Persistent re- experiencing of the event	At least one of the following: B1. Intrusive recollections of the event B2. Recurrent distressing dreams of the event B3. A sudden feeling that the event is recurring	At least one of the following: B1. Recurrent and intrusive disturbing recollections of the event B2. Recurrent distressing dreams of the event B3. Sudden acting or feeling as if the event was recurring B4. Intense psychological distress at exposure to events that symbolize or resemble an aspect of the event	At least one of the following: B1. Recurrent and distressing recollections of the event B2. Recurrent distressing dreams of the event B3. Acting or feeling if the traumatic event were recurring B4. Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the event	At least one of the following: B1. Recurrent, involuntary, and intrusive distressing memories of the event(s) B2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the event(s) B3. Dissociative reactions in which the individual feels or acts as if the traumatic event(s) were recurring

Table 1. Overview of the diagnostic criteria of posttraumatic stress disorder across the different versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM).

Continuance of Table1 on the following page.

Criterion/ Manual	DSM-III	DSM-III-TR	DSM-IV/ DSM-IV-TR	DSM-5
Persistent re- experiencing of the event (continued)			B5. Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the event	<ul> <li>B4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the event(s)</li> <li>B5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the event(s)</li> </ul>
Numbing <sup>A</sup> resp. Persistent avoidance of stimuli associated with the event <sup>B, C</sup>	At least one of the following: C1. Loss of interest C2. Detachment from others C3. Constricted affect	At least three of the following: C1. Efforts to avoid thoughts or feelings associated with the event C2. Efforts to avoid activities or situations that arouse recollections of the event C3. Inability to recall an important aspect of the event C4. Markedly diminished interest in significant activities C5. A feeling of detachment or estrangement from others C6. Restricted feeling of affect C7. Sense of a foreshortened future	At least three of the following: C1. Efforts to avoid thoughts, feelings, or conversations associated with the event C2. Efforts to avoid activities, places, or people that arouse recollections of the event C3. Inability to recall an important aspect of the event C4. Markedly diminished interest or participation in significant activities C5. A feeling of detachment or estrangement from others C6. restricted range of affect C7. sense of a foreshortened future	At least one of the following: C1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the event(s) C2. Avoidance of or efforts to avoid external reminders that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s)

*Table 1.* Overview of the diagnostic criteria of posttraumatic stress disorder across the different versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (continued).

Continuance of Table1 on the following page.

Table 1. Overview of the diagnostic criteria of posttraumatic stress disorder across the different versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM)
(continued).

Criterion/ Manual	DSM-III	DSM-III-TR	DSM-IV/ DSM-IV-TR	DSM-5
Persistent arousal	At least two of the following:	At least two of the following:	At least two of the following:	At least two of the following:
and avoidance A	D1. Exaggerated startle response	D1. Difficulty falling or staying	D1. Difficulty falling or staying	D1. Inability to remember an
resp.	D2. Sleep disturbances	asleep	asleep	important aspect of the event(s)
Persistent in-	D3. Survival guilt	D2. Irritability or outbursts of anger	D2. Irritability or outbursts of anger	D2. Persistent and exaggerated
creased arousal <sup>B</sup> resp.	D4. Memory impairment or trouble concentrating	D3. Difficulty in concentrating D4. Hypervigilance	D3. Difficulty in concentrating D4. Hypervigilance	negative beliefs or expectations about oneself, others, the world
Negative	D5. Avoidance of activities that	D5. Exaggerated startle response	D5. Exaggerated startle response	D3. Persistent, distorted cognitions
alterations in	remind of the event	D6. Physiological reactivity upon		about the cause or consequences of
cognition and mood <sup>C</sup>	D6. Intensification of symptoms by reminders	exposure to events that symbolize or resemble an aspect of the traumatic		the traumatic event(s) that lead the individual to blame himself/herself
		event		or others
				D4. Persistent neg. emotional state
				D5. Markedly diminished interest or
				participation in activities
				D6. Feelings of detachment or
				estrangement from others
				D7. Persistent inability to experience positive emotions
Marked				At least two of the following:
alterations in				E1. Irritable behavior, angry out-
arousal and				bursts typically expressed as verbal/
reactivity <sup>C</sup>				physical aggression
				E2. Reckless or self-destructive
				behavior
				E3. Hypervigilance
				E4. Exaggerated startle response
				E5. Problems with concentration
				E6. Sleep disturbance

Continuance of Table1 on the following page.

Criterion/ Manual	DSM-III	DSM-III-TR	DSM-IV/ DSM-IV-TR	DSM-5
Time / Duration		Duration of at least one month	Duration is more than one month	Duration is more than one month
General impairment			Clinically significant distress or impairment in social, occupational, or other important areas of functioning	Clinically significant distress or impairment in social, occupational, or other important areas of functioning
Medical condition				Not attributable to the physiological effects of a substance or another medical condition
Further specifications		'Delayed onset' if the onset of symptoms was at least six months after the trauma	'Delayed onset' if the onset of symptoms is at least six months after the stressor	'Delayed expression' if the diagnostic criteria are not met until at least 6 months after the event
			<ul><li>'Acute' if the duration of symptoms is less than three months</li><li>'Chronic' if the duration of symptoms is three months or more</li></ul>	<ul> <li>'With dissociative symptoms, Depersonalization': Experiences of feeling detached from oneself, and as if one were an outside observer of one's processes or body</li> <li>'With dissociative symptoms, Derealization': experiences of the unreality of surroundings</li> </ul>

*Table 1.* Overview of the diagnostic criteria of posttraumatic stress disorder across the different versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (continued).

*Note.* <sup>A</sup>, Criterion in the DSM-III; <sup>B</sup>, Criterion in the DSM-III-TR and DSM-IV/DSM-IV-TR; <sup>C</sup>, Criterion in the DSM-5.

### 1.1.3. PTSD in the International Statistical Classification of Diseases and Related Health Problems

The ICD is published by the World Health Organization (WHO) and is of the highest worldwide relevance with respect to the diagnosis of mental and non-mental health conditions in (mental) health clinics and other (mental) health institutions. The ICD aims at providing an internationally accepted, clinically useful, and user-friendly diagnostic catalogue of physical and mental health conditions to be used in the context of diagnosis and treatment of (mental) health disorders. Moreover, the manual constitutes the common ground for health insurance billing and health insurance services in Germany and beyond. The first version of the ICD was published in 1900, but only with its sixth version in 1948 were non-lethal and mental health conditions included (Hirsch et al., 2016). The ICD-9 included a category V.308 'Acute reactions to stress', which conceptualized stress reactions as transient disturbances in healthy individuals in response to extraordinary physical or mental stress (Cooper, 1988; Slee, 1978). The ICD-10 (World Health Organization, 1992) introduced the diagnosis 'Posttraumatic stress disorder' (F43.1) in section F.43 'Reactions to severe stress and adjustment disorders'. The 11<sup>th</sup> revision was renamed as the ICD-11 for Mortality and Morbidity Statistics, ICD-11 MMS (World Health Organization, 2018), and groups PTSD (6B40) in the section 'Disorders specifically associated with stress'. Moreover, it introduces the diagnosis of complex PTSD (cPTSD, 6B41). Factor structure and latent profile analyses support a distinction between PTSD and cPTSD, insofar as patients with cPTSD report overall elevated PTSD symptoms, overall greater dysfunction and impairment, and accompanying symptoms of disturbed selforganization and self-regulation, in contrast to patients who fall into the diagnostic category of PTSD (Achterhof, Huntjens, Meewisse, & Kiers, 2019; Ben-Ezra et al., 2018; Böttche et al., 2018; Brewin et al., 2017; Cloitre et al., 2013; Cloitre et al., 2009; Currier, Foster, Karatzias, & Murphy, 2021; Folke, Nielsen, Andersen, Karatzias, & Karstoft, 2019; Frost et al., 2019; Hyland, Murphy, et al., 2017; Karatzias et al., 2016; Knefel & Lueger-Schuster, 2013; Maercker, Brewin, Bryant, Cloitre, van Ommeren, et al., 2013; Mordeno, Nalipay, & Mordeno, 2019; Tian et al., 2020). Table 2 presents an overview of the diagnostic criteria of PTSD referring to the ICD-10 and the ICD-11.

#### 1.1.4. Diagnostic agreement between the different versions of the DSM and the ICD.

The empirical literature reveals heterogeneous findings concerning the correspondence of PTSD prevalence rates between the different versions of the DSM and the ICD, and discussions about the appropriateness of the different criteria and their changes over time are ongoing. For instance, extensions to the trauma criterion are associated with significantly increased PTSD rates from the DSM-III(-TR) to the DSM-IV (Breslau & Kessler, 2001; Weathers & Keane, 2007), and most studies report an overall only limited concordance between the DSM-III(-TR) and the DSM-IV (Solomon & Horesh, 2007), between the DSM-IV and the DSM-5 (Hoge, Riviere, Wilk, Herrel, & Weathers, 2014; Kilpatrick et al., 2013), between the DSM-5 and the proposed ICD-11 (O'Donnell et al., 2014), between the ICD-10 and the DSM-IV (Andrews, Slade, & Peters, 1999; Rosner & Powell, 2009), and between the ICD-10 and the proposed ICD-11 (Knefel & Lueger-Schuster, 2013). Indeed, studies reporting satisfactory agreement rates between the different manuals are scarce (Crespo López & Gómez Gutiérrez, 2016; Morina, van Emmerik, Andrews, & Brewin, 2014).

*Table 2.* Overview of the diagnostic criteria of posttraumatic stress disorder across the different versions of the International Statistical Classification of Diseases and Related Health Problems (ICD).

Criterion/ Manual	ICD-10	ICD-11 <sup>A</sup>		
		Posttraumatic Stress Disorder	Complex Posttraumatic Stress Disorder	
Trauma Criterion	Exposure to a stressful event or situation (either brief or long-lasting) of exceptionally threatening or catastrophic nature, which would be likely to cause pervasive distress in almost anyone.	Exposure to an extremely threatening or horrific event or series of events.	Exposure to an event or series of events of ar extremely threatening or horrific nature, mos commonly prolonged or repetitive events from which escape is difficult or impossible.	
Persistent re- experiencing of the event	<ul> <li>At least one of the following:</li> <li>B1. Intrusive 'flashbacks'</li> <li>B2. Vivid memories</li> <li>B3. Recurring dreams</li> <li>B4. Experiencing distress when exposed to circumstances resembling or associated with the stressor</li> </ul>	B. Re-experiencing the traumatic event or events in the present in the form of vivid intrusive memories, flashbacks, or nightmares. Re- experiencing may occur via one or multiple sensory modalities and is typically accompanied by strong or overwhelming emotions, particularly fear or horror, and strong physical sensations.	B. Re-experiencing the traumatic event or events in the present in the form of vivid intrusive memories, flashbacks, or nightmares. Re experiencing may occur via one or multiple sensory modalities and is typically accompanied by strong or overwhelming emotions, particularly fear or horror, and strong physical sensations.	
Persistent avoidance of stimuli associated with the event	C. Exhibit an actual or preferred avoidance of circumstances resembling or associated with the stressor, which was not present before exposure	C. Avoidance of thoughts and memories of the event(s), or avoidance of activities, situations, or people reminiscent of the event(s).	C. Avoidance of thoughts and memories of the event(s), or avoidance of activities, situations, or people reminiscent of the event(s).	
Persistent arousal and avoidance <sup>B</sup> resp. Sense of threat <sup>C</sup>	<ul> <li>At least one of the following:</li> <li>D1. Inability to recall, either partially or completely, some important aspects of the period of exposure to the stressor.</li> <li>D2. Persistent increased psychological sensitivity and arousal (not present before exposure), shown by at least two of the following: <ul> <li>Difficulty in falling or staying asleep</li> <li>Irritability or outbursts of anger</li> <li>Difficulty in concentrating</li> <li>Exaggerated startle response</li> </ul> </li> </ul>	D. Persistent perceptions of heightened current threat, for example as indicated by hypervigilance or an enhanced startle reaction to stimuli such as unexpected noises.	D. Persistent perceptions of heightened current threat, for example as indicated by hypervigilance or an enhanced startle reaction to stimuli such as unexpected noises.	

Continuance of Table 2 on the following page.

*Table 2.* Overview of the diagnostic criteria of posttraumatic stress disorder across the different versions of the International Statistical Classification of Diseases and Related Health Problems (ICD) (continued).

Criterion/ Manual	ICD-10	ICD	-11 <sup>A</sup>	
		Posttraumatic Stress Disorder	Complex Posttraumatic Stress Disorder	
Affective			Severe and persistent problems in affect	
Dysregulation			regulation.	
Negative Self-			Severe and persistent beliefs about oneself as	
concept			diminished, defeated, or worthless, accompanied	
			by feelings of shame, guilt, or failure related to the traumatic event.	
Disturbances in			Severe and persistent difficulties in sustaining	
relationships			relationships and in feeling close to others, such as feeling distant or cut-off from others.	
Time / Duration		The symptoms persist for at least several weeks	The symptoms persist for at least several weeks	
General impairment		The symptoms cause significant impairment in personal, family, social, educational, occupational, or other important areas of functioning	The symptoms cause significant impairment in personal, family, social, educational, occupational, or other important areas of functioning	
Further specifications	The symptoms must be met within 6 months of the stressful event or at the end of a period of stress. Onset delayed more than 6 months can be included, but this should be specified	'Delayed onset' if the onset of symptoms was at least six months after the trauma	'Delayed onset' if the onset of symptoms was at least six months after the trauma	

*Note*. <sup>A</sup>, Diagnosis of posttraumatic stress disorder and complex posttraumatic stress disorder is mutually exclusive; <sup>B</sup>, Criterion in the ICD-10; <sup>C</sup>, Criterion in the ICD-11.

#### 1.1.5. Prevalence rates of PTSD

According to large-scale international investigations, up to 80% of the population is confronted with at least one traumatic event during the lifetime, up to 67% experience two or more traumatic events, and up to 30% report four or more events (Benjet et al., 2016; Hyland et al., 2021). The most common traumatic events are witnessing death or serious injury, being confronted with the unexpected death, illness, or accident of a loved one, being physically or sexually assaulted, being involved in a serious accident, and experiencing a life-threatening illness or injury (Benjet et al., 2016; Hyland et al., 2021). Estimations of 12-month PTSD prevalence rates range between 4% and 17% for single and non-man-made traumata, increasing to 35% for survivors of natural disasters, and up to 56% for refugees and survivors of childhood abuse, domestic violence, and war/ genocide/ mass violence (Berger et al., 2012; Cusack et al., 2019; Hyland et al., 2021; Kessler et al., 2017; Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012; Neria, Nandi, & Galea, 2008; Oakley, Kuo, Kowalkowski, & Park, 2021; Petrie et al., 2018; Santiago et al., 2013; Spottswood, Davydow, & Huang, 2017).

#### 1.1.6. Epidemiological findings in brief

Fortunately, not every trauma survivor develops (persisting) PTSS or PTSD. It is acknowledged that diverse interpersonal, sociodemographic, cultural, geographic, and traumarelated variables interact in a complex chorus on the path from traumatization to PTSD. Factors that have been found to increase the risk of developing PTSD in the aftermath of a traumatic event include female gender (Bowler et al., 2017; Cusack et al., 2019; Di Crosta et al., 2020; Frans, Rimmö, Åberg, & Fredrikson, 2005; Garza & Jovanovic, 2017; Guina, Nahhas, Kawalec, & Farnsworth, 2019; Kessler et al., 2005; Pietrzak, Goldstein, Southwick, & Grant, 2011; Silove et al., 2017; Tang, Deng, Glik, Dong, & Zhang, 2017), a younger age when experiencing the traumatic event (Bowler et al., 2017; Kessler et al., 2017; Kessler et al., 2017; Pietrzak et al., 2011), a lower educational and socioeconomic status (Abedzadeh-Kalahroudi, Razi, & Sehat, 2018; Bowler et al., 2017; Carmassi et al., 2018; Di Crosta et al., 2020), living in territories with unstable political and economic conditions (de Jong, Komproe, Van Ommeren et al., 2001; Keane, Marshall, & Taft, 2006), and exposure to (iterative) human-made or interpersonal traumatic events (Croft et al., 2019; Cusack et al., 2019; Guina et al., 2019; Kessler et al., 2017; Pietrzak et al., 2011).

#### 1.1.7. Comorbidities

Comorbid mental health disorders are commonly reported among trauma survivors and PTSD patients, and include generalized anxiety disorder, agoraphobia with and without panic disorder and major depressive disorder (Campbell et al., 2007; Galatzer-Levy, Nickerson, Litz, & Marmar, 2013; Garabiles, Lao, Wang, & Hall, 2020; Kar & Bastia, 2006; Karatzias et al., 2020; Leskin & Sheikh, 2002; Li, Duan, & Chen, 2020; Nichter, Haller, Norman, & Pietrzak, 2020; Tao, Wang, Guo, & Guo, 2020), substance-related addiction disorders (Brady, McCauley, & Back, 2021; Galatzer-Levy et al., 2013; Najavits et al., 2020; Norman, Haller, Hamblen, Southwick, & Pietrzak, 2018; Turner & Lloyd, 1995), and suicidal ideation and suicidal attempts (Kratovic, Smith, & Vujanovic, 2021; Nichter, Haller, et al., 2020; Sareen, Houlahan, Cox, & Asmundson, 2005). Concomitant poor (autonomic) physical health outcomes are also frequently reported, such as digestive disorders, cancer, diabetes and arthritis (Norman et al., 2006), migraine and chronic headache (Peterlin et al., 2011; Peterlin, Tietjen, Meng, Lidicker, & Bigal, 2008), and (congestive) heart diseases, asthma, eczema and psoriasis (Qureshi, Pyne, Magruder, Schulz, & Kunik, 2009). Mental and physical health comorbidities contribute to the risk of chronicity of PTSD (Cougle, Resnick, & Kilpatrick, 2013; Gandubert et al., 2016; Müller et al., 2018; Roy-Byrne et al., 2004; Zlotnick et al., 2004) and to a reduced quality of life and increased mortality (Abedzadeh-Kalahroudi et al., 2018; Croft et al., 2019; Gustavsson et al., 2011; Kessler et al., 2017; Kozarić-Kovačić & Borovečki, 2005; Müller et al., 2018; Najavits et al., 2020; Smith, Schnurr, & Rosenheck, 2005).

### 1.2. A population at high risk: PTSD in military personnel

#### 1.2.1. Military-related stressors and traumatization

Over the time of their career, military staff are highly likely to engage in one or multiple foreign deployments that can last for many weeks or months. Throughout these deployments, they are separated from their families and live under unaccustomed circumstances. During deployment, soldiers are faced with an array of severe and potentially traumatizing events, such as being confronted with bombed-out villages, experiencing direct combat duties, being harmed during battlefield action, taking part in peacekeeping missions and operations in war zones under difficult and stressful conditions, and witnessing or hearing of the death or serious injury of a comrade (Campbell & Nobel, 2009; Day & Livingstone, 2001; Xue et al., 2015). Although military personnel receive intense training before deployment as well as postdeployment care, being deployed abroad constitutes a highly distressing challenge per se, demanding high physical and psychological resilience from military personnel. Given this ongoing and repeated exposure to severely stressful and life-threatening events, veterans bear an increased occupational risk of being traumatized, accompanied by a substantially increased lifetime risk for PTSD (Ahmadian, Neylan, Metzler, & Cohen, 2019; Bergman, Przeworski, & Feeny, 2017; Blais et al., 2021; Iversen et al., 2009; Loignon, Ouellet, & Belleville, 2020; Mobbs & Bonanno, 2018; Murdoch et al., 2017; Nichter, Norman, Haller, & Pietrzak, 2019; Norman et al., 2018; Sareen et al., 2007; Smith et al., 2008; Stanley, Rogers, Hanson, Gutierrez, & Joiner, 2019; Vasterling et al., 2010).

### 1.2.2. Prevalence of PTSD in military samples

The lifetime prevalence rates of PTSD in military samples range up to 68% (Bergman et al., 2017; Hines, Sundin, Rona, Wessely, & Fear, 2014; Hoge et al., 2004; Kessler, Sonega, Bromet, Hughes, & Nelson, 1995; Lew et al., 2009; Loignon et al., 2020; Mobbs & Bonanno,

2018; Murdoch et al., 2017; Ramchand, Rudavsky, Grant, Tanielian, & Jaycox, 2015; Richardson, Frueh, & Acierno, 2010; Stanley et al., 2019). Concurrently, the probability of meeting the diagnostic criteria for cPTSD is substantially increased in military trauma samples compared to trauma samples in the general population (Wolf et al., 2015), with studies showing that up to 80% of all service members within military cohorts meet the criteria for cPTSD (Howard et al., 2021; Letica-Crepulja et al., 2020). PTSD prevalence rates vary substantially between nations and between different military cohorts from the same nation. Accordingly, Richardson et al. (2010) reported lifetime PTSD prevalence rates between 6% and 31% in deployed US-American soldiers, whilst Canadian samples showed lifetime prevalence rates between 2.7% and 10.3%. It is assumed that sample- and trauma-related factors (e.g., frequency and duration of deployment, extent of pre-deployment training and post-deployment care, military structures, sociodemographic and intrapersonal characteristics), symptomrelated factors at the time of assessment (e.g., PTSS severity, chronicity, onset, comorbidity), and methodological aspects of the respective studies (e.g., sampling strategy, sample size, comparison group, measurements) influence the reported prevalence rates of combat-related PTSD across the literature (Brewin, Andrews, & Valentine, 2000; Hines et al., 2014; McFarlane, 2000; Polusny et al., 2011; Ramchand et al., 2015; Richardson et al., 2010; Rona et al., 2012; Xue et al., 2015). Wittchen et al. (2012) reported a 12-month PTSD prevalence rate of 2.9% in deployed veterans of the German Armed Forces (GAF) and found a two- to fourfold increased risk of PTSD in soldiers who had been deployed abroad relative to soldiers who had never been deployed abroad. The authors thus assumed a high number of unreported PTSD cases in GAF personnel, guessing that about 50% of German veterans with PTSD are not properly diagnosed (Wittchen et al., 2012).

#### 1.2.3. PTSD and comorbidity in military personnel

Veterans with deployment-related PTSD often report co-occurring adverse mental or physical health outcomes, such as major depressive disorder, anxiety disorders, substance-related addictive disorders and substance misuse, suicidal ideation and suicide attempts, and impairments in cognitive, mental, and physical functioning (Ahmadian et al., 2019; Blais et al., 2021; Kessler et al., 1995; Murdoch et al., 2017; Nichter et al., 2019; Norman et al., 2018; Schwartz & Shrira, 2019; Stander, Thomsen, & Highfill-McRoy, 2014; Stanley et al., 2019). Results from the National Health and Resilience in Veterans Study showed strong associations between PTSS/ PTSD and a range of somatic complaints such as respiratory and sleep disorders, osteoporosis and osteopenia, migraine, diabetes, cancer, and generalized mental and physical distress (El-Gabalawy, Blaney, Tsai, Sumner, & Pietrzak, 2018). Notably, a diagnosis of PTSD does not seem to be a prerequisite for the occurrence of multiple functional impairments; rather, subthreshold PTSS seem to be sufficient for multi-morbidity in traumatized veterans (Bergman et al., 2017).

#### **1.3.** Treatment of PTSD and the relevance of internet-based interventions

#### 1.3.1. Cognitive behavioral therapy for PTSD

Cognitive behavioral therapy (CBT) is a well-established and evidence-based treatment approach for PTSD (Blanchard et al., 2003; Bryant, Harvey, Dang, Sackville, & Basten, 1998; Devilly & Spence, 1999), with trauma-focused CBT (TF-CBT) in particular being recommended by international evidence-based guidelines (Forbes et al., 2007; National Collaborating Centre for Mental Health, 2005; Schäfer et al., 2019). TF-CBT combines cognitive behavioral techniques such as psychoeducation, exposure in sensu/ vivo, and cognitive reappraisal (Kar, 2011). Habituation to the stressful event and increasing the patient's abilities of cognitive reframing, emotion regulation, and cognitive control, including mental and cognitive processing of the traumatic event, are assumed to be contributing mechanisms of change (Gallagher, 2017; Harvey, Bryant, & Tarrier, 2003; Pfeiffer, Sachser, de Haan, Tutus, & Goldbeck, 2017; Schoutrop, Lange, Hanewald, Duurland, & Bermond, 1997; Yang et al., 2018). Bilateral stimulation such as Eye Movement Desensitization and Reprocessing (EMDR) and tapping have been shown to significantly improve PTSD symptoms and to increase (CBT) treatment efficacy when used as an adjunct (Boudewyns & Hyer, 1996; Church, Stapleton, Yang, & Gallo, 2018; Karatzias, Brown, et al., 2019; Perlini et al., 2020; Seidler & Wagner, 2006; Shapiro, 1996; Waterman & Cooper, 2020).

#### 1.3.2. Psychotherapeutic treatment options for veterans with PTSD

A body of literature has revealed evidence that veterans with PTSD benefit more from TF-CBT compared to treatments that are based on other approaches (Bradley, Greene, Russ, Dutra, & Westen, 2005; Goodson et al., 2011; Haagen, Smid, Knipscheer, & Kleber, 2015; Kitchiner, Lewis, Roberts, & Bisson, 2019; Steenkamp, Litz, Hoge, & Marmar, 2015). As a limiting factor, however, military personnel have often been found to benefit less from psychotherapy relative to PTSD patients with a history of civilian traumatization (Haagen et al., 2015; Kitchiner et al., 2019; Kitchiner, Roberts, Wilcox, & Bisson, 2012; Steenkamp et al., 2015; Straud, Siev, Messer, & Zalta, 2019).

#### 1.3.3. Uptake of psychotherapy and barriers to uptake in patients with PTSD

The provision of adequate psychotherapeutic treatment at an early stage of symptom presentation predicts treatment efficacy and diminishes the risk of chronicity of PTSD and secondary adverse health effects and comorbidities (Bisson, Shepherd, Joy, Robert, & Newcombe, 2004). If untreated or not appropriately treated, PTSD tends to become chronic (Davidson, Stein, Shalev, & Yehuda, 2014). Treatment provision is hindered by fact that the onset of PTSD can be delayed by years or decades. Moreover, trauma exposure is often not reported by trauma survivors, and heterogeneous symptom presentations along with comorbidities increase the risk of misdiagnosis, inappropriate treatment provision, or late intervention onset (Brewin, Andrews, Hejdenberg, & Stewart, 2012; Matto, McNiel, & Binder, 2019). On average, less than 50% of traumatized individuals with PTSD are in touch with the health care system (Kartha et al., 2008; Kessler et al., 1999; Polusny et al., 2008; Slewa-Younan et al., 2017; Stein, McQuaid, Pedrelli, Lenox, & McCahill, 2000) and only 20% to 33% of sufferers seek psychological treatment (Calhoun, Bosworth, Grambow, Dudley, & Beckham, 2002; Hoge et al., 2004; Kim et al., 2018; Rayburn et al., 2005; Roberts, Gilman, Breslau, Breslau, & Koenen, 2011; Slewa-Younan et al., 2017; Spoont, Murdoch, Hodges, & Nugent, 2010). Although effective treatment options for PTSD are available, these are not widely applied in clinical practice (Bisson et al., 2013; Chen, Olin, Stirman, & Kaysen, 2017; Keller, Stevens, Lui, Murray, & Yaggie, 2014; Kirkpatrick & Heller, 2014; Sayer et al., 2017), resulting in a limited infrastructure of low-threshold, easily accessible face-to-face psychotherapy for PTSD along with long waiting lists (Schulz, Barghaan, Harfst, & Koch, 2008; Trusz, Wagner, Russo, Love, & Zatzick, 2011). At the same time, trauma survivors often experience difficulties in establishing and maintaining interpersonal relationships and struggle with self-disclosure, which impedes the therapeutic bond, therapeutic process, treatment outcome, and treatment adherence (Besser & Neria, 2012; Campbell & Renshaw, 2013; Charuvastra & Cloitre, 2008). In contrast to non-trauma-focused psychotherapy, dropout is considerably higher (Lewis, Roberts, Andrew, Starling, & Bisson, 2020). PTSD patients often report fears of stigmatization, embarrassment, judgment, or exclusion and associated feelings of shame (Hoge, Auchterlonie, & Milliken, 2006; Hoge et al., 2004; Hoge et al., 2014; Kantor, Knefel, & Lueger-Schuster, 2017; Kim et al., 2018), negative beliefs about mental health care services, and negative past experiences with the health care system (Blais, Tsai, Southwick, & Pietrzak, 2015; Kantor et al., 2017; Possemato, Wray, Johnson, Webster, & Beehler, 2018). Moreover, they report a lack of trust in mental health care providers and negative beliefs about PTSD and its curability (Kantor et al., 2017; Possemato et al., 2018), as well as barriers regarding location and time of treatment appointments (Kim et al., 2018; Possemato et al., 2018).

# *1.3.4. Treatment-seeking behavior and barriers to psychotherapy uptake in military personnel*

Only a minority of military personnel seek psychological support during the first year after returning from deployment (Wittchen et al., 2012), and few veterans with PTSS/ PTSD contact the mental health care system to receive psychotherapy (Finnegan, Jackson, & Simpson, 2018; Karlin et al., 2010; Mott, Hundt, Sansgiry, Mignogna, & Cully, 2014; Possemato et al., 2018; Simpson & Leach, 2015; Wittchen et al., 2012). Veterans seem to be more likely to seek help from general practitioners and other non-mental health services (Calhoun et al., 2002; Elhai, Reeves, & Frueh, 2004; Hoge et al., 2006; Spoont, Hodges, Murdoch, & Nugent, 2009; Wittchen et al., 2012) and to take psychotropic medication rather than undergo psychotherapy (Fortney et al., 2017). Furthermore, they are more likely to seek treatment for somatic and sleep problems than for stress, anxiety, or mood-related complaints (Gutner, Pedersen, & Drummond, 2018). Of all veterans who seek psychotherapy, only 2% to 10% adhere to the intervention as proposed by the practitioner and the manual (Mott et al., 2014; Seal et al., 2010; Smith, Sippel, Rozek, Hoff, & Harpaz-Rotem, 2019). In parallel, up to more than half of treatment-seeking veterans tend to terminate treatment prematurely (Byllesby, Dickstein, & Chard, 2019; Crocker et al., 2018; Edwards-Stewart et al., 2021; Eftekhari, Crowley, Mackintosh, & Rosen, 2020; Fischer, Bhatia, Baddeley, Al-Jabari, & Libet, 2018; Gilmore et al., 2020; Hundt et al., 2020; Norona, Borsari, Armstrong, & Shonkwiler, 2020; Sciarrino, Bartlett, Smith, Martin, & Williams, 2021). Most of the aforementioned barriers, such as negative beliefs about psychotherapy and its efficacy, a lack of trust in psychotherapy or the psychotherapist, negative beliefs about PTSD and its curability, fear of stigmatization, shame, and time constraints (Blais & Renshaw, 2013; Dingfelder, 2009; Elhai et al., 2004; Graziano & Elbogen, 2017; Hoge et al., 2004; Hoge et al., 2014; Pietrzak, Johnson, Goldstein, Malley, & Southwick, 2009;

Possemato et al., 2018; Spoont et al., 2009; Spoont et al., 2010; Vogt, 2011), also apply to military personnel. In addition, and more specifically to this population, veterans report the experience of moral injury during deployment, which seems to be negatively associated with treatment-seeking behavior in military members (Paige, Renshaw, Allen, & Litz, 2019), as well as a lower perception of the need for care and social support (Graziano & Elbogen, 2017). Veterans describe meaningful concerns regarding the confidentiality of treatment, leading to worries about social and occupational exclusion, judgment, and disadvantages for their career in the case of therapy uptake (Brown et al., 2011; Hoge et al., 2004; Hoge et al., 2014; Pietrzak et al., 2009; Possemato et al., 2018; Sudom et al., 2012).

# 1.3.5. Internet-based interventions for PTSD

Internet-based interventions (IBI) are psychological treatments that are usually based on well-established and evidenced treatment face-to-face approaches such as CBT (internet-based CBT, iCBT) and are delivered via the internet. Participants are provided with disorder-specific treatment modules on a weekly to twice-weekly basis, often including complementary components such as activity planning, applied relaxation training, social skills training, stress management, behavioral activation, or guided imagery (Carpenter, Stoner, Schmitz, McGregor, & Doorenbos, 2014; Ebert & Erbe, 2012; Eichenberg & Ott, 2012; Lau, Smit, Fleming, & Riper, 2017; Litz, Engel, Bryant, & Papa, 2007; Putois et al., 2019; Steinmetz, Benight, Bishop, & James, 2012; Wang, Wang, & Maercker, 2013). IBI can be supported by remote contact with a therapist via chat, e-mail, or video-conferencing systems, and is then termed therapist-guided IBI/ iCBT (Berger, 2017). Mostly, the support takes the form of asynchronous written feedback from the therapist. Alternatively, IBI can be conceived as a self-help program with automated feedback, only offering on-demand contact with the therapist in the case of symptom deterioration or when technical support is needed, and is then termed unguided IBI/ iCBT (Olthuis, Watt, Bailey, Hayden, & Stewart, 2016; Probst, Berger, & Flückiger, 2019). IBI are

associated with several advantages: They are easily accessible, low-threshold, independent from time and location, provide visual anonymity and discreteness, are contemporary, and are useful for a structured and repeatable presentation of psychoeducation and homework material. Moreover, they can be tailored to minority groups and different age cohorts (Apolinário-Hagen, Vehreschild, & Alkoudmani, 2017; Berger & Andersson, 2009; Berger et al., 2012; Ebert & Erbe, 2012; Eichenberg & Ott, 2012; Erbe, Eichert, Riper, & Ebert, 2017; Olthuis, Watt, et al., 2016; Schuster, Pokorny, Berger, Topooco, & Laireiter, 2018). In addition, IBI can reduce patients' fears of stigmatization, judgment, or exclusion, which in turn decrease internal barriers and foster the willingness to seek treatment (Berger et al, 2012; Ebert & Erbe, 2012; Eichenberg & Ott, 2012; Olthuis, Watt, et al., 2016). Furthermore, IBI can contribute to reducing healthcare costs and supporting the health care system to provide psychotherapy access (Krupnick et al., 2017; Lewis, Roberts, Bethell, Robertson, & Bisson, 2018). Despite all of these advantages, however, practitioners and treatment-seeking individuals express ambivalent attitudes and concerns about IBI, such as the lack of nonverbal signals, limitations about handling crises, and an assumed restricted therapeutic bond (Apolinário-Hagen et al., 2018; Apolinário-Hagen et al., 2017; Schuster et al., 2018). The program Interapy (Lange et al., 2003; Lange et al., 2000; Lange, van de Ven, Schrieken, & Emmelkamp, 2001) is a pioneering TF-iCBT intervention for PTSD that is well evaluated and widely accepted (e.g. Ruwaard, Lange, Schrieken, & Emmelkamp, 2011). Patients complete three modules with a total of 10 online writing assignments over five weeks. Each assignment is expected to take 45 minutes to be completed. A trauma psychotherapist asynchronously guides the client through the assignments by providing supportive and encouraging written email feedback during and after each module. First, the client writes about the trauma in the first person and present tense to confront him/herself with the event and associated thoughts and feelings (self-confrontation). Second, the client writes encouraging and supportive letters to a hypothetical friend who is experiencing the same or a comparable trauma to instill new views about it, regain a sense of control, and

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correct dysfunctional beliefs and feelings (cognitive restructuring). Third, in symbolic farewell letters to a significant other or him/herself, the client reflects on the therapeutic process and on how to deal with the trauma in the future (social sharing). Figure 1 depicts the treatment protocol of Interapy (Lange et al., 2003; Lange et al., 2000; Lange et al., 2001). An alternative approach is internet-based expressive writing (iEW), which is based on theories of emotional disclosure (e.g. Pennebaker, 1997). IEW is shorter in duration, not manual-based, the writing assignments are not structured, and therapeutic support is not commonly provided (Possemato, 2007).

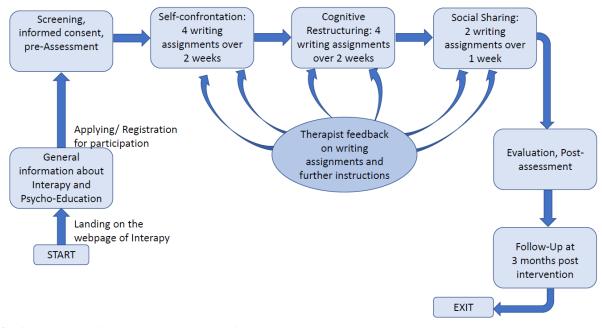


Fig. 1 Illustration of the treatment protocol of the intervention Interapy.

# 1.3.6. Efficacy of internet-based interventions for PTSD

*Interapy* has been found to produce large effect sizes (Knaevelsrud & Maercker, 2007; Lange et al., 2003), with significantly reduced PTSD symptomatology, reduced levels of comorbid depression and anxiety, and a stable treatment effect after an 18-month follow-up period (Knaevelsrud & Maercker, 2007). Over the last two decades, various IBI programs for PTSD have been developed and a large body of randomized controlled trials (RCT) have continuously evaluated their efficacy. Prior to the present thesis, available meta-analyses and

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systematic reviews established the efficacy of IBI, particularly iCBT, in different populations with PTSD and anxiety disorders (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Andrews et al. 2010; Barak, Hen, Boniel-Nissim, & Shapira, 2008; Sijbrandij, Kunovski, & Cuijpers, 2016; Spek et al., 2007). Moreover, participants' ratings of the therapeutic alliance indicated that IBI/ iCBT are acceptable and compatible with the formation of a solid therapeutic working alliance (Baumeister, Reichler, Munzinger, & Lin, 2014; Cook & Doyle, 2002; Klein et al., 2009; Knaevelsrud & Maercker, 2007; Melville, Casey, & Kavanagh, 2010; Preschl, Maercker, & Wagner, 2011; Wagner, Brand, Schulz, & Knaevelsrud, 2012).

# 1.3.7. Military personnel with PTSD and internet-based interventions

Veterans generally seem to show an open-minded attitude to mental health technology and internet systems (e-mental health), supporting the view that military personnel may be receptive to alternative web-based treatment opportunities (Erbes et al., 2014; Whealin, Seibert-Hatalsky, Willett Howell, & Tsai, 2015). Before the present thesis, research on IBI/ iCBT in military populations was limited, and the available studies examined US-American samples of military personnel only. Table 3 provides a brief overview of the available programs at that time. For more details on the treatments and effect sizes, please refer to the original studies. Table 3. Brief overview of available programs and evaluation studies on internet-based intervention programs for

Author/ Program	Intervention and its components	Main study findings
Belsher et al. (2015) afterdeployment.org	8 sessions of self-help website Psychoeducation, training to identify triggers, relaxation and breathing techniques, problem- solving skills, cognitive reframing Accompanied by between-sessions homework assignments	<ul> <li>50% of subjects adhered to ≥ 4 sessions</li> <li>40% of subjects showed significantly reduced PTSS</li> </ul>
Engel et al. (2015) <i>DESTRESS-PC</i>	6-8-week study nurse assisted iCBT Psychoeducation, anger management, sleep hygiene, stress management, relaxation techniques, breathing techniques, cognitive reframing, positive self-talk Accompanied by telephone calls of the study nurse, regularly written feedback, and homework assignments	<ul> <li>Significant PTSD improvement in the intervention arm relative to the control arm</li> <li>Treatment effect was not sustained over time</li> </ul>
Hobfoll, Blais, Stevens, Walt, and Gengler (2016) <i>Vets Prevail</i>	7-session iCBT Psychoeducation, skill training, adaptive coping behavior, problem-solving, avatar- based storytelling, serious gaming in-time chat rooms to get in contact with other users	<ul> <li>Significant reduction on PTSD in contrast to the control arm</li> <li>75% completed ≥ 5 sessions</li> <li>Around 25% dropped out</li> </ul>
Kuhn et al. (2014) <i>PTSD coach</i>	Mobile application self-management tool Psychoeducation, CBT-based coping tools, breathing techniques, relaxation, tracking of symptoms, identification of triggers, and management of triggers	<ul> <li>Participants rated the app as being helpful to handle PTSD</li> <li>Participants rated the app as being acceptable and satisfying to use</li> </ul>
Litz et al. (2007) <i>DESTRESS</i>	8-week self-management iCBT Psychoeducation, trauma trigger self- monitoring, skill-training, negative affect management, sleep hygiene, graduated exposure, cognitive restructuring, relapse prevention Accompanied by one face-to-face-session, regularly written feedback, telephone calls of study therapists, and homework assignments	<ul> <li>Dropout rate 30%</li> <li>Small effect size at post- treatment assessment favored the intervention relative to an active control condition</li> <li>Treatment effect vanished at 3- month follow up and recurred as a large effect at the 6-month- follow up</li> </ul>

posttraumatic stress disorder in military populations.

# **1.4.** Visual attention and autonomic responses in PTSD

# 1.4.1. A brief introduction to the essentials of visual attention processes

According to cognitive models, visual information processing is characterized by different stages of processing (Adaval, Saluja, & Jiang, 2019; Hopfinger & West, 2006; Norman, 2002). It is assumed that stimuli are registered and evaluated in the early stages of information processing (LeDoux, 1995; LeDoux, 2003; Öhman, 1993). It is further assumed that these orienting processes to stimuli are generated in a bottom-up fashion, with preconsciously controlled and automated eye gazes in response to exogenous stimulus presentation (Corbetta & Shulman, 2002; LeDoux, 2000; Vuilleumier, 2005). At this stage of processing, *vigilance* is believed to play a central role as an important mental and behavioral capacity to enable the individual to attend and react to unexpected and sudden changes in the surrounding environment (Mackworth, 1956; Oken, Salinsky, & Elsas, 2006; Posner, 2008). Later stages of information processing are purported to rely on more strategically and deliberately controlled attentional processes (LeDoux, 1995; LeDoux, 2003; Öhman, 1993). Endogenous, top-down regulated eye gazes are thought to rely on rather goal-directed processes in terms of voluntarily and willingly engaging, maintaining, disengaging, and shifting attention from one location to another (Fox, Russo, Bowles, & Dutton, 2001). In these later stages of processing, attentional *control*, that is the ability to direct attention willingly and flexibly and to focus one's attention despite distractors, is thought to act as a key component of the voluntary coordination of eye gazes (Derryberry & Reed, 2002; Engle, 2018). Once it enters the cortical visual system, the information is further processed by subsequent neurological circuits that run diverse processes such as contextualization of the stimulus (Chica & Lupiáñez, 2009; Gilbert & Li, 2013; Sincich & Horton, 2005; Zhang, Kolodkin, Wong, & James, 2017; Ziesche & Hamker, 2014).

# 1.4.2. A brief introduction to the technique of eye-tracking

The technology of eye-tracking is an advantageous technique to experimentally measure eye gazes and is utilized in diverse domains, such as traffic behavior research, market and consumer research, user experience and interface research, professional sports training, educational science, clinical/ medical research, psychology and neuroscience, development research, and virtual reality technologies (Duchowski, 2002, 2007; Holmqvist et al., 2011; Poole & Ball, 2006; Wedel & Pieters, 2017). Infrared light that is safe and invisible for human vision is projected from the eye-tracking system to the eyes and is reflected differently by the retina depending on the position of the pupil (see Figure 2a/2b).

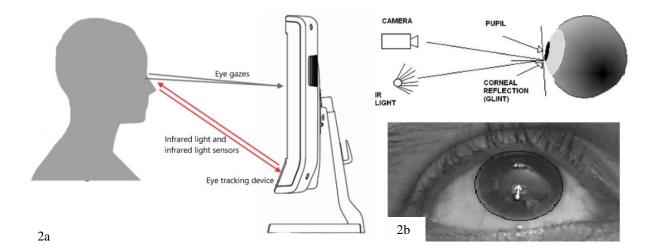


Fig. 2. Schematic illustration of the recording mechanism of an eye-tracking-based apparatus<sup>2</sup>.

This reflection constitutes a signal that is recorded by the eye-tracking system, consisting of a direction vector and a distance factor. Based on these data, the eye-tracking software can output a plurality of gaze variables (Duchowski, 2002, 2007; Holmqvist et al., 2011; Poole & Ball, 2006; Wedel & Pieters, 2017). Eye-tracking paradigms provide a convenient experimental approach to obtain temporal and spatial continuous recordings of participants' gazes and glances on certain areas of interest (AOI). Eye-tracking thus provides a proximal measurement

<sup>&</sup>lt;sup>2</sup> Figure 2a adapted from https://www.hs-esslingen.de/en/computer-science-and-engineering/research/projects/internal-projects/#&gid=1&pid=2 Figure 2b adapted from https://www.semanticscholar.org/paper/iris-Center-Corneal-Reflection-Method-for-Gaze-Sigut-Sidba/854cee85e677866be084881842713c104c2f2cf3/figure/0

of attentional processes, and eye-tracking data can be distinguished from reaction time and other conscious behavioral responses of the participant, making this technique less susceptible to associated confounding variables (Armstrong & Olatunji, 2012). The technique allows a variable to be operationalized by different outcome variables, such as latency, dwell time, number of revisits, first fixation duration, and fixation sequences. Visual indicators such as heat maps and scan paths can be useful for visualization.

# 1.4.3. Theories and fundamental empirical findings on attentional bias in PTSD

Attentional bias is described as an involuntarily facilitated and increased attentional response that is directed to (or away from) trauma reminders or alternate sources of potential hazard and stress in trauma survivors with PTSD or PTSS (Bomyea, Johnson, & Lang, 2017). Meta-analytical evidence shows that individuals with anxiety and stress-related disorders show patterns of attentional bias to threat that are absent in healthy controls, and that conscious and subconscious processes of perception contribute to attentional bias in stress-related disorders (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007). It is assumed that (trauma) memory traces and fear structures involve various biases (e.g., emotional, intentional, cognitive, attentional) that interact with each other and lead to self-perpetuating vicious cycles of increased arousal, continuing avoidance, insufficient re-interpretation of cues, sustained alertness, and an increased perception of threat and stress (Amir, Foa, & Coles, 1998; Birrer & Michael, 2011; Bomyea et al., 2017; Dalgleish et al., 2003; Foa, Feske, Murdock, Kozak, & McCarthy, 1991; Herzog, D'Andrea, & DePierro, 2019; Lissek, 2012; Michael, Ehlers, Halligan, & Clark, 2005; Mogg, Bradley, De Bono, & Painter, 1997; Pineles et al., 2011; Powers et al., 2019; Steil & Ehlers, 2000; Williams, Watts, MacLeod, & Mathews, 1988). So far, three main hypotheses on attentional bias in PTSD have been discussed. The hypervigilance hypothesis assumes that relative to healthy subjects, PTSD patients' visual search processes at early stages of information processing are characterized by an excessively increased and facilitated detection of potentially threatening stimuli, leading to an excessive orientation towards trauma reminders (Corbetta & Shulman, 2002; Ehlers & Clark, 2000; Fani et al., 2012; LeDoux, 2000; Terpou et al., 2019; Vuilleumier, 2005). Such hypervigilant orienting has been found to play a crucial role in initiating, maintaining, and exacerbating arousal, anxiety, intrusive thoughts, re-experiencing, and concentration disturbances, giving rise to the assumption that a forward feedback loop of increased initial attention towards stimuli of a potential threat and *increased arousal* leads to a maintenance or increase of anxiety and stress symptoms (Ehlers & Clark, 2000; Kimble et al., 2014; Norman, Stein, & Davidson, 2007; Pineles et al., 2009; Terpou et al., 2019). The maintenance hypothesis assumes that an attentional bias emerges after threat detection, based on irregularities on higher (i.e., later) stages of information processing, i.e., on an endogenous, goal-directed level of attentionsustaining top-down processes (Fox et al., 2001). It is assumed that in contrast to healthy individuals, patients with PTSD present difficulties or disturbances to willingly disengage and shift attention from one stimulus to another, resulting in increased *persistence* of attention on the target stimulus (Esterman et al., 2019; Lazarov, Suarez-Jimenez, Tamman, et al., 2019). The literature has revealed evidence of PTSD-associated impairments of attentional control (Bardeen & Fergus, 2016; Bardeen, Fergus & Orcutt, 2015; Cox & Olatunji, 2017), and such deficits in attentional control are thought to induce, increase, and maintain ruminative and intrusive thoughts in PTSD. Accordingly, rumination in PTSD is conceptualized as a rather automated process (Birrer & Michael, 2011). Moreover, deficient attentional control has been shown to affect overall PTSD symptom severity, maintenance, and chronicity (Birrer & Michael, 2011; Ehring, Frank, & Ehlers, 2008; Michael, Ehlers, Halligan, & Clark, 2005) and is assumed to play a key role in PTSD-related maintenance biases (Aupperle, Melrose, Stein, & Paulus, 2012; Badura-Brack et al., 2015; El Khoury-Malhame, Reynaud, et al., 2011; Esterman et al., 2019; Olatunji, Armstrong, McHugo, & Zald, 2013; Schoorl, Putman, Van Der Werff, & Van Der Does, 2014). The hypothesis of attentional bias variability (ABV) takes temporal dynamics of attention into account, assuming that individuals with PTSD show a sequence of shifting attention towards and away from threat that is absent in healthy controls (Alon, Naim, Pine, Bliese, & Bar-Haim, 2019; Bardeen & Daniel, 2017; Buckner, Maner, & Schmidt, 2010; Clarke et al., 2020; Zvielli, Bernstein, & Koster, 2014). The hypothesis of ABV reflects within-subject fluctuations of engagement and disengagement of attention on trauma-related stimuli (Iacoviello et al., 2014; Swick & Ashley, 2017). It approaches attentional bias in PTSD in terms of hypervigilance towards threat at early stages of information processing, followed by repeated efforts of the individual to avoid threat- or trauma-related cues at later stages of processing. Such attention fluctuation in terms of repeated *engagement – disengagement – engagement* seems to be specific to PTSD, in contrast to specific phobias, social anxiety, and trait anxiety (Naim et al., 2015). Furthermore, ABV correlates with overall PTSD severity (Iacoviello et al., 2014; Naim et al., 2015; Swick & Ashley, 2017; Yuval, Zvielli, & Bernstein, 2016) and with emotion dysregulation (Bardeen, Daniel, Hinnant, & Orcutt, 2017).

# 1.4.4. A brief overview of eye-tracking-based operationalization of and findings on attentional bias in PTSD

The direction of orienting (location of initial fixation) and speed of orienting after stimulus onset (latency) have been established as operators of hypervigilant orienting in PTSD. An increased orienting, and reduced latencies, to trauma cue AOIs would support the assumption of an orienting (hypervigilance) bias in PTSD (Armstrong & Olatunji, 2012; Lazarov, Suarez-Jimenez, Tamman, et al., 2019). Attentional maintenance in PTSD has been previously operationalized using dwell time (the time spent gazing at a stimulus). An increased dwell time on trauma-related or threat cues would indicate a maintenance bias in PTSD (Armstrong & Olatunji, 2012; Lazarov, Suarez-Jimenez, Tamman, et al., 2019). So far, ABV has not been systematically operationalized in eye-tracking-based research. An earlier meta-analysis of the eye-tracking literature suggested that patterns of attentional bias can be observed

in patients with anxiety and stress-related disorders relative to healthy controls (Armstrong & Olatunji, 2012). As a limitation, Armstrong and Olatunji (2012) included only two primary investigations on PTSD. Recently, Lazarov, Suarez-Jimenez, Tamman, et al. (2019) reviewed the existing eye-tracking literature with an exclusive focus on PTSD. The authors concluded that there is no robust evidence of hypervigilant orienting to threat (hypervigilance bias) in PTSD. However, they found a solid body of eye-tracking-based evidence of increased dwell times on trauma and threat cues in patients with PTSD when compared to healthy controls, supporting the presumed maintenance bias in PTSD (Lazarov, Suarez-Jimenez, Tamman, et al., 2019).

# 1.4.5. Modifiability of attentional bias in PTSD

In the same vein as psychotherapeutic interventions that aim to modify the patient's cognitions, emotions, and behavioral responses by addressing beliefs, appraisals, and conditioned responses, specific attentional bias modification (ABM) programs have been established with the aim of reducing attentional bias. Meta-analyses and systematic reviews give reason to assume that attentional bias in PTSD can be modified by ABM programs, with pre-to-post treatment effect sizes on measures of attentional bias ranging from small to moderate (Bar-Haim, 2010; Beard, 2011; Emmelkamp, 2012; Hakamata et al., 2010; Hallion & Ruscio, 2011; MacLeod & Clarke, 2015; Mogg, Waters, & Bradley, 2017; Mogoaşe, David, & Koster, 2014).

# 1.4.6. Posttraumatic stress disorder and autonomic physiological responses

Keeping in mind that the experience of a potentially traumatizing event is a prerequisite for the diagnosis of PTSD, the conceptualization of the disorder as a *response* to traumatization is emphasized (American Psychiatric Association, 2013) . Accordingly, to gain a deeper understanding of PTSD, it is necessary to scrutinize physiological and psychological responses to trauma (Yehuda & LeDoux, 2007). Functional stress reactions diminish after some time, whereas individuals with PTSD show an enduring or sustained and altered stress response relative to (non-)traumatized healthy controls (Pineles et al., 2011; Simeon et al., 2007; Solomon & Mikulincer, 2006; Southwick et al., 2007). As such, the following can be observed in individuals with PTSD: An increased heart rate along with a reduced heart rate variability, an increased startle response, deficits in fear extinction and fear inhibition (Shvil, Rusch, Sullivan, & Neria, 2013), elevated perspiration, shortness of breath, increased pupil dilation (Cascardi, Armstrong, Chung, & Paré, 2015; Murray, Keifer Jr, Ressler, Norrholm, & Jovanovic, 2013; Shvil et al., 2013), and elevated blood pressure and skin conductance levels (Arditte Hall, Osterberg, Orr, & Pineless, 2018; Fonkoue et al., 2020). The extent of these autonomic imbalances emphasizes the complex and self-perpetuating circuit of stress reactions in the trauma survivor, with interwoven relationships between neural mechanisms, autonomic correlates, physiological reactions, and psychological symptoms of PTSD (Rodriguez-Paras & Sasangohar, 2017; Seligowski et al., 2019; Shvil et al., 2013). The present thesis refrains from providing a detailed introduction to these topics. Instead, essential studies<sup>3</sup> and associated publications that have been produced in the context of the larger research project<sup>4</sup> are highly recommended at this juncture.

# **1.5.** Framework of this dissertation and its research purpose

This dissertation is part of a larger research project that was conducted in a collaboration work between the Freie Universität Berlin, Department of Education and Psychology/ Division of Clinical Psychological Intervention, and the Military Hospital Berlin, Department for Military Mental Health. The larger research project aimed at evaluating the efficacy and

<sup>&</sup>lt;sup>3</sup> For detailed introductions to PTSD and its associations with the neuro-hormonal-stress system please see, e.g.:

Chrousos, G. P. (2009). Stress and disorders of the stress system. Nature Reviews Endocrinology, 5(7), 374-381. doi:10.1038/nrendo.2009.106

Daskalakis, N. P., Lehrner, A., & Yehuda, R. (2013). Endocrine Aspects of Post-traumatic Stress Disorder and Implications for Diagnosis and Treatment. Endocrinology and Metabolism Clinics of North America, 42(3), 503-513. doi:http://dx.doi.org/10.1016/j.ecl.2013.05.004.
 <sup>4</sup> For further readings in the context of the larger research project and beyond, please see, e.g.:

Schumacher, S., Engel, S., Niemeyer, N., Kuester, A., Burchert, S., Skoluda, N., Rau, H., Nater, U., Willmund, G.-D., & Knaevelsrud, C. (accepted). Salivary cortisol and alpha-amylase in posttraumatic stress disorder and their potential role in the evaluation of cognitive behavioral treatment outcomes. *Journal of Traumatic Stress*.

Engel, S., Schumacher, S., Niemeyer, H., Küster, A., Burchert, S., Klusmann, H., Rau, H., Willmund, G.-D., & Knaevelsrud, C. (2021). Associations between oxytocin and vasopressin concentrations, traumatic event exposure and posttraumatic stress disorder symptoms: Group comparisons, correlations, and courses during an internet-based cognitive-behavioral treatment. European Journal of Psychotraumatology, 12(1), 1886499. https://doi.org/10.1080/20008198.2021.1886499

Schumacher, S.\*, Niemeyer, H.\*, Engel, S., Cwik, J.C., Laufer, S., Klusmann, H., & Knaevelsrud, C. (2019). HPA axis regulation in posttraumatic stress disorder: A meta-analysis focusing on potential moderators. *Neuroscience and Biobehavioral Reviews, 100*, 35-57. https://doi.org/10.1016/j.neubiorev.2019.02.005

#### INTRODUCTION AND THEORETICAL BACKGROUND

acceptance of a therapist-guided iCBT program in a sample of GAF service members with PTSS. The trial was registered with the Australian Clinical Trials Registry [ACTRN12616000956404] and the study protocol has been described in more detail in Niemeyer et al. (2020). Besides evaluating treatment efficacy and acceptance (Niemeyer et al., 2020), associated research interests targeted associations between difficulties in emotion regulation and PTSS (Spies et al., 2020), associations of oxytocin and vasopressin concentrations with trauma exposure, PTSS, and treatment efficacy (Engel, 2020; Engel et al., 2021; Engel et al., 2020), and associations of cortisol and alpha-amylase levels with trauma exposure, PTSS ,and treatment efficacy (Schumacher et al., 2021; Schumacher et al., 2019).

# 1.5.1. STUDY 1: Comparison of DSM-5 and proposed ICD-11 criteria for PTSD with DSM-IV and ICD-10: Changes in PTSD prevalence in military personnel

For this thesis, STUDY 1 represents a preliminary investigation to evaluate the agreement on PTSD diagnostic status when transiting between the different versions of the DSM (DSM-IV, DSM-5) and the ICD (ICD-10, ICD-11 proposal) in a sample of military personnel of the GAF.

**Comparing all four diagnostic systems.** At the time of conceptualization of STUDY 1, most investigations contrasted either DSM-IV to DSM-5 (Carmassi et al., 2013; Crespo López & Gómez Gutiérrez, 2016; Elhai, Ford, Ruggiero, & Frueh, 2009; Elhai et al., 2012; Forbes et al., 2011; Gentes et al., 2014; Kilpatrick et al., 2013; Miller et al., 2013), DSM-IV to the proposed ICD-11 (Morina et al., 2014; Stammel, Abbing, Heeke, & Knaevelsrud, 2015; van Emmerik & Kamphuis, 2011), DSM-5 to the proposed ICD-11 (Wisco et al., 2016), or ICD-10 to the proposed ICD-11 (Knefel & Lueger-Schuster, 2013). Only two investigations were available that compared all four diagnostic systems simultaneously and yielded inconsistent

findings (O'Donnell et al., 2014; Stein et al., 2014). STUDY 1 intends to supplement this research area by comparing the PTSD prevalence rates under all four diagnostic systems.

**Reporting agreement rates between systems.** Most of the existing investigations in this field mainly report differences in PTSD rates between the systems, while only a minority of relevant publications include consistency or agreement analyses. Reporting increases or reductions in diagnoses when transiting between systems limits the interpretation of findings, and reporting accordance or agreement rates is strongly recommended (Byrt, Bishop, & Carlin, 1993; Spitznagel & Helzer, 1985; Vach, 2005). Nevertheless, STUDY 1 intends to contribute to the existing data by reporting agreement on PTSD diagnostic status when transiting between the versions of the DSM and the ICD by calculating indicators of concordance.

**Examining a population of GAF veterans.** To date, available studies have examined diverse (non-) clinical samples of survivors of various types of civilian traumatization (Elhai et al., 2012; Forbes et al., 2011; Kilpatrick et al., 2013; Miller et al., 2013; O'Donnell et al., 2014; van Emmerik & Kamphuis, 2011; Wisco et al., 2016), earthquake survivors (Carmassi et al., 2013), and adult survivors of childhood institutional abuse (Knefel & Lueger-Schuster, 2013). At the time of conceptualization of STUDY 1, studies examining the transition of PTSD diagnostic status between the different systems in military veteran samples were limited, the findings were heterogeneous, and the research was particularly restricted to US American and British samples (Gentes et al., 2014; Miller et al., 2013; Morina et al., 2014; Wisco et al., 2016). There was no study examining GAF veterans, leaving it unclear to what extent the different manuals agree regarding PTSD diagnostic status in this population. STUDY 1 strives to fill this gap by providing data on PTSD prevalence concordance rates under the four systems in a sample of GAF veterans.

# 1.5.2. STUDY 2: Internet-based interventions for posttraumatic stress: A metaanalysis of randomized controlled trials

STUDY 2 of this thesis presents a preliminary investigation with the aim of conducting a metaanalytical evaluation of the efficacy and acceptance of IBI in populations with PTSD or PTSS.

**Conducting a meta-analysis**. At the time of conceptualization of STUDY 2, only two publications were available that focused on IBI for PTSD and other stress-related disorders, and both were conceptualized as systematic reviews (Amstadter, Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009; Herbert & Brunet, 2009). Interpreting findings of systematic reviews is restricted to a descriptive (qualitative) level, limiting their overall informative value (Borenstein, Hedges, Higgins, & Rothstein, 2011; Lipsey & Wilson, 2001). STUDY 2 therefore aims to provide a meta-analysis of the efficacy of IBI for PTSD, yielding quantitative data.

**Evaluating stand-alone IBI**. Prior to STUDY 2, two meta-analyses on technologybased interventions for PTSD were available, which synthesized a heterogeneous assortment of technology-assisted interventions (e.g., virtual reality, CD-ROM programs, video conferencing, online programs) and included stand-alone programs as well as adjuncts to conventional psychotherapy (Bolton & Dorstyn, 2015; Sloan, Gallagher, Feinstein, Lee, & Pruneau, 2011). Synthesizing results on diverse technologies and differing conceptualizations impede the interpretation of findings, hamper the evaluation of efficacy of treatment modes, and limit the explanatory value of findings (Ebert & Erbe, 2012; Eichenberg & Ott, 2012). STUDY 2 thus includes primary investigations that examined stand-alone IBI for PTSD only.

**Including RCT studies only.** At the time of conceptualization of STUDY 2, metaanalyses on the efficacy of technology- or online-based interventions for PTSD included RCT, quasi-experimental trials, uncontrolled pre-post trials, and non-randomized trials (Bolton & Dorstyn, 2015; Sloan et al., 2011). RCT represent the highest standard in empirical research (Rorty, 2009), whereas the inclusion of non-randomized trials is assumed to limit the generalizability and reliability of meta-analytical findings (Borenstein et al., 2011; Lipsey & Wilson, 2001). STUDY 2 included only such primary investigations that were designed as RCT and that reported between-group effect sizes on PTSD symptoms at least from pre- to post-intervention.

**Focusing on a PTSD specificity of primary investigations**. To date, meta-analyses and systematic reviews are available that summarize PTSD together with other disorders, such as anxiety and mood disorders (Cuijpers et al., 2009; Grist & Cavanagh, 2013; Reger & Gahm, 2009; Spek et al., 2007). Although this procedure improves the overall number of included studies, subsequent subgroup analyses are necessary to achieve disorder-specific effect sizes. The associated inevitable numerical reduction of effect sizes entered into these disorder-specific subgroup analyses limits the interpretation of the calculated disorder-specific effects (Borenstein et al., 2011; Lipsey & Wilson, 2001). Aiming to bridge this gap, STUDY 2 examined primary investigations that evaluated IBI for the treatment of PTSD only.

**Conducting subgroup analyses**. Subgroup analyses enable an examination of the impact of study- or treatment-related factors on the overall effect size (Borenstein et al., 2011; Lipsey & Wilson, 2001). Earlier meta-analyses inspected the effect of some online treatment components on the overall efficacy (Andersson & Cuijpers, 2009; Cowpertwait & Clarke, 2013; Grist & Cavanagh, 2013; Richards & Richardson, 2012; Spek et al., 2007). As a limitation, however, these analyses largely differed regarding the components under scrutiny, the results were heterogeneous, and conclusions were particularly limited in terms of their meaning for PTSD. STUDY 2 seeks to supplement earlier meta-analyses by providing an assortment of subgroup analyses concerning the impact of treatment components on the efficacy of IBI for PTSD.

# 1.5.3. STUDY 3: Attentional bias in GAF veterans with and without PTSS – An eyetracking investigation and group comparison

STUDY 3 analyzed cross-sectional data that were collected within the larger research project, with the aim of comparing GAF veterans with and without traumatization and with and without PTSS with respect to patterns of attentional bias to threat prior to the provision of the iCBT.

Utilizing an eye-tracking paradigm. To date, most experimental investigations on attentional bias consist of reaction time/ behavioral response paradigms. These techniques are limited by the fact that they depend on the participant's behavioral response and are susceptible to recording biases that can impede the interpretation of data (Miller, 1991; van Ens, Schmidt, Campbell, Roefs, & Werthmann, 2019; Whelan, 2008). By contrast, eye-tracking-based data are detachable from conscious behavioral responses and reaction time (Armstrong & Olatunji, 2012). So far, comparably little eye-tracking research on attentional bias in PTSD is available, especially regarding the population of military veterans. STUDY 3 provides cross-sectional eye-tracking-based data on attentional bias in (traumatized) GAF veterans with and without PTSS.

Selecting multiple stimulus categories. The selection of stimuli is one of the facets that vary across earlier investigations, with studies presenting either words (Bryant et al., 1995; Felmingham, Rennie, Manor, & Bryant, 2011), faces (Armstrong, Bilsky, Zhao, & Olatunji, 2013; Beevers, Lee, Wells, Ellis, & Telch, 2011; Disner et al., 2013; Lee & Lee, 2014), or pictorial cues (Kimble et al., 2010; Lee & Lee, 2012; Thomas, Goegan, Newman, Arndt, & Sears, 2013). The question of which type of stimulus may be sufficiently complex, salient, and trauma (un-) specific to measure attentional bias in trauma survivors in general and in veterans in particular has been subject to debate (Armstrong et al., 2013; Bryant et al., 1995; Kimble et al., 2010; Thomas et al., 2013). STUDY 3 strives to tackle this by concurrently presenting

participants with multiple stimulus categories, including trauma-related pictorial cues, pictorial cues of a broader ambiguous/threatening context, and faces.

Including multiple control groups. Existing investigations differ with respect to sample composition: Some studies included cases with subclinical PTSS (Kimble et al., 2010; Lee & Lee, 2012; Lee & Lee, 2014; Thomas et al., 2013) while others included full diagnostic PTSD cases only (Armstrong et al., 2013; Bryant et al., 1995; Felmingham et al., 2011). Moreover, control group designs also vary, with studies incorporating no control group (Kimble et al., 2010), a healthy trauma control group (Felmingham et al., 2011; Lee & Lee, 2014), or a trauma control group plus a non-trauma control group (Armstrong et al., 2013; Thomas et al., 2013). STUDY 3 compared three study groups simultaneously: Veterans with PTSS versus traumatized veterans without PTSS versus non-traumatized healthy veterans. Moreover, STUDY 3 added an alternative grouping approach, consisting of traumatized veterans with a full PTSD diagnosis according to the DSM-5 versus traumatized veterans with subsyndromal PTSS versus non-exposed healthy veterans.

# 1.5.4. STUDY 4: Attentional bias in veterans with deployment-related PTSD before and after iCBT – An eye-tracking investigation

STUDY 4 analyzed longitudinal data from the larger research project with the aim of evaluating the efficacy of the provided iCBT to modify patterns of attentional bias in treatment-seeking GAF veterans with PTSD. The study sought to contribute data that examine the modifiability of patterns of attentional bias in trauma-exposed veterans with PTSD after receiving iCBT.

**Evaluating the efficacy of iCBT to modify attentional bias**. Evidence exists regarding the efficacy of ABM programs (Bar-Haim, 2010; Beard, 2011; Emmelkamp, 2012; Hakamata et al., 2010; Hallion & Ruscio, 2011; MacLeod & Clarke, 2015; Mogoaşe et al., 2014). Regarding the efficacy of more general (psychotherapeutic) interventions to modify patterns of attentional bias, the literature is extremely scarce. In a pioneering work, El Khoury-Malhame,

Reynaud, et al. (2011) investigated the efficacy of EMDR to modify attentional bias in PTSD. However, it remains largely unclear to what extent psychotherapeutic interventions that do not specifically target attention (bias) may be helpful to modify patterns of attentional bias in PTSD. In particular, at the time of STUDY 4, there were no available studies examining the efficacy of an iCBT program on attentional bias in PTSD. STUDY 4 sought to fill this research gap by evaluating the efficacy of an iCBT program to modify patterns of attentional bias in treatmentseeking veterans with PTSD.

Using an eye-tracking paradigm to measure modifications of attentional bias. Analyses on the efficacy of ABM programs have mainly included reaction time- / behavioral response-based paradigms (Bar-Haim, 2010; Beard, 2011; Emmelkamp, 2012; Hakamata et al., 2010; Hallion & Ruscio, 2011; MacLeod & Clarke, 2015; Mogoaşe et al., 2014), and El Khoury-Malhame, Lanteaume, et al. (2011) used the emotional Stroop and detection of target tasks. At the time of conceptualization of STUDY 4, only one eye-tracking-based investigation in the field of attentional bias modification research was available (Wadlinger & Isaacowitz, 2008). Wadlinger and Isaacowitz (2008) provided a sample of non-clinically depressed undergraduate students with one session of ABM. To date, eye-tracking-based research on the efficacy of interventions to modify attentional bias in PTSD is sparse. STUDY 4 aims to fill this gap by contributing eye tracking-based data on the efficacy of an iCBT program to modify patterns of attentional bias in veterans with PTSS.

In the following, STUDY 1, STUDY 2, STUDY 3, and STUDY 4 are presented to the reader. Due to copyright restrictions, the original manuscript of STUDY 3 is not available in the online version of this thesis. The respective pages are therefore omitted. The reader is provided with the abstract of STUDY 3 and with the respective reference information and the DOI link to access the study online.

# **CHAPTER 2 – STUDY 1**

# Comparison of DSM-5 and proposed ICD-11 criteria for PTSD with DSM-IV and ICD-10: Changes in PTSD prevalence in military personnel

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#### Abstract

Background. Recently, changes have been introduced to the diagnostic criteria for posttraumatic stress disorder (PTSD) according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD). Objectives. This study investigated the effect of the diagnostic changes made from DSM-IV to DSM-5 and from ICD-10 to the proposed ICD-11. The concordance of provisional PTSD prevalence between the diagnostic criteria was examined in a convenience sample of 100 members of the German Armed Forces (GAF). Method. Based on guestionnaire measurements, provisional PTSD prevalence was assessed according to DSM-IV, DSM-5, ICD-10, and proposed ICD-11 criteria. The consistency of the diagnostic status across the diagnostic systems was statistically evaluated. Results. Provisional PTSD prevalence was the same for DSM-IV and DSM-5 (both 56%), and comparable under DSM-5 versus ICD-11 proposal (48%). Agreement between DSM-IV and DSM-5, and between DSM-5 and the proposed ICD-11 was high (both p < .001). Provisional PTSD prevalence was significantly increased under ICD-11 proposal compared to ICD-10 (30%) which was mainly due to the deletion of the time criterion. Agreement between ICD-10 and the proposed ICD-11 was low (p = .014). Conclusion. This study provides preliminary evidence for a satisfactory concordance between provisional PTSD prevalence based on the diagnostic criteria for PTSD that are defined using DSM-IV, DSM-5, and proposed ICD-11. This supports the assumption of a set of PTSD core symptoms as suggested in the ICD-11 proposal, when at the same time a satisfactory concordance between ICD-11 proposal and DSM was given. The finding of increased provisional PTSD prevalence under ICD-11 proposal in contrast to ICD-10 can be of guidance for future epidemiological research on PTSD prevalence, especially concerning further investigations on the impact, appropriateness, and usefulness of the time criterion included in ICD-10 versus the consequences of its deletion as proposed for ICD-11.

# Highlights

- The consistency between provisional PTSD prevalence according to DSM-IV, DSM-5, ICD-10, and the proposed ICD-11 criteria was examined in a sample of 100 members of the German Armed Forces.
- The provisional PTSD prevalence was the same under DSM-IV and DSM-5, and comparable under DSM-5 and the ICD-11 proposal, indicating a satisfactory agreement between these systems.
- The provisional PTSD prevalence was significantly increased under the ICD-11 proposal compared to ICD-10, mainly due to the deletion of the time criterion in the ICD-11 proposal.
- Preliminary support for the assumption of a concise set of six PTSD core symptoms and for the deletion of the time criterion as presented in the ICD-11 proposal.
- Satisfactory consistency between preliminary PTSD prevalence based on DSM-IV,
   DSM-5, and the ICD-11 proposal and overall support for the changes made to DSM and
   ICD.
- Future research needs to examine what diagnostic requirements are necessary and sufficient for diagnosing PTSD and whether these are approximated by the ICD-11 proposal.

**Keywords**: posttraumatic stress disorder; DSM; ICD; military; epidemiology; prevalence, concordance; PTSD.

# 1. Introduction

In the last decade, there has been substantial criticism of the criteria for posttraumatic stress disorder (PTSD) in the 4<sup>th</sup> edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association, 2000) and the 10<sup>th</sup> edition of the International Classification of Mental and Behavioral Disorders (ICD-10, World Health Organization, 1993). First, concerns have been raised about the overlap of particular PTSD symptoms with symptoms of depression and anxiety (Maercker et al., 2013; Steel et al., 2009); second, a potential overuse of PTSD diagnoses in trauma-exposed populations has been discussed (Afana, 2012; Maercker et al., 2013; Steel et al., 2009); third, the trauma criterion has been criticized as not being adequately defined with respect to the selection of potentially traumatizing events (Breslau & Kessler, 2001; McNally, 2003; Rosen, 2004) as well as regarding the narrow interpretation of responses to trauma. PTSD can be associated with a wide range of reactions to trauma (Brewin, Andrews, & Rose, 2000; Kilpatrick et al., 1998), and moreover can develop in the absence of responses of fear, helplessness, or horror (Adler, Wright, Bliese, Eckford, & Hoge, 2008; Breslau & Kessler, 2001). Thus, the already published 5<sup>th</sup> Edition of the DSM (DSM-5, American Psychiatric Association, 2013) as well as the proposal for the 11<sup>th</sup> revision of the ICD (ICD-11, World Health Organization, 2012) introduced major changes to the diagnostic criteria for PTSD in adults that are described in detail below.

#### 1.1.DSM-IV versus DSM-5

First, the DSM-5 (American Psychiatric Association, 2013) expanded the A1 criterion to 'exposure to sexual violence', and removed the A2 criterion due to insufficient clinical utility and limited predictive value (Friedman, 2013). This expands the context of PTSD to a disorder following a broader range of stressful events and including reactions associated with other states than fear or anxiety (Brewin et al., 2000; Friedman, Resick, Bryant, & Brewin, 2011). Second, the three symptom clusters known from DSM-IV were replaced by four symptom clusters by

splitting the formerly known DSM-IV cluster C into two distinct categories (Cluster C: avoidance of stimuli; Cluster D: alterations in cognitions and mood) (Friedman, 2013; Friedman et al., 2011; Gentes et al., 2014). Moreover, the DSM-5 criteria D and E (formerly criterion D in DSM-IV) now comprise three additional symptoms that had not been included in DSM-IV, and two symptoms known from DSM-IV were rephrased for DSM-5. Thus, the number of qualifying and of necessarily endorsed symptoms differs between DSM-IV and DSM-5. According to DSM-IV, one re-experiencing, three avoidance, and two arousal- and reactivity-related symptoms need to be met out of 17 qualifying symptoms. Contrary, DSM-5 demands one re-experiencing, one avoidance, two cognition- and mood-related, and two arousal- and reactivity-related symptoms out of twenty qualifying symptoms. However, both versions require symptoms to be present for at least one month, and impairment in at least one area of functioning.

#### 1.2.ICD-10 versus ICD-11 proposal

First, whereas the ICD-10 asks for one re-experiencing, one avoidance, and one feeling of continued threat symptom out of 17 qualifying symptoms, the ICD-11 proposal defines six qualifying symptoms, two on each of the three subscales only. This parsimonious conceptualization of PTSD aims at simplifying the assessment and at reducing over-diagnosing and false-positive comorbidities (Brewin et al., 2009; Cloitre et al., 2013; Maercker et al., 2013; Stein et al., 2007), assuming that these symptoms represent characteristics that are salient to all PTSD cases (Brewin et al., 2009; Maercker et al., 2013). Besides, the ICD-11 proposal clarifies that impairment in one area of functioning and a duration of at least one month must be reported (Maercker et al., 2013). Moreover, the traumatic event does not need to cause immediate distress (Brewin et al., 2009; Maercker et al., 2013), and the symptom onset can be delayed more than six months post trauma (Andrews, Brewin, Philpott, & Stewart, 2007).

#### 1.3.Epidemiological research

To date, literature evaluating the consistency between PTSD prevalence between the four diagnostic systems has yielded inconsistent results. The majority of publications comparing DSM-IV to DSM-5 report no differences (Carmassi et al., 2013; Elhai, Ford, Ruggiero, & Christopher Frueh, 2009; Elhai et al., 2012; Gentes et al., 2014; Kilpatrick et al., 2013; Miller et al., 2013; O'Donnell et al., 2014), with the exception of Forbes et al. (2011) who found lower PTSD prevalence under DSM-5. Of those who reported consistency (Carmassi et al., 2013; Elhai et al., 2009; Gentes et al., 2014; Kilpatrick et al., 2013) all reported satisfying high agreement between both versions of the DSM. Comparing the proposed ICD-11 to DSM-IV criteria, Stammel, Abbing, Heeke, and Knaevelsrud (2015) reported reduced PTSD prevalence according to the proposed ICD-11 criteria. In contrast, van Emmerik and Kamphuis (2011) as well as Morina, van Emmerik, Andrews, and Brewin (2014) found no differences. To our knowledge, only two studies to date have systematically compared all four diagnostic systems, again yielding inconsistent results. Whereas Stein et al. (2014) found no differences in PTSD prevalence at all, O'Donnell et al. (2014) reported no differences between DSM-5 and DSM-IV, but lower PTSD prevalence under the proposed ICD-11 compared to DSM-IV, DSM-5, and ICD-10. Notably, although interpretation of prevalence differences between different diagnostic systems is limited when no consistency is reported, analyses of agreement between the diagnostic systems are provided only by some authors (Carmassi et al., 2013; Elhai et al., 2009; Gentes et al., 2014; Kilpatrick et al., 2013; Morina et al., 2014; Stammel et al., 2015).

War veterans and active soldiers represent a population at increased risk for PTSD since they are confronted with potentially traumatizing events almost daily. However, this population must show a high level of physical and mental fitness, emphasising the need for reliable and valid diagnostic systems and instruments and thus underlining the importance of investigating the concordance and appropriateness of the different diagnostic systems for this trauma

population. However, we are aware of only a few studies that examined PTSD prevalence among veterans of war or active soldiers (Gentes et al., 2014; Miller et al., 2013; Morina et al., 2014; Wisco et al., 2016). Although, Gentes et al. (2014), as well as Miller et al. (2013) report comparable PTSD prevalence between DSM-IV and DSM-5, and Morina et al. (2014) found comparable PTSD prevalence between the ICD-11 proposal and DSM-IV, Wisco et al. (2016) report significantly reduced PTSD prevalence under the ICD-11 proposal compared to DSM-5 as well as compared to ICD-10, indicating an unsatisfactory concordance between these systems. However, no simultaneous comparison of all these diagnostic systems, i.e., the ICD-11 proposal, ICD-10, DSM-IV, and DSM-5, is available.

The main purpose of this study was to expand the empirical evidence on concordance of PTSD prevalence between the diagnostic systems DSM-IV, DSM-5, ICD-10, and the ICD-11 proposal. We focused on the population of war veterans and active soldiers by recruiting treatment-seeking members of the German Armed Forces (GAF) with reported lifetime traumatization. Of special concern for this study was the concordance when self-rated questionnaires were scored following the diagnostic rules of DSM-IV, DSM-5, ICD-10, and proposed ICD-11 criteria for PTSD. It is of note that most earlier studies in this area used clinician-administered interviews to check for a positive diagnosis of PTSD (Elhai et al., 2009; Forbes et al., 2011; Gentes et al., 2014; Morina et al., 2014; O'Donnell et al., 2014; Stein et al., 2014; van Emmerik & Kamphuis, 2011; Wisco et al., 2016). While this is without doubt the gold standard for clinical research, clinical practice often heavily relies on self-administered instruments, underlining the importance of investigating the consistency when self-rating instruments for PTSD are provided. Based on research findings, we expected that the PTSD prevalence would be the same using DSM-IV versus DSM-5 criteria (Carmassi et al., 2013; Elhai et al., 2009; Gentes et al., 2014; Kilpatrick et al., 2013; Miller et al., 2013; O'Donnell et al., 2014; Stein et al., 2014), but would be reduced under the ICD-11 proposal as compared to ICD-10 and DSM-5 (O'Donnell et al., 2014; Wisco et al., 2016).

#### 2. Method

#### 2.1. Participants and Procedure

Data were collected in a convenience sample of 100 treatment-seeking members of the GAF who had returned from deployment, were over the age of 18, reported a history of lifetime traumatization, and were fluent in German. Participants were recruited and assessed between June 2014 and February 2015 in collaboration with the inpatient and outpatient clinics of the GAF hospital in Berlin. Of the patients invited to the study, 57% agreed to and participated in the study. Participants consented to participate after they had been informed about the study's content, data confidentiality, and anonymity. Data were collected by utilizing paper-and-pencil questionnaires. Participants were told that they would receive a number of questionnaires that deal with different aspects of physical and mental health. Further, they were instructed that although some of the questions throughout the questionnaires may seem to be very similar, they should not feel confused by this, and that they must answer each item. The questionnaires of interest for the present study were part of a larger survey, permitting so that the presentation of the questionnaires of interest was not back-to-back but interleaved by other inventories, reducing the risk of order effects. First, after filling in a short questionnaire on demographic information, participants filled in the German version of the Life Events Checklist for DSM-5 (German version: Ehring, Knaevelsrud, Krüger, & Schäfer, 2014a, see Appendix; LEC-5, Weathers et al., 2013), and the German version of the Posttraumatic Stress Disorder Checklist for DSM-5 (German version: Ehring et al., 2014b; PCL-5, Weathers et al., 2013). Afterwards, six distinct inventories of 219 items in total were given to the participants. Finally, the participants received the German version of the Posttraumatic Stress Diagnostic Scale (German version: PDS-D, Ehlers, Steil, Winter, & Foa, 1996; PDS, Foa, 1995). The study was approved by the Review Board of the University of Muenster.

Participants were on average 35.22 years (SD = 8.84) old and predominantly male (86%). Most participants lived together with a partner (60%) or in a single household (24%).

Subjects reported being in a relationship (32%), married (37%), single (21%), or divorced (10%). Two-thirds were employed full-time (66%), whereas the remaining worked part-time (6%), were unemployed (5%), retired (3%), or studying/ on parental leave/ unfit for work (18%); two participants gave no information.

#### 2.2. Measures

# 2.2.1. PTSD symptoms

The German version of the Posttraumatic Stress Diagnostic Scale (PDS-D, Ehlers et al., 1996; PDS, Foa, 1995) was used to assess PTSD symptoms and provisional PTSD diagnostic status referring to DSM-IV and ICD-10. Section 3 of the PDS-D assesses PTSD symptoms during the past month based on 17 items on a 4-point scale (0, 'never/ only once during the past month' to 3, '5 times per week or more/ nearly always'). Participants' ratings of 1 ('once a week or less/ once in a while') or higher indicated that a symptom was endorsed. Section 4 checks for impairment in at least one area of functioning. Participants were instructed to complete the PDS-D based on a 'worst event that still troubles them the most today'. The PDS-D is one of the most commonly used and well validated instruments to assess PTSD, as supported by Griesel, Wessa, and Flor (2006) who reported satisfactory psychometric properties and high internal consistency (.88 <  $\alpha$  < .94 for symptom clusters and total scale). In this study, Cronbach's alpha was satisfactory (total scale  $\alpha$  = .95; intrusion  $\alpha$  = .94; avoidance  $\alpha$  = .89; hyperarousal  $\alpha$  = .86).

The German version of the Posttraumatic Stress Disorder Checklist for DSM-5 (German version: Ehring et al., 2014b; PCL-5, Weathers et al., 2013) was used to assess PTSD symptoms and provisional PTSD diagnostic status following DSM-5 and the ICD-11 proposal. Twenty items assess PTSD symptoms on a 5-point scale (0, 'not at all' to 4, 'extremely'), whereby all questions refer to the past month. Participants' ratings of 2 ('moderately') or higher indicated that a symptom was endorsed. Participants were instructed to complete the PCL-5 based on a

'worst event that still troubles them the most today'. The PCL-5 was developed based on the DSM-5 criteria, and preliminary psychometric evaluations revealed high internal consistency ( $\alpha = .94$ ), good test-retest reliability (.56 < r < .82), and high discriminability and convergence (Blevins, Weathers, Davis, Witte, & Domino, 2015; Krüger-Gottschalk et al., 2017). In the current study, internal consistency was satisfactory (total scale  $\alpha = .97$ ; intrusion  $\alpha = .93$ ; avoidance  $\alpha = .88$ ; cognitions and mood  $\alpha = .91$ ; hyperarousal  $\alpha = .89$ ).

#### 2.2.2. Trauma exposure

Traumatic events were measured using the trauma list of the PDS-D providing eleven traumatic events as well as by providing the German version of the Life Events Checklist for DSM-5 (German version: Ehring et al., 2014a, see Appendix; LEC-5, Weathers et al., 2013) providing 17 traumatic events. In both instruments participants were asked to name one worst event that still troubles them the most today.

# 2.2.3. Provisional diagnostic status based on DSM-IV versus DSM-5

For a provisional diagnosis based on DSM-IV, participants had to endorse one reexperiencing, three avoidance, and two hyperarousal symptoms out of 17 qualifying symptoms for the past month, with symptom ratings of 1 or higher on the PDS-D. They had to report feelings of fear, helplessness, or horror during trauma exposure, as well as current impairment in at least one area of functioning. For a provisional diagnosis based on DSM-5, participants needed to meet one re-experiencing, one avoidance, two alterations in cognition and mood, and two alterations in arousal and reactivity symptoms out of 20 qualifying symptoms for the past month, with symptom ratings of 2 or higher on the PCL-5. Current impairment in at least one area of daily functioning was required.

#### 2.2.4. Provisional diagnostic status based on ICD-10 versus the ICD-11 proposal

For a provisional diagnosis based on ICD-10, participants had to endorse one reexperiencing, one avoidance, and one hyperarousal symptom out of 17 qualifying symptoms, with symptom ratings of 1 or higher on the PDS-D. Participants had to report distress during trauma exposure, and symptom onset within six months post trauma. For receiving a provisional diagnosis based on the ICD-11 proposal, we followed the suggestions put forward by Brewin et al. (2009) and Maercker et al. (2013). Participants needed to fulfil one re-experiencing, one avoidance, and one sense of threat symptom out of six qualifying symptoms, with symptom rating of 2 or higher on the PCL-5. Symptoms had to be present for at least one month, and current impairment in at least one area of functioning was required.

# 2.3. Data Analysis

Analyses were conducted using SPSS 22.0 (IBM Corporation, 2013). As there was only a small amount of missing data (0.2%) that was missing at random, the performance of an expectation-maximization algorithm was justified to impute a single new data set without missing data. We calculated the proportions of participants meeting the diagnostic criteria for justifying a provisional PTSD diagnosis under DSM-IV, DSM-5, ICD-10, and the ICD-11 proposal. We then calculated the proportion of participants changing (i.e., gaining or losing) or maintaining the provisional diagnostic status when the transition from DSM-IV to DSM-5, from ICD-10 to ICD-11, and from DMS-5 to the ICD-11 proposal was applied. Two-tailed binomialapproximation tests for proportions were applied for PTSD prevalence between the different diagnostic systems, and Cohen's kappa was calculated for concordance between the different diagnostic systems. Significance was set at p < .05 for all analyses.

# 3. Results

#### 3.1. Trauma exposure

On average, 4.14 (SD = 1.61) traumatic events in the PDS-D and 9.02 (SD = 3.54) events in the LEC-5 were reported. The most frequently reported events were exposure to serious accident/fire/explosion (84%), deployment to or battle action in an area of war (84%), and severe human suffering (78%), all of which took place in a military context, and they were at the same time those events that still troubled them the most today. On average, 5.93 (SD = 5.47) years had passed since the traumatic event. Whereas 53.1% of participants reported that they experienced symptoms such as irritability, sleep disturbances, intrusive thoughts, or flashbacks within the first six months post trauma, the remainder reported a late symptom onset.

# 3.2. Provisional diagnosis based on DSM-IV versus DSM-5

The prevalence of provisional PTSD was the same under DSM-IV and DSM-5 (Table 1). Eleven participants gained the provisional diagnosis when the transition from DSM-IV to DSM-5 was made, whereas another eleven participants lost it. The difference was not significant (p = .54), and level of agreement was satisfactory (78%,  $\kappa = .55$ , p < .001). Table 1 illustrates the concordance between both systems. Participants who lost the diagnosis did not meet the required DSM-5 symptoms of negative alterations in cognitions and mood (N = 9, 81.8%), alterations in arousal and reactivity (N = 7, 63.6%), avoidance (N = 6, 54.5%), or re-experiencing (N = 2, 18.2%). Two (18.2%) participants gained the diagnosis under DSM-5 due to the deletion of the A2 criterion, the remaining changes were attributable to differences in symptom requirements between both versions. No differences between participants that received the provisional diagnosis under DSM-IV but not under DSM-5 and vice versa were found regarding age, gender, time since trauma, number of traumatic events, and mean PTSD symptom severity (.152  $\leq p \leq .949$ ).

Prevalence (N, %) of provisional diagnosis		Prevalence ( <i>N</i> , %) of provisional diagnosis based on DSM-5 <sup>2</sup>	
based on DSM-IV <sup>1</sup>		Diagnosis given	Diagnosis not given
		56 (56.0%)	44 (44.0%)
Diagnosis given	56 (56.0%)	45 (80.4%)	11 (19.6%)
Diagnosis not given	44 (44.0%)	11 (25.0%)	33 (75.0%)

Table 1. Prevalence of provisional PTSD diagnosis based on DSM-IV and DSM-5, N = 100.

*Note.*<sup>1</sup> Proportions based on PDS-D; <sup>2</sup> Proportions based on PCL-5.

#### 3.3. Provisional diagnoses based on ICD-10 versus ICD-11 proposal

Significantly more participants met the criteria for a provisional PTSD diagnosis under the ICD-11 proposal (48%) than under ICD-10 (30%) (p < .001). As depicted in Table 2, 28 participants gained a provisional diagnosis when moving from ICD-10 to the ICD-11 proposal, whereas 10 lost it. Agreement was low (62%,  $\kappa = .228$ , p = .014). Table 2 illustrates the concordance between both diagnostic systems. Participants who lost their provisional diagnosis did not meet the proposed ICD-11 criterion of re-experiencing (N = 7, 70%), alterations in sense of threat (N = 4, 40%), or avoidance (N = 3, 30%). In contrast, 24 (85.7%) participants gained the provisional diagnosis due to the deletion of the time criterion, and two (7.1%) reported reactions to trauma that did not involve high distress. The remaining changes were attributable to differences in symptom requirements between both versions. No differences between participants that received the provisional diagnosis under ICD-10 but not under the ICD-11 proposal and vice versa were found regarding age, gender, time since trauma, number of traumatic events, and mean PTSD symptom severity (.233  $\leq p \leq .951$ ).

Prevalence (N, %) of provisional diagnosis		Prevalence (N, %) of provisional diagnosis based on ICD-11		
based on ICD-10 <sup>1</sup>		proposal <sup>2</sup>		
		Diagnosis given	Diagnosis not given	
		48 (48%)	52 (52%)	
Diagnosis given	30 (30%)	20 (66.7%)	10 (33.3%)	
Diagnosis not given	70 (70%)	28 (40.0%)	42 (60.0%)	

Table 2. Prevalence of provisional PTSD diagnosis based on ICD-10 and ICD-11 proposal, N = 100.

Note.<sup>1</sup> Proportions based on PDS-D; <sup>2</sup> Proportions based on PCL-5.

# 3.4. Provisional diagnostic status based on DSM-5 versus the ICD-11 proposal

The difference in provisional PTSD prevalence under DSM-5 (56%) versus ICD-11 proposal (48%) was not significant (p = .066). Table 3 illustrates the concordance between both diagnostic systems. As can be seen, nine participants lost their diagnostic status under the ICD-11 proposal, whereas only one gained it. Eight (88.9%) did not meet the criterion for reexperiencing and two (22.2%) did not meet the criterion for alterations in arousal and sense of threat under the ICD-11 proposal. However, agreement was satisfactory (90%,  $\kappa = .801$ , p <.001). No differences between participants that received the provisional diagnosis under the ICD-11 proposal but not under DSM-5 and vice versa were found regarding age, gender, time since trauma, number of traumatic events, and mean PTSD symptom severity (.182  $\leq p \leq .922$ ).

Prevalence (N, %) of provisional diagnosis		Prevalence (N, %) of provisional diagnosis based on ICD-11	
based on DSM-5 <sup>1</sup>		proposal <sup>1</sup>	
		Diagnosis given	Diagnosis not given
		48 (48%)	52 (52%)
Diagnosis given	56 (56%)	47 (83.9%)	9 (16.1%)
Diagnosis not given	44 (44%)	1 (2.3%)	43 (97.7%)

*Table 3.* Prevalence of provisional PTSD diagnosis based on ICD-11 proposal and DSM-5, N = 100.

*Note.* <sup>1</sup> Proportions based on PCL-5.

# 4. Discussion

In line with our hypothesis and consistent with previous findings (Carmassi et al., 2013; Elhai et al., 2009; Elhai et al., 2012; Gentes et al., 2014; Kilpatrick et al., 2013; Miller et al., 2013; O'Donnell et al., 2014; Stein et al., 2014), no change in provisional PTSD prevalence was identified when the criteria shifted from DSM-IV to DSM-5. Although, DSM-IV and DSM-5 include a different number of qualifying symptoms, group these symptoms into specific clusters, and thus implicitly demand specific symptom characteristics to be present in a minimum number and specific combination, possibly leading to the identification of somewhat different patient populations in the present study, the agreement between both systems was satisfactory. Although, this may raise the question of the necessity and appropriateness of the changes made to DSM, earlier research that dealt with latent factor structures supported the four-factor approach that is now implemented in the DSM-5 (Forbes et al., 2011; Gentes et al., 2014; Miller et al., 2013). However, in the current study the deletion of the A2 criterion contributed to a diagnostic change for some participants that have met all required symptoms but did not report fear, horror, or helplessness during traumatization. This finding supports earlier research that reveals that a proportion of trauma survivors with clinically significant PTSD symptoms report a range of peri-traumatic reactions different from fear or helplessness, indicating a limited prognostic value of the A2 criterion for the development of PTSD, and suggesting an extension of the range of possible peri-traumatic reactions (Brewin et al., 2000; Friedman, 2013; Friedman et al., 2011).

In contrast to our assumption and to earlier research (O'Donnell et al., 2014; Stein et al., 2014; Wisco et al., 2016), the provisional PTSD prevalence was increased under the ICD-11 proposal compared to ICD-10. However, the increase was mainly due to the deletion of the time criterion, accounting for a tendency of late symptom onset in the present sample. This finding provides further preliminary support for the deletion of the time criterion and supports a systematic review that reports on delayed PTSD onset, particularly among individuals exposed to combat or war (Andrews et al., 2007). One might think of underlying mechanisms that may facilitate a late symptom onset, especially among populations of military personnel that are presented with long lasting and repeated traumatization. Possibly, during or immediately after this ongoing and repeated traumatization these individuals may be able to compensate for the psychological stress, keeping their physical and mental fitness as high as possible, and thus placing them at a higher chance of survival during these tough times. However, their psychological resilience may be significantly reduced on a sustained basis, making them even more vulnerable to stressors and crises that in turn may have the potential to activate PTSD later in life, long after the traumatic event or period has ended. However, this assumption needs further evaluation and future research dealing with the mechanism of late-onset PTSD in diverse populations of trauma survivors.

Although the proposed ICD-11 criteria include only six qualifying symptoms, while the DSM-5 includes twenty, the results of the current study indicate an overall satisfactory agreement between both systems. This finding of the current study contrasts with Wisco et al. (2016) who found significantly reduced PTSD prevalence under the ICD-11 proposal compared to DSM-5. This significant reduction of qualifying symptoms under the ICD-11 proposal when at the same time the concordance between both systems is still satisfactory gives preliminary reason to assume that the parsimonious collection of PTSD symptoms under ICD-11 (Brewin

et al., 2009; Maercker et al., 2013) may be appropriate and reliable. This is in line with a review providing evidence that PTSD screening instruments with fewer items can perform as well as or even better than longer and more complex measures (Brewin, 2005).

However, future research is needed to further verify the adequacy and sufficiency of the six core symptoms that are chosen for the ICD-11 proposal. Furthermore, since both diagnostic criteria seem to fit equally well to the present sample, the question arises whether there is a 'latent' PTSD towards which the different diagnostic systems are iteratively approaching (Kendler, Zachar, & Craver, 2011). Kendler et al. (2011) argue that psychological processes and structures may be underlying the phenotypes of psychiatric disorders demanding some degree of abstraction that may be solved by diagnostic systems. Further research is needed to shed a deeper light on the question whether this abstraction may be portrayed in the most concise way in the ICD-11 proposal, as suggested by earlier research (Brewin et al., 2009; Maercker et al., 2013).

The current study expands the field of research that deals with populations of war veterans or active soldiers (Gentes et al., 2014; Miller et al., 2013; Morina et al., 2014). Whereas the findings of the current study support earlier findings of comparable PTSD prevalence under DSM-IV and DSM-5 (Gentes et al., 2014; Miller et al., 2013), the study's findings concerning the transition from DSM-5 to the ICD-11 proposal as well as from ICD-10 to the ICD-11 proposal are innovative and add knowledge to research and to the literature. Moreover, the current study expands the field of research that compares PTSD prevalence among all four diagnostic systems (O'Donnell et al., 2014; Stein et al., 2014). Although the current study contributes to the inconsistency of research findings that is reported to date, its results preliminarily support the diagnostic changes made to DSM and to ICD. However, future research is needed to strengthen our findings.

## 4.1. Limitations

Several limitations of the current study need to be mentioned. First, PTSD diagnostic status was based on self-report questionnaires only and can therefore provide estimations of probable PTSD prevalence only. Although verification of the provisional diagnostic status by application of structured clinical interviews such as the Clinician Administered PTSD Scale for DSM-5 (CAPS-5, Weathers et al., 2013) is generally regarded as the gold standard, research has shown good agreement between PTSD diagnoses based on self-report questionnaires and on clinical interviews (Ehring et al., 2007). Besides, self-report ratings represent an important component in clinical practice and research today, thus underlining the high relevance of the current study to specifically evaluate the concordance of provisional PTSD diagnostic status that is based on well-established self-report inventories.

Second, in the current study two different diagnostic instruments were utilized, namely the PDS-D for DSM-IV and ICD-10, and the PCL-5 for DSM-5 and the ICD-11 proposal. We cannot rule out that differences between the provisional prevalence of PTSD reported in the present study may be partly due to differences between the diagnostic instruments, i.e., both systems require different symptom severity ratings to count a symptom as being endorsed, which makes it hard to tell whether the participants understood 'once a week or less/ once in a while' in the same way they interpreted 'moderately'. However, the application of the PDS-D and the PCL-5 was justified since the PDS-D is one of the most commonly used and well validated instruments to assess PTSD referring to ICD-10 and DSM-IV criteria (Griesel et al., 2006), and the PCL-5 was developed based on the DSM-5 criteria. However, at the time of planning the current study, no instrument was yet available to assess the proposed ICD-11 criteria (Brewin et al., 2009; Maercker et al., 2013). We are aware that in the meantime an instrument assessing the proposed ICD-11 criteria was developed (Cloitre et al., 2015) that has been used in recent research (Dokkedahl et al., 2015). However, this instrument has not been well enough established and validated up to now.

Finally, the sample was a comparably small convenience sample, and one might argue that the study was not sufficiently powered. However, the current study aims specifically at the population of GAF, to add knowledge to the field of research that deals with military personnel as a specific population that is at increased risk for PTSD due to ongoing, repeated, and work-related trauma exposure (Gentes et al., 2014; Miller et al., 2013; Morina et al., 2014). With respect to the scarce literature that deals with PTSD prevalence concordance between DSM-IV, DSM-5, ICD-10, and ICD-11 proposal in military personnel to date, the current study should be considered as an exploratory approach providing some guidance for future investigations to corroborate our findings.

## 4.2. Conclusion

The current study provides preliminary evidence for the impact that the changes of the DSM and the ICD diagnostic criteria for PTSD can have on the diagnostic status in a population of GAF that is exposed to military-related traumatic experiences, which is of relevance for future investigations on measuring and studying PTSD. On the one hand, promising results are provided regarding the concordance between DSM-5 and proposed ICD-11 criteria, and between DSM-IV and DSM-5, as well as concerning the appropriateness of changes made to DSM and ICD in general. On the other hand, the concordance between DSM-IV and DSM-5 as well as between DSM-5 and proposed ICD-11 raises the question of a 'latent' PTSD structure that may be underlying the well-known broad diagnostic instruments and that may be found in a more parsimonious concept of PTSD, that may be approached by the proposed ICD-11 criteria.

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## **CHAPTER 3 – STUDY 2**

# Internet-based interventions for Posttraumatic Stress: A meta-analysis of randomized controlled trials

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## Abstract

Posttraumatic stress disorder (PTSD) is a prevalent and highly distressing affliction, but access to trauma-focused psychotherapy is limited. Internet-based interventions (IBIs) could improve the delivery of and access to specialized mental health care. Currently, no meta-analytical evidence is available on IBIs for PTSD. We conducted a meta-analysis of 20 randomized controlled studies, including 21 comparisons, in order to summarize the current state of efficacy for the treatment of PTSD and to identify moderator variables. Studies tested internet-based cognitive behavioral therapy (CBT) and expressive writing (EW) against active or passive comparison conditions, including subclinical and clinical samples. Results show that at postassessment CBT-IBIs are significantly more efficacious than passive controls, resulting in medium to large effects on the PTSD sum and all sub-symptom scores (0.66 < g < 0.83), but both EW and CBT are not superior to active controls. EW differed from controls only at followup in reducing intrusions and hyperarousal but based on merely two studies. Subgroup analyses reveal that for CBT none of the program components such as provision of therapeutic support, reminders, or number of sessions serves as a moderator. Overall, results for CBT-IBIs are promising, but the number of includable studies for subgroup analyses was low, limiting statistical power. Future research is necessary to systematically investigate the impact of treatment components and test against active controls with optimal power.

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## Highlights

- CBT-IBIs reduce PTSD symptoms significantly at post-test compared to passive controls
- CBT-IBIs with different components are all more efficacious than passive controls
- CBT- and EW-IBIs are not superior to active control conditions
- Efficacy of CBT-IBIs is given at post-test, but does not carry through to follow-up
- However, the number of studies was low for sufficiently powered testing

**Keywords**: Posttraumatic Stress; PTSD; Internet intervention; Online therapy; Meta-analysis; Systematic review.

## 1. Introduction

## 1.1. Introduction to posttraumatic stress disorder

Around 65% of the world population experience at least one potentially traumatic event at some point during the lifespan (National Collaborating Centre for Mental Health 2005). A recent survey of the lifetime occurrence of posttraumatic stress disorder (PTSD) in the US adult population found prevalence rates of 11.7% in women and 4 % in men (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). Depending on a number of risk factors such as an interpersonal nature of the traumatic event (Phelps et al., 2014), female gender (Kessler et al., 2012), repeated traumatic exposure for occupational reasons (e.g. Hoge et al., 2004; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995), residency in an unstable political and economic country (de Jong, Komproe, Van Ommeren, & et al., 2001; Keane, Marshall, & Taft, 2006), and being member of an ethnic minority (Roberts, Gilman, Breslau, Breslau, & Koenen, 2011), prevalence rates of lifetime PTSD have been found to vary between 5% and 55% (Terhakopian, Sinaii, Engel, Schnurr, & Hoge, 2008). In addition, due to repeated revisions of diagnostic criteria and a variety of available measures, reports on the prevalence of PTSD differ across studies despite comparable sample characteristics (Terhakopian et al., 2008).

Following the recently updated DSM-5 criteria (American Psychiatric Association, 2013), PTSD comprises four symptom clusters: (a) the *avoidance* of external and internal stimuli that may trigger traumatic memories; (b) the *re-experiencing* of the traumatic event in the form of intrusive thoughts, nightmares or flashbacks; (c) *negative cognitions and mood,* which is characterized by senses of blame, guilt or shame, estrangement, withdrawal and the inability to experience or to express positive emotions; (d) *alterations in arousal and reactivity* (*hyperarousal*), that may lead to excessive alertness, aggressive behavior, recklessness, sleep disturbances, safety behavior and jumpiness. The previous version, DSM-IV-TR (American Psychiatric Association, 2000), on which most research is still based, includes three symptom clusters: avoidance, re-experiencing and hyperarousal.

## 1.2. Psychological treatment of posttraumatic stress disorder

Trauma-focused cognitive behavioral therapy (TF-CBT) combines well-established cognitive-behavioral techniques such as confrontation with trauma-associated stimuli (exposure in sensu or in vivo) with habituation and mental processing of the traumatic event as assumed mechanisms of change, and cognitive reappraisal, which specifically aims at the identification and modification of maladaptive cognitive distortions associated with PTSD. TF-CBT is the best evaluated approach for PTSD, resulting in the highest number of studies providing consistent evidence of efficacy with large effect sizes when compared to wait list or usual care (Bisson, Roberts, Andrew, Cooper, & Lewis, 2013; Bradley, Greene, Russ, Dutra, & Westen, 2014; Diehle, Schmitt, Daams, Boer, & Lindauer, 2014).

However, although effective treatments for PTSD are available, these are not widely applied in clinical practice, leading to drawbacks concerning the clinical practice of evidencebased medicine in face-to-face psychotherapy for the treatment of PTSD (Bisson et al., 2013; Keller, Stevens, Lui, Murray, & Yaggie, 2014; Kirkpatrick & Heller, 2014). Moreover, only a minority of traumatized individuals who experience symptoms of PTSD are in touch with the health care system (Kessler et al., 1999) and only around one in five patients seeks psychological treatment (Calhoun, Bosworth, Grambow, Dudley, & Beckham, 2002; Hoge et al., 2004; Rayburn et al., 2005; Roberts et al., 2011; Spoont, Murdoch, Hodges, & Nugent, 2010), due to fear of stigmatization, embarrassment, judgment or exclusion (Hoge et al., 2004; Hoge et al., 2014), or negative beliefs about mental health care services (Blais, Tsai, Southwick, & Pietrzak, 2015). Moreover, difficulties in establishing personal relationships can make it difficult for patients to open up during therapy (Besser & Neria, 2012; Campbell & Renshaw, 2013). Trauma survivors with PTSD often experience distress in interpersonal relationships, which can also affect the therapeutic relationship in terms of diminished trust and selfdisclosure and enhance the fear of being emotionally flooded in therapy when recollecting the traumatic experience (Charuvastra & Cloitre, 2008). These difficulties with being vulnerable in

the therapeutic context affect the benefit from the treatment. Above all, there is a pronounced lack of availability of psychotherapy for PTSD, with long waiting times and inadequate psychotherapy infrastructure (Trusz, Wagner, Russo, Love, & Zatzick, 2011). This disparity of need for psychotherapy and availability is crucial, and alternative means of providing access to treatment are needed, since PTSD severely affects life satisfaction as well as functioning and has a tendency to become chronic if untreated (Davidson, Stein, Shalev, & Yehuda, 2014).

#### 1.3. Internet based intervention programs

Most internet-based interventions (IBIs) are psychological treatments, usually based on established approaches such as CBT that are delivered exclusively via the internet, and that provide participants with disorder-specific treatment modules on a weekly to biweekly basis (e.g. Ebert & Erbe, 2012). The unique characteristic of being independent from seeing a therapist face-to-face provides IBIs with the distinct advantages of being easily accessible, lowthreshold and visually anonymous, highlighting the potential of IBIs to reach specific populations that might not otherwise seek treatment. Depending on the particular program, a range of complementary components can be found, e.g., activity planning, applied relaxation training and social skill training. In addition, multimedia components are often integrated, such as video/ audio vignettes or interactive trainings (e.g. cognitive bias modification training), or reminder messages to the client after a particular time of absence (e.g. Ebert & Erbe, 2012; Eichenberg & Ott, 2012). Furthermore, they can be supported by remote contact to a therapist via chat, email, or video-conference-systems. Or IBIs can be conceptualized as self-help programs with automated feedback offering only on-demand contact to a therapist in case of symptom deterioration, or technical support if the patient has trouble using the program.

Various IBIs exist for the treatment of PTSD. *Interapy* (Lange et al., 2000) is one well evaluated and widely accepted IBI CBT-based program (e.g. Ruwaard, Lange, Schrieken, & Emmelkamp, 2011) that encompasses three main components: self-confrontation (exposure),

cognitive restructuring, and social sharing/restoration by means of 11 structured writing assignments. During the self-confrontation assignments, the client writes about his trauma in first person and present tense in order to confront himself with the event and his associated thoughts and feelings. During the cognitive restructuring assignments, the client writes encouraging and supportive letters to a hypothetical friend who is experiencing the same or a comparable trauma with the aim of instilling new views about it, reflecting on positive aspects in the client's life, regaining a sense of control and detecting and correcting dysfunctional or automated thoughts, unrealistic beliefs and burdensome feelings. During the assignments of social sharing/restoration the client reflects in symbolic farewell letters to a significant other or alternatively to himself on the therapeutic process and on how to deal with the trauma in the future. A specially trained trauma-psychotherapist guides the client through the interventions and by remote communication provides supportive and encouraging written feedback after each module and on a weekly basis. Besides Interapy, there are other internet treatment programs based on TF-CBT that complement trauma exposure and cognitive restructuring with additional CBT interventions, such as stress management, guided imagery or relaxation (Carpenter, Stoner, Schmitz, McGregor, & Doorenbos, 2014; Litz, Engel, Bryant, & Papa, 2007; Steinmetz, Benight, Bishop, & James, 2012; Wang, Wang, & Maercker, 2013). An alternative approach that has been transferred to the internet is expressive writing (EW), which is based on theories of emotional disclosure (e.g. Pennebaker, 1997) and encourages the patient to write in detail about the trauma and to disclose her feelings and thoughts associated with it. In contrast to CBT-based treatment programs, EW delivered via the internet is generally shorter in duration and mainly not manual-based, the writing assignments are rather unstructured and therapeutic support is not commonly provided. Nevertheless, both EW and CBT have in common the fact that they are based on writing assignments. There is also a range of other treatments that rely on the use of media, e.g., the use of video conferencing between face-to-face therapy sessions. These can use computer software or CD-ROMs as well as new technology, such as virtual

reality that creates a realistic three-dimensional virtual environment for the patient (Gonçalves, Pedrozo, Coutinho, Figueira, & Ventura, 2012; McLay et al., 2014; Motraghi, Seim, Meyer, & Morissette, 2014). Generally, these treatments are not independent of face-to-face therapy, but rather accompany conventional therapy and are therefore not considered as IBIs.

## 1.4. Research on internet-based intervention programs

Thus far, meta-analytical research evaluating IBIs for PTSD has not been done. We are aware of two recent meta-analyses (Bolton & Dorstyn, 2015; Sloan, Gallagher, Feinstein, Lee, & Pruneau, 2011) that investigate the efficacy of technology assisted interventions for PTSD including virtual reality, CD-ROM accompanied interventions, video conferencing as well as internet-delivered programs. However, subsuming several technologies that in some cases combine conventional therapy with these technologies makes it impossible to evaluate the efficacy of the particular modes of delivery (e.g. Ebert & Erbe, 2012; Eichenberg & Ott, 2012). Furthermore, both include randomized controlled trials (RCTs) as well as uncontrolled and/or non-randomized trials and restrict their data sets to CBT-based interventions, thereby omitting alternative approaches. To our knowledge, only one publication focusing on internet-delivered treatments has been produced, but rather as a qualitative review than a quantitative analysis (e.g. Herbert & Brunet, 2009), thus restricting the findings to a descriptive level. A number of meta-analyses have analyzed PTSD together with several other disorders (Cuijpers et al., 2009; Grist & Cavanagh, 2013; Reger & Gahm, 2009; Spek et al., 2007), making it impossible to specify the efficacy for PTSD. A number of meta-analyses of IBIs for other disorders examine the role of particular program components on efficacy. These include the provision of therapeutic support (Andersson & Cuijpers, 2009; Cowpertwait & Clarke, 2013; Grist & Cavanagh, 2013; Richards & Richardson, 2012; Spek et al., 2007), the number of treatment sessions (Richards & Richardson, 2012), as well as the implementation of additional components such as reminder functions or multimedia (Cowpertwait & Clarke, 2013).

However, the results are conflicting and more meta-analytical research is needed here. Furthermore, psychotherapy research has shown that manual-guidance of treatment significantly improves treatment outcome (Laska, Gurman, & Wampold, 2014), but this common factor has hardly been investigated in IBIs.

## 1.5. Objectives

The aim of this study was to conduct a comprehensive meta-analysis of all RCTs that evaluate IBIs for the treatment of subclinical or clinical PTSD in the adult population. As diagnostic interviews and symptom measures in recent research on PTSD mostly still utilized the three-part definition of PTSD that includes avoidance, intrusion and hyperarousal according to the DSM-V-TR (American Psychiatric Association, 2000), we focused on these three symptom clusters. First, we aimed at evaluating the efficacy of IBIs using different therapeutic approaches with regard to both the global and the sub-symptom scales of avoidance, intrusion and hyperarousal. Second, we assess the role of particular program components for efficacy, namely the provision of therapeutic support, the number of intervention modules, standardization/manual use, and the use of reminder functions as well as of multimedia components. Third, we descriptively evaluate dropout and completer characteristics.

## 2. Method

## 2.1. Inclusion criteria

Studies were required to meet the following inclusion criteria: 1) the program was an internet based intervention program; 2) the program aimed at reducing subclinical or clinical PTSD in an adult population; 3) results were reported at the PTSD sum and/or symptom cluster levels; 4) valid and reliable assessments were used; 5) the study design was a RCT that compared an active intervention group to an active or passive comparison group by assessing symptom levels at least post treatment. Additionally applied exclusion criteria were: 1) exclusion of trials dealing with *secondary* PTSD, defined as the experience of PTSD-like

symptoms after being confronted with reports of the trauma of a third person, which is especially prominent in social/therapeutic occupations, e.g. social workers (Figley, 1995). We excluded such trials because we aimed at focusing on directly trauma-exposed populations and because we anticipated increased heterogeneity in the data and interpretational problems if the constructs of PTSD and *secondary* PTSD were mixed; 2) interventions designed for computer based/virtual reality/ mixed reality environments or face-to-face psychotherapy supplemented by computer technology; 3) interventions designed as smartphone applications, because the mode of presentation (mobile versus stable device), handling (smartphone touchscreen versus computer keyboard) and the potential utilization (on the way versus at home) presumably would lead to an increased heterogeneity, which might restrict the generalizability and reliability of the results.

## 2.2. Identification and selection of studies

To comprehensively identify all relevant studies, we conducted the literature search following the search strategies recommended by Lipsey and Wilson (2001). We screened the databases Medline, CINAHL, PsycARTICLES, PsycINFO, Psyndex, PubMed, Web of Science, PILOTS and SCOPUS for articles that had been published and for references of unpublished dissertations in English or German language up to 24th February 2015. The search included the terms [("internet intervention" OR "web intervention" OR "online intervention" OR "internet psychotherapy" OR "web psychotherapy" OR "online psychotherapy") AND ("posttraumatic stress" OR "posttraumatic stress symptoms" OR "posttraumatic stress disorder" OR "trauma\*" OR "victim\*")]. See Appendix A for an example of the full electronic search strategy. We repeated the search on 7<sup>th</sup> April 2015 to double-check and also look for new articles that had been published in the meantime. We also searched through the grey literature by examining abstracts of conference contributions, posters, and commentaries, and searched within the study register of http://clinicaltrials.gov. In addition, a snowball search system was

used for the identification of further potentially relevant studies by screening the reference lists of already entailed studies and through personal communication with experts in the field. Two independent raters (AK, HN) decided on the inclusion or exclusion of each study and discussed in the case of dissent.

## 2.3. Data extraction

We extracted the sample sizes and the reported outcome statistics of the PTSD scales (mean and standard deviation or standard error, or Cohen's *d* with its 95% confidence interval) for intervention and comparison groups at pre and post treatment and, if available, also at the follow-up assessment, including the follow-up time interval. If more than one outcome measure was reported, two independent raters (AK, HN) decided which one to include in the present analyses, based on validity, reliability, and appropriateness (e.g., online self-assessment versus non-blinded telephone interview). Thus, only one measure was included in the analysis to prevent violating the independence of the data (Borenstein, Hedges, Higgins, & Rothstein, 2011). Furthermore, for the same reason, if the treatment effect was tested against different comparison conditions, only one control condition was included. The raters decided which to use based on comparability and appropriateness with regard to the majority of available comparison conditions in the other included studies.

Following the criteria in the Cochrane Handbook (Higgins & Green, 2008) we gathered the following information on study design: PTSD measures, exclusion/inclusion criteria for participants, screening procedures, recruitment process, participants' flow, randomization procedure, attrition/ dropout/ completer analyses, comparison group, blinding of participants, blinding of study assessors to participants' allocation to treatment condition. Moreover, we extracted data concerning sample variables: age (mean, standard deviation), gender ratio, sample (e.g. students, clinic patients), trauma type, symptom severity, ethnicity; and concerning treatment characteristics: therapeutic approach, program content, therapeutic support,

standardization (manual use), duration of sessions, number of sessions, duration of intervention, delay of feedback, tailoring of feedback, reminder functions, multimedia components (e.g. video files, audio vignettes). With respect to therapeutic support, we labeled all programs in which a therapist was in remote contact with the client and provided therapeutic feedback messages as 'support'. In contrast, programs that were either fully automated, provided only non-therapeutic moderation such as the supervision of forum posts, or solely technical assistance, were considered as 'no support'.

## 2.4. Effect size calculations

As advocated in the literature (Borenstein et al., 2011), Hedges' g was used to measure effect size at both the primary study and meta-analytical level. The difference between the means of treatment and comparison conditions at post as well as at follow-up assessment, divided by the pooled standard deviation and adjusted for a small-sample bias (Hedges, 1981) is used to calculate g. Following a common rule of thumb (Cohen, 1988), effect sizes 0.2 < g <0.5 are considered small, 0.5 < g < 0.8 medium, and  $g \ge 0.8$  large. Positive effect sizes with the 95% confidence interval (95% CI) excluding zero indicate that the treatment condition was superior to the control condition. In addition, we tested whether two between-effect sizes significantly differed from each other by applying the Q-statistic, with a p-value below .05 indicating a significant difference (Borenstein et al., 2011).

## 2.5. Meta-analytical procedure

We utilized the random effects model (REM) for the primary effect size calculations. This is based on the assumption that the individual effect sizes stem from a pool of true effect sizes and thus vary to a certain degree, leading to a generous 95% CI and lowering the risk for type 1 error and lending relatively more weight to small-sample studies at the same time (Borenstein et al., 2011). All subgroup analyses were conducted using mixed effects analysis (MEA), which pools the studies within the respective subgroups by using the REM and then tests for a

significant difference between these subgroups using the fixed effects model (FEM) which assumes that all observed effect sizes are estimators of the same underlying true effect and all deviations occur due to random error (Borenstein et al., 2011). Mean effect sizes were calculated if at least two primary studies' effects were available to constitute a subgroup. All meta-analytical calculations were performed using the software package Comprehensive Meta Analyses (Version 3.3.070 Biostat, 2014).

## 2.5.1. Primary analyses of therapeutic approach and comparison condition

All IBIs were grouped according to their treatment approach (e.g., CBT). Control conditions were divided into passive (i.e., wait list) and active (e.g., psychoeducation, control writing task) conditions. We calculated effect sizes for the differences between each treatment approach and passive or active comparison conditions on the PTSD sum, avoidance, hyperarousal, and intrusion scales, for both post and follow-up assessments. Forest plots were used to present the analyses (Appendix B).

## 2.5.2. Subgroup analyses of program components

In addition to the treatment approach, we investigated the impact of specific program components on efficacy, specifically therapeutic support, number of sessions, manual use, use of reminder functions and use of multimedia components. These analyses were conducted for all symptom scores at post assessment. However, no subgroup analysis was applicable if a substantial confounding between treatment approach and component was present (i.e., a component was the same across all studies but one, e.g., one study used a reminder whereas all others did not). Furthermore, in case of a complete overlap of a component with the therapeutic approach (e.g., all programs based on a certain approach were manual based), it was impossible to disentangle the impact of the particular component from the impact of the interventions on the outcome.

## 2.6. Dropout analysis

We calculated the dropout rate in percentage for each treatment and comparison condition and summarized the primary studies' reports about differences between dropouts and completers in particular characteristics on a descriptive level.

## 2.7. *Heterogeneity*

Heterogeneity was examined using the *Q*-statistic. The level of significance was set to p < .05, indicating that heterogeneity was present (Borenstein et al., 2011). In addition, we used the *I*<sup>2</sup>-index as an estimate of the proportion of the observed variance that reflects true differences in effect sizes between the studies. Values of 25%, 50%, and 75% were interpreted as low, moderate and high levels of heterogeneity (Crombie & Davies, 2009). Of note is that moderate to high heterogeneity leads to difficulties in interpreting mean effect size, and possible moderators that might contribute to the heterogeneity should be examined (Borenstein et al., 2011; Crombie & Davies, 2009).

## 2.8. Publication bias

Begg and Mazumdar's rank correlation (Begg & Mazumdar, 1994), Egger's regression test (Egger, Smith, Schneider, & Minder, 1997), and Duval and Tweedie's trim-and-fill procedure (Duval & Tweedie, 2000) were applied in all data sets that fulfilled the requirements for their application, i.e. those that included at least six studies and were homogeneous. The detection of publication bias is unreliable and of low power if less than six studies are analyzed (Egger et al., 1997; Sterne, Becker, & Egger, 2005), and since these methods are based on a homogeneity assumption, they can lead to false alarms if this assumption is violated (Ioannidis & Trikalinos, 2007; Sterne, Gavaghan, & Egger, 2000; Terrin, Schmid, Lau, & Olkin, 2003). If asymmetry is detected, the trim-and-fill procedure provides a corrected effect size estimate. The difference between the original and the corrected effect size estimates was tested for significance by investigating whether the original still fell within the confidence limits of the

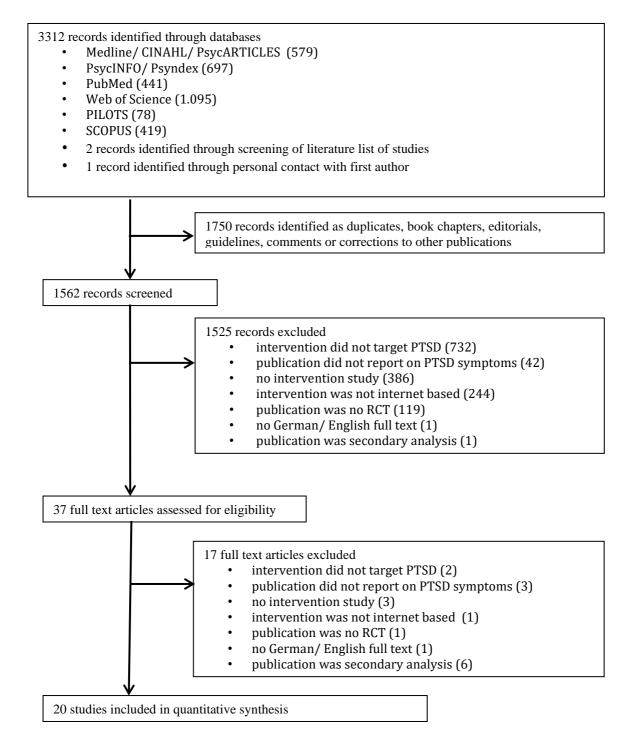
bias-corrected effect estimate (Niemeyer, Musch, & Pietrowsky, 2013). Finally, sensitivity analyses were used to identify outliers that might have contributed to the significant heterogeneity in the data sets. We inspected all heterogeneous data sets to find those studies with a substantially divergent effect size (Borenstein et al., 2011), If a primary study's effect differed substantially from the remaining effects of a particular data set, being either much larger or smaller. In such cases, we omitted the outlier and tentatively re-calculated the mean effect and tested for heterogeneity in the remaining data set. Furthermore, we descriptively examined whether the respective study was different in any characteristics that might have contributed to the substantial difference.

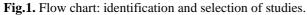
## 3. Results

## 3.1. Literature search

The literature search identified 3312 records. Of these, 1750 were excluded because they were identified as duplicates, book chapters dealing with fundamentals and basic principles, editorials, guidelines, comments, or corrections to other publications. From the remaining 1562 records 1525 were excluded after screening title and abstract for the following reasons: 732 did not target PTSD; 42 did not report on PTSD outcome, but rather used PTSD scores as covariates; 386 were identified as correlational reports, discussion papers or theoretical publications; 244 evaluated virtual/mixed reality interventions or other forms of psychotherapy or alternative therapies; 119 were either case studies, uncontrolled/non-randomized trials, or study protocols; for one it was impossible to gain access to a full text in German or English; and one was identified as a secondary analysis. We read the full text of the 37 remaining publications and excluded another 17, because 2 did not target PTSD, 3 did not report on PTSD, 3 were no intervention studies, 1 was no internet intervention, 1 was no RCT, 6 were secondary analyses and for 1 no German/English full text was available. We finally included 20 studies that fulfill all our expectations. All included studies are marked with an asterisk in the reference

list. All of these were published in scientific journals, except for Beyer (2011) which was an unpublished dissertation thesis. Figure 1 presents the selection process and reasons for study exclusion.





## 3.2. Included Studies

We included k = 20 studies comprising 21 comparisons of IBIs to control conditions with a total of N = 973 participants in the active treatment groups and N = 805 subjects in the comparison groups. Of these, 5 studies tested IBIs based on EW (Beyer, 2011; Hirai, Skidmore, Clum, & Dolma, 2012; Possemato, Ouimette, & Geller, 2010; Stockton, Joseph, & Hunt, 2014; Winzelberg et al., 2003) and 15 tested IBIs based on CBT (Carpenter et al., 2014; Hirai & Clum, 2005; Kersting et al., 2013; Kersting, Kroker, Schlicht, Baust, & Wagner, 2011; Knaevelsrud, Brand, Lange, Ruwaard, & Wagner, 2015; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange, van de Ven, Schrieken, & Emmelkamp, 2001; Litz et al., 2007; Owen et al., 2005; Spence et al., 2011; Spence et al., 2014; Steinmetz et al., 2012; Wagner, Knaevelsrud, & Maercker, 2006; Wang et al., 2013). Only the study by Wang and colleagues (2013) included two independent treatment to control group comparisons, and both were included as separate comparisons in the current analysis.

## 3.3. Quality of included studies

The studies' quality was overall sufficient. All studies reported recruitment procedures and participant flow and conducted the randomization using a computerized algorithm or independent third party. However, with respect to the reporting standards for study publication (APA Publications, 2008) the following shortcomings need to be mentioned. Fifteen studies did not sufficiently specify the applied diagnostic and screening procedures and did not provide detailed information on the subclinical or clinical status of the included samples (Carpenter et al., 2014; Hirai & Clum, 2005; Hirai et al., 2012; Kersting et al., 2013; Kersting et al., 2011; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Owen et al., 2005; Possemato et al., 2010; Steinmetz et al., 2012; Stockton et al., 2014; Wagner et al., 2006; Wang et al., 2013; Winzelberg et al., 2003). Furthermore, four studies did not provide sufficient information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., information on participants' inclusion/exclusion criteria (Hirai et al., 2012; Possemato et al., 2010; Steinmetz et al., 2012; Stockton et al., 2014). Overall, information on blinding of participants/ study assessors to participants' allocation to treatment condition was insufficient. Only nine studies provided reasons for attrition (Kersting et al., 2013; Kersting et al., 2011; Knaevelsrud et al., 2015; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Spence et al., 2011; Wagner et al., 2006; Winzelberg et al., 2003). Seven studies applied completer analyses (Beyer, 2011; Hirai et al., 2012; Lange et al., 2003; Lange et al., 2001; Owen et al., 2005; Stockton et al., 2014; Wagner et al., 2006), whereas 11 applied intention-to-treat-analyses (Carpenter et al., 2014; Kersting et al., 2013; Kersting et al., 2011; Knaevelsrud et al., 2015; Knaevelsrud & Maercker, 2007; Litz et al., 2007; Spence et al., 2011; Spence et al., 2014; Steinmetz et al., 2012; Wang et al., 2013; Winzelberg et al., 2003). Two did not provide information on this, but reported sample size together with the outcome (Hirai & Clum, 2005; Possemato et al., 2010).

## 3.4. Samples

The studies included diverse samples that had experienced a range of different traumatic events, inter alia general public exposed to different potential traumatic events (Beyer, 2011; Hirai & Clum, 2005; Hirai et al., 2012; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Spence et al., 2011; Spence et al., 2014; Wang et al., 2013), women diagnosed with breast cancer (Carpenter et al., 2014; Owen et al., 2005; Winzelberg et al., 2003), patients after kidney transplantation (Possemato et al., 2010), victims of natural disasters (Steinmetz et al., 2012; Wang et al., 2013), survivors of war, torture and terror (Knaevelsrud et al., 2015; Litz et al., 2007), prenatal loss (Kersting et al., 2013; Kersting et al., 2011), and loss of a significant person (Wagner et al., 2006). Four studies included participants with clinical symptom levels of PTSD that were confirmed by diagnostic screening procedures (Knaevelsrud et al., 2015; Litz et al., 2007; Spence et al., 2011; Spence et al., 2014), and one study clearly stated the inclusion of a subclinical sample (Beyer, 2011). As reported in 3.3., all remaining

studies made no clear specification on the samples' symptom level. The sample sizes varied between N = 24 (Stockton et al., 2014) and N = 228 (Kersting et al., 2013), of which 13 studies included N < 100 participants (Hirai & Clum, 2005; Kersting et al., 2011; Knaevelsrud & Maercker, 2007; Lange et al., 2001; Litz et al., 2007; Owen et al., 2005; Possemato et al., 2010; Spence et al., 2011; Steinmetz et al., 2012; Stockton et al., 2014; Wagner et al., 2006; Wang et al., 2013; Winzelberg et al., 2003) and the remaining included N > 100 (Beyer, 2011; Carpenter et al., 2014; Hirai et al., 2012; Kersting et al., 2013; Knaevelsrud et al., 2015; Lange et al., 2003; Spence et al., 2014; Wang et al., 2013). As reported in 3.2., Wang et al. (2013) included two independent treatment to control group comparisons (see also Table 1). The studies were conducted in the USA, Germany, the Netherlands, Australia, Switzerland, Great Britain, China, and the Middle East, and thus the included samples represent diverse ethnicities.

## 3.5. Outcome assessments

The majority of applied outcome measures were self-ratings of PTSD symptoms with the assessment conducted via the internet. These self-rating scales were the following: Impact of Event Scale-Revised (IES-R; Weiss & Marmar, 1997), Impact of Event Scale (IES; Horowitz, Wilner, & Alvarez, 1979), Posttraumatic Diagnostic Scale (PDS; Foa, Cashman, Jaycox, & Perry, 1997), PTSD Check List (PCL; Weathers, Litz, Herman, & Huska), PTSD Check List-Civilian Version (PCL-C; Andrykowski, Cordova, Studts, & Miller, 1998), Stressful Responses Questionnaire-Frequency (SRQF; Clum, 1999), and Modified PTSD Symptom Scale (MPSS; Falsetti, Resnick, Resick, & Kilpatrick, 1993). One study reported more than one assessment (Hirai & Clum, 2005). In this case, we included the SRQF (online self-assessment) rather than the IES-R (paper-pencil self-assessment). Test validity and reliability of the SRQF are comparable to the IES-R. By including the online self-assessment rather than the paper-pencil self-assessment we were able to reduce the expected heterogeneity across the studies with regard to the outcome measurement, since all the remaining self-report outcome assessments

were also conducted via the internet. Finally, one study (Litz et al., 2007) applied a face-to-face assessment by utilizing the PTSD Symptom Scale – Interview Version (PSSI; Foa & Tolin, 2000). Nine studies reported PTSD sum scores only (Carpenter et al., 2014; Kersting et al., 2011; Litz et al., 2007; Owen et al., 2005; Spence et al., 2011; Spence et al., 2014; Steinmetz et al., 2012; Wang et al., 2013; Winzelberg et al., 2003), 7 reported subscale scores only (Hirai & Clum, 2005; Hirai et al., 2012; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Stockton et al., 2014; Wagner et al., 2006), and 4 reported both (Beyer, 2011; Kersting et al., 2013; Knaevelsrud et al., 2010). Six publications reported follow-up assessments (Carpenter et al., 2014; Hirai et al., 2012; Litz et al., 2007; Spence et al., 2014; Stockton et al., 2014; Wang et al., 2013) that tracked the course of symptomatology from 5 up to 24 weeks post intervention.

## 3.6. Internet-based interventions

## 3.6.1. Programs based on cognitive behavioral therapy

Fifteen studies evaluated IBIs based on CBT (CBT-IBI). Seven adapted the CBT manual of *Interapy* to different trauma types and samples (Kersting et al., 2013; Kersting et al., 2011; Knaevelsrud et al., 2015; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Wagner et al., 2006). All *Interapy*-based programs were characterized by the same number of sessions, the provision of therapeutic support, and none of them used multimedia components and reminder functions. The remaining programs, namely *Coping with Cancer* (Carpenter et al., 2014), *My Trauma Recovery* (Wang et al., 2013), *DESTRESS* (Litz et al., 2007), *My Disaster Recovery* (Steinmetz et al., 2012) and others that were not specified by name (Hirai & Clum, 2005; Owen et al., 2005; Spence et al., 2011; Spence et al., 2014) combined general and trauma specific CBT techniques such as self-confrontation and cognitive restructuring. Some included interventions derived from social cognitive theory, or adaptive coping techniques and stress management trainings (Litz et al., 2007; Spence et al., 2014),

relaxation (Carpenter et al., 2014; Steinmetz et al., 2012; Wang et al., 2013), self-monitoring (Litz et al., 2007) or social skills trainings (Carpenter et al., 2014; Owen et al., 2005; Spence et al., 2011).

## 3.6.2. Programs based on expressive writing

Five programs followed emotional disclosure theories (e.g. Pennebaker, 1997), using EW approaches (Beyer, 2011; Hirai et al., 2012; Possemato et al., 2010; Stockton et al., 2014; Winzelberg et al., 2003). Four of these were quite similar with respect to the interventions and instructions to the participant (Beyer, 2011; Hirai et al., 2012; Possemato et al., 2010; Stockton et al., 2014), which were to write about the traumatic event and to disclose their deepest thoughts and feelings associated with it. In contrast, the program *Bosom Buddies* (Winzelberg et al., 2003) embedded the main task of expressive writing in a discussion forum in which participants shared each other's experiences, thoughts and feelings. Here, different topics were captured for the expressive writing tasks, such as 'self and body image', 'meaning of life', 'friendship' or 'sexuality'. Table 1 gives an overview of the characteristics of the studies and programs, grouped by therapeutic approach.

## 3.7. Comparison conditions

Thirteen studies (12 CBT-IBIs and 1 EW-IBI) used a waiting list design, i.e. a passive control condition (Carpenter et al., 2014; Hirai & Clum, 2005; Kersting et al., 2013; Kersting et al., 2011; Knaevelsrud et al., 2015; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Owen et al., 2005; Spence et al., 2011; Wagner et al., 2006; Wang et al., 2013; Winzelberg et al., 2003). The remaining 3 CBT-IBIs used active comparison conditions, either psychoeducation that was described as 'information-only websites' (Spence et al., 2014; Steinmetz et al., 2012), or control writing, i.e. writing about non-trauma related daily hassles (Litz et al., 2007). Of note is that Steinmetz et al. (2012) compared the treatment group to a second active comparison condition involving usual care in a face-to-face setting. We chose to

#### Author Year Country Manual/ Population Symptom Trauma Outcome Intervention N Control N Therap. Sessions/ Assessment reminder/ Duration <sup>1</sup> level support media Interventions based on expressive writing Beyer 2011 USA GP, Sub-IES-R N/ Y/ N BL, Post Diverse n.n., 39/36/40 \* CW. 36 \* Differs 3/1.5 students clinical (S, A, I, H) Hirai 2012 USA GP, NOS IES-R CW, 50 \* N/ Y/ N 3/1 BL, Post, Diverse n.n., 54\* No (A, I, H) FU (5) students Possemato USA GP. NOS Kidney PCL n.n., 25 Δ CW, 23 $\Delta$ N/N/N3/1,5 **BL**. Post No 2010 patients transplant (S, A, I, H) GP NOS IES-R n.n., 14\* CW, 10 \* N/Y/N3/1 BL, Post, Stockton Great Diverse No 2014 Britain (A, I, H) FU (8) USA Winzelberg GP, NOS Bosom Buddies. Y/Y/N12/12BL, Post Cancer PCL-C(S) WL, 36 † No 2003 36 † women Interventions based on cognitive behavioral therapy USA WL, 61 † Y/ Y/ Y BL, Post, Carpenter GP, NOS Cancer IES (S) Coping with No 10/102014 Cancer, 71 † FU (20) women USA SRQF Hirai 2005 GP NOS Diverse n.n., 13 Δ WL, 14 Δ Y/Y/Y8/8 BL, Post No (A, I, H) IES-R BL, Post Kersting, Germany GP, NOS Pregnancy Interapy, 115 † WL, 113 † Yes Y/N/N10/5 2013 (S, A, I, H) loss parents Kersting, Germany GP, NOS IES (S) Interapy, 45 † WL, 33 † Y/N/N10/5 BL, Post Pregnancy Yes 2011 women loss

STUDY 2

Table 1.	Characteristics	of included studie	s, grouped b	y therapeutic appr	oach the interventio	on is based on

Continuation of Table 1 on the following page.

Author Year	Country	Population	Symptom	Trauma	Outcome	Intervention N	Control N	Therap.	Manual/	Sessions/	Assessment
			level					support	reminder/	Duration <sup>1</sup>	
									media		
Knaevelsrud	Middle	GP	Clinical	War, terror	PDS	Interapy, 79 †	WL, 80 †	Yes	Y/ N/ N	10 / 5	BL, Post
2015	East				(S, A, I, H)						
Knaevelsrud	Nether-	GP	NOS	Diverse	IES-R	Interapy, 49 †	WL, 47 †	Yes	Y/N/N	10 / 5	BL, Post
2007	lands				(A, I, H)						
Lange 2003	Nether-	GP,	NOS	Diverse	IES (A, I)	Interapy, 69 *	WL,32 *	Yes	Y/N/N	10 / 5	BL, Post
	lands	students									
Lange 2001	Nether-	GP	NOS	Diverse	IES (A, I)	Interapy, 13 *	WL, 12 *	Yes	Y/N/N	10 / 5	BL, Post
	lands										
Litz 2007	USA	GP, service	Clinical	War, terror	PSSI (S)	DESTRESS, 24	CW, 21 †	Yes	Y/N/N	6 / 8	BL, Post,
		members				†					FU (12, 24)
Owen 2005	USA	GP,	NOS	Cancer	IES (S)	n.n. , 26 *	WL, 27 *	No	Y/Y/Y	6 / 12	BL, Post
		women									
Spence 2014	Australia	GP	Clinical	Diverse	IES-R (S)	n.n., 59 †	PE, 66 †	Yes	Y/Y/Y	6 / 8	BL, Post,
											FU (12)
Spence 2011	Australia	GP	Clinical	Diverse	PCL-C (S)	n.n., 23 †	WL, 21 †	Yes	Y/Y/Y	7 / 8	BL, Post
Steinmetz	USA	GP	NOS	Natural	MPSS (S)	My Disaster	PE, 19†	No	Y/Y/Y	6 / 4	BL, Post
2012				disaster		Recovery, 18 †					

Table 1	(cont.).	Characteristics	of included studies	s. grouped b	v therapeutic	approach the	e intervention is	based on

Continuation of Table 1 on the following page.

Author Year	Country	Population	Symptom level	Trauma	Outcome	Intervention N	Control N	Therap. support	Manual/ reminder/ media	Sessions/ Duration <sup>1</sup>	Assessment
Wagner 2006	Switzer- land	GP	NOS	Loss	IES (A, I)	Interapy, 26*	WL, 25 *	Yes	Y/ N/ N	10 / 5	BL, Post
Wang 2013	China	GP	NOS	Diverse / Natural disaster	PDS (S)	My Trauma Recovery, 49 † / 50 † N <sub>analyzed</sub> = 973	WL, 45 †/ 53 †, N analyzed = 805	No	Y/ N/ Y	6 / 4	BL, Post, FU (12)

### Table 1 (cont.). Characteristics of included studies, grouped by therapeutic approach the intervention is based on

Note. <sup>1</sup>, number of session/ duration in weeks; A, PTSD avoidance; BL, Baseline; FU (xx), Follow Up (weeks); GP, General population; H, PTSD hyperarousal; I, PTSD intrusion; n.n., non nomen; NOS, not otherwise specified; PE, Psychoeducation; Post, Post assessment; S, PTSD global sum; WL, Waiting list; \*, N analyzed in completeranalysis; †, N analyzed in intention-to-treat analysis; Δ, no information provided on applied analysis.

include the psychoeducation control condition, because all other active comparison conditions across studies were internet-based and without face-to-face contact. Four EW-IBIs used active control writing exercises, mostly writing about the daily routine or time management (Beyer, 2011; Hirai et al., 2012; Possemato et al., 2010; Stockton et al., 2014).

## 3.8. Program components

Table 2 gives an overview of the program components tested in the subgroup analyses. The subgroup analyses had to be restricted to CBT due to a substantial or total confounding of the components' specifications with the therapeutic approach of EW. Furthermore, for CBT the analyses had to be restricted to the PTSD sum scale at post assessment due to a lack of studies that reported outcome on the sub-symptom scales. The subgroup analysis on manual use was also not applicable for CBT, because we identified a total confounding with the therapeutic approach.

## 3.8.1. Therapeutic support

Ten of the 15 CBT-IBIs provided therapeutic support (Kersting et al., 2013; Kersting et al., 2011; Knaevelsrud et al., 2015; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Litz et al., 2007; Spence et al., 2011; Spence et al., 2014; Wagner et al., 2006). The therapeutic feedback was delayed and tailored to the clients written reports. Of the EW-IBIs, only Beyer (2011) tested support conditions ('no contact', 'immediate contact', 'delayed contact'). The remaining EW-IBIs did not provide therapeutic support.

## 3.8.2. Number of sessions, manual use

Of all CBT programs, 5 provided 6 sessions over 4 to 12 weeks (Litz et al., 2007; Owen et al., 2005; Spence et al., 2014; Steinmetz et al., 2012; Wang et al., 2013), 1 provided 7 sessions over 8 weeks (Spence et al., 2011), 1 provided 8 sessions over 8 weeks (Hirai & Clum, 2005) and 8 provided 10 sessions over 5 to 10 weeks (Carpenter et al., 2014; Kersting et al., 2013;

Kersting et al., 2011; Knaevelsrud et al., 2015; Knaevelsrud & Maercker, 2007; Lange et al., 2003; Lange et al., 2001; Wagner et al., 2006). All CBT-IBIs were manual-based. Four of the 5 EW-IBIs included 3 writing sessions within one up to one and a half week (10 days) and were not manual-based. Only Winzelberg et al. (2003) was manual-based and comprised 12 sessions during 12 weeks.

Ther.	number	Manual	Reminder	Multimedia	Therapeutic support		
Appr.	sessions				Therapeutic support	No therapeutic support	
EW	3	no	yes	no	Beyer, 2011 <sup>1</sup> * †	Beyer, 2011 <sup>1</sup> * †	
						Hirai, 2012*	
						Stockton, 2014*	
EW	3	no	no	no		Possemato, 2010*†	
EW	12	yes	yes	no		Winzelberg, 2003†	
CBT	10	yes	no	no	Kersting, 2013* †		
					Kersting, 2011 †		
					Knaevelsrud, 2015* †		
					Knaevelsrud, 2007*		
					Lange, 2003*,		
					Lange, 2001*		
					Wagner, 2006*		
CBT	10	yes	yes	yes		Carpenter, 2014 †	
CBT	8	yes	yes	yes		Hirai, 2005 *	
CBT	7	yes	yes	yes	Spence, 2011†		
CBT	6	yes	no	no	Litz, 2007 †		
CBT	6	yes	no	yes		Wang, 2013 †	
CBT	6	yes	yes	yes	Spence, 2014 †	Owen, 2005 †	
						Steinmetz, 2012†	

Table 2. Classification of programs

Note. <sup>1</sup>, intervention compared different treatment groups testing both conditions against each other; †, study reported on PTSD sum scale; \*, study reported on sub-symptom level.

## 3.8.3. Multimedia components, reminder functions

Seven CBT-IBIs used multimedia components, e.g. videos or audio vignettes (Carpenter et al., 2014; Hirai & Clum, 2005; Owen et al., 2005; Spence et al., 2011; Spence et al., 2014; Steinmetz et al., 2012; Wang et al., 2013) and 6 used reminder functions (Carpenter et al., 2014;

Hirai et al., 2012; Owen et al., 2005; Spence et al., 2011; Spence et al., 2014; Steinmetz et al., 2012). All but one EW-IBI (Possemato et al., 2010) used reminders, none used multimedia.

## 3.9. Primary analyses of therapeutic approach and comparison condition

All mean effect sizes are displayed in Table 3. Appendix B displays the forest plots for the analyses of PTSD sum, avoidance, intrusion, and hyperarousal scales. Due to the small number of studies available, only the comparisons displayed in table 3 were applicable. Consequently, also differences between the effect sizes of the subgroups were testable for the respective comparisons, only.

## 3.9.1. CBT-IBIs versus active and passive control conditions at post assessment

CBT was associated with large effect sizes for PTSD sum (k = 8, g = 0.95, p < .001) when compared to passive control conditions, but the data set was heterogeneous. Sensitivity analyses identified Carpenter et al. (2014) as an outlier that significantly contributed to the wide confidence interval, and its exclusion resulted in a homogeneous data set with a moderate mean effect size (k = 7, g = 0.72, 95% CI [0.57 - 0.86], p < .001). Large effects of CBT were found for avoidance (k = 7, g = 0.83, p < .001) and intrusion (k = 7, g = 0.82, p < .001), while a medium effect was found for hyperarousal (k = 4, g = 0.66, p < .001), all cases compared to passive control conditions. When compared to active control conditions, the effect for PTSD sum scale was not significant, indicating that CBT-IBI was not superior to the active control treatment.

## 3.9.2. EW-IBIs versus active and passive control conditions at post assessment

When compared to an active control condition, none of the effect sizes for PTSD sum scale, avoidance, intrusion and hyperarousal were significant, indicating that EW-IBI did not outperform active treatment.

## 3.9.3. Follow-up assessment

With regard to PTSD sum score at follow-up, all includable studies were CBT-based. A large but non-significant effect was found in comparison to passive control conditions. Sensitivity analysis again identified Carpenter et al. (2014) as an outlier causing the wide confidence interval. Excluding this study eliminated the heterogeneity in the data set and reduced the effect size, still resulting in a non-significant difference between the CBT-IBIs and passive control conditions on the PTSD total score (k = 2, g = 0.48, 95% CI [-0.11 – 1.07], p = .109). The comparison to active control conditions also did not result in a significant effect. To sum up, at follow-up CBT-based IBIs did not outperform either active or passive control conditions on the PTSD sum score. Regarding avoidance, intrusion and hyperarousal, all includable studies were EW-based and each compared the treatment to active control writing conditions. Whereas no significant follow-up effect was given for avoidance, the effect sizes for intrusion (k = 2, g = 0.50, p < .01) and hyperarousal (k = 2, g = 0.46, p < .05) were small to medium and significant. Thus, over a follow-up period of 5 to 8 weeks, EW outperformed control writings in reducing intrusive and hyperarousal symptoms.

## 3.9.4. 'Interapy' based programs

In addition, we tested the efficacy of this specific CBT subgroup in a separate data set, as all components were kept similar across the seven studies applying *Interapy* 'based programs. With regard to the PTSD sum, avoidance and intrusion scales, large effects were achieved (0.81 < g < 0.84, all p < .001), as well as a medium effect on hyperarousal (k = 3, g = 0.68, p < .001). All comparisons utilized passive control groups. There was no heterogeneity.

Assessment	k	Hedges' g [95% CI]♦	Q, significance of Q, I <sup>2</sup>	Comparison †	
PTSD global sum s	scale	, post assessment			
CBT <sup>1</sup>	8	0.95*** [0.46 - 1.43]	$Q = 80.07,  p < .001,  I^2 = 91.26$	n. a.	
$EW^{-1}$	1	0.43 [-0.03 - 0.90]	n. a.		
CBT <sup>2</sup>	3	0.09 [-0.19 - 0.36]	$Q = 0.30, p = .862, I^2 = 0$	p = .491	
EW <sup>2</sup>	2	0.24 [-0.11 – 0.59]	$Q = 0.64, p = .420, I^2 = 0$		
Avoidance, post as	sessi	nent			
CBT <sup>1</sup>	7	$0.83^{***} \left[ 0.67 - 0.98 \right]$	$Q = 5.32, p = .504, I^2 = 0$		
EW <sup>2</sup>	4	0.20 [-0.05 - 0.44]	$Q = 1.23, p = .747, I^2 = 0$		
Intrusion, post ass	essm	ent			
CBT <sup>1</sup>	7	0.82*** [0.64 - 1.01]	$Q = 7.46, p = .281, I^2 = 19.52$		
EW <sup>2</sup>	4	0.28 [-0.01 - 0.56]	$Q = 3.77, p = .287, I^2 = 20.45$		
Hyperarousal, post assessment					
CBT <sup>1</sup>	4	$0.66^{***} [0.48 - 0.83]$	$Q = 2.24, p = .525, I^2 = 0$		
EW <sup>2</sup>	4	0.21 [-0.04 - 0.46]	$Q = 1.12, p = .771, I^2 = 0$		
Follow Up – CBT					
PTSD sum <sup>1</sup>	3	1.64 [-0.34 – 3.61]	$Q = 114.34,  p < .001,  I^2 =$		
			98.25		
PTSD sum <sup>2</sup>	2	0.21 [-0.14 - 0.55]	$Q = 1.12, p = .269, I^2 = 18.01$		
Follow $Up - EW^2$					
Avoidance	2	0.31 [-0.03 - 0.66]	$Q = 0.00, p = .950, I^2 = 0$		
Intrusion	2	0.50 ** [0.15 - 0.84]	$Q = 0.00, p = .987, I^2 = 0$		
Hyperarousal	2	0.46 * [0.11 - 0.80]	$Q = 0.07, p = .789, I^2 = 0$		
Interapy based pro	ogran	is <sup>1</sup>			
PTSD sum	3	$0.81^{***} \left[ 0.62 - 1.00 \right]$	$Q = 0.42, p = 0.81, I^2 = 0$		
Avoidance	6	$0.84^{***} \left[ 0.68 - 1.00 \right]$	$Q = 4.97, p = 0.419, I^2 = 0$		
Intrusion	6	$0.82^{***}$ [ $0.62 - 1.02$ ]	$Q = 7.14, p = 0.211, I^2 = 29.94$		
Hyperarousal	3	$0.68^{***} \left[ 0.49 - 0.86 \right]$	$Q = 1.48, p = 0.478, I^2 = 0$		

Table 3. Primary analyses on therapeutic approach

Note.  $\blacklozenge$ , analysis based on random effects model;  $\dagger$ , analysis based on mixed effects analysis; <sup>1</sup>, analysis included passive control conditions only; <sup>2</sup>, analysis included active control conditions only; CBT, cognitive behavioral therapy; EW, expressive writing; k, number of studies; n. a., not applicable; \*, p < .05; \*\*, p < .01; \*\*\*, p < .001.

## 3.10. Subgroup analyses on program components

As described in 3.8, the number of subgroup analyses was somewhat restricted due to confounding and the small number of studies. Furthermore, examining the differences between the effect sizes for significance was possible for subgroups utilizing passive comparison conditions, only. The results are displayed in table 4 and described below.

### 3.10.1. Therapeutic support

When compared to passive control conditions IBIs that did not provide therapeutic support resulted in a large but non-significant effect size with a very wide confidence interval. Sensitivity analysis again identified Carpenter et al. (2014) as an outlier. The exclusion reduced the heterogeneity to non-significance, leaving a moderate and significant effect (k = 3, g = 0.54, 95% CI [0.22 – 0.86], p = .001). IBIs that provided therapeutic support resulted in a large effect size (k = 4, g = 0.80, p < .001) when compared to passive control conditions. However, there were no significant differences between the effect sizes for IBIs with and without therapeutic support, either including (p = .584) or excluding (p = .164) the outlier. Finally, compared to active control conditions neither the mean effect size for IBIs providing support nor the effect size of the one study without support differed significantly from zero.

## 3.10.2. Number of sessions

IBIs providing 10 sessions yielded a large effect size (k = 4, g = 1.33, p < .01) with a wide confidence interval when compared to passive comparison conditions. Again, we identified Carpenter et al. (2014) as an outlier and the exclusion of this study reduced the heterogeneity to non-significance, leaving a large effect with adequate 95% CI limits (k = 3, g = 0.81, 95% CI [0.62 - 1.00], p < .001). IBIs providing less than ten sessions achieved a medium effect size (k = 4, g = 0.57, p < .001) when compared to passive comparison conditions. However, both with (p = .098) and without (p = .136) the outlier study there was no significant difference between the effect sizes for longer and for shorter IBIs. Compared to active comparison conditions, the effect size for IBIs providing less than ten sessions was not significant. No studies with ten treatment sessions and active comparison conditions were available.

### 3.10.3. Reminder functions

Compared to passive control conditions IBIs without reminder function resulted in a medium effect size (k = 5, g = 0.76, p < .001). IBIs that provided reminders yielded a large but

non-significant effect. Once more, sensitivity analysis identified Carpenter et al. (2014) as an outlier; excluding it resulted in a homogeneous data set with a small and non-significant effect (k = 2, g = 0.43, 95% CI [-0.04 – 0.91], p = .073). The difference between both effect sizes was not significant, either including or excluding the outlier (p = .550, p = .199). When testing against active control conditions no significant effect was found for IBIs providing reminders, and the one study that did not apply a reminder also resulted in a non-significant primary effect.

### 3.10.4. Multimedia component

Both IBIs that used multimedia components and those that did not resulted in large effect sizes when compared to passive comparison conditions (k = 5, g = 1.04, p < .05; k = 3, g = 0.81, p < .001, resp.). Removing the outlier (Carpenter et al., 2014) from this multimedia subgroup left a homogeneous data set with a medium effect (k = 4, g = 0.57, 95% CI [0.33 – 0.82], p < .001). The difference between IBIs with and without multimedia was not significant, both including and excluding the outlier (p = .637, p = .136). IBIs using multimedia components did not significantly differ from active control groups. None of the studies tested IBIs without multimedia components against active comparison conditions.

Subgroup	k	Hedges' g [95% CI] ♦	Q, significance of Q, I <sup>2</sup>	Comparison †
Therapeutic support				
Not given <sup>1</sup>	4	1.12 [-0.02 - 2.27]	$Q = 76.53, p < .001, I^2 = 96.08$	p = .584
Given <sup>1</sup>	4	0.80*** [0.62 - 0.98]	$Q = 0.54, p = .909, I^2 = 0$	
Not given <sup>2</sup>	1	0.12 [-0.51 - 0.75]	n. a.	n. a.
Given <sup>2</sup>	2	0.08 [-0.22 - 0.38]	$Q = 0.28, p = .595, I^2 = 0$	
Number of sessions				
Ten <sup>1</sup>	4	1.33 ** [0.47 – 2.19]	$Q = 65.09, p < .001, I^2 = 95.39$	p = .098
Less than ten <sup>1</sup>	4	0.57 *** [0.33 – 0.82]	$Q = 3.31, p = .346, I^2 = 9.37$	
Ten <sup>2</sup>	0	n. a.	n. a.	n. a.
Less than ten <sup>2</sup>	3	0.09 [-0.19 - 0.36]	$Q = 0.30, p = .862, I^2 = 0$	

Table 4. Subgroup analyses on program components for CBT, PTSD sum score at post assessment

Table 4 is continued on the following page.

Subgroup	k	Hedges' g [95% CI] ♦	Q, significance of Q, I <sup>2</sup>	Comparison †
Reminder				
Not given <sup>1</sup>	5	$0.76^{***} \left[ 0.60 - 0.92 \right]$	$Q = 2.28, p = .687, I^2 = 0$	p = .550
Given <sup>1</sup>	3	1.30 [-0.46 - 3.06]	$Q = 63.68, p < .001, I^2 = 96.86$	
Not given <sup>2</sup>	1	0.21 [-0.24 – 0.37]	n.a.	n. a.
Given <sup>2</sup>	2	0.05 [-0.26 - 0.36]	$Q = 0.06, p = .806, I^2 = 0$	
Multimedia				
Not given <sup>1</sup>	3	0.81*** [0.62 - 1.00]	$Q = 0.42, p = .810, I^2 = 0$	p = .637
Given <sup>1</sup>	5	1.04* [0.10 – 1.98]	$Q = 77.72, p < .001, I^2 = 94.85$	
Not given <sup>2</sup>	0	n. a.	n. a.	n. a.
Given <sup>2</sup>	3	0.09 [-0.19 – 0.36]	$Q = 0.30, p = .862, I^2 = 0$	

Table 4 (cont.). Subgroup analyses on program components for CBT, PTSD sum score at post assessment

Note.  $\blacklozenge$ , analysis based on random effects model;  $\dagger$ , analysis based on mixed effects analysis;<sup>1</sup>, analysis included passive control conditions only; <sup>2</sup>, analysis included active control conditions only; CBT, cognitive behavioral therapy; k, number of studies; \*, p < .05; \*\*, p < .01; \*\*\*, p < .001.

## 3.11. Dropout analysis

For the purpose of this meta-analysis, the dropout rate was defined as the percentage of participants that did not complete the whole course of treatment after having been assigned to a condition. For EW-IBIs, on average 15.83% of participants in the treatment, 16.7% in the passive and 15.98% in the active comparison conditions were reported as dropouts. EW-IBIs providing no support lost 18.74% compared to 8.55% participants in supported treatments. Over all CBT-IBIs, on average 23.23% of the participants allocated to treatment, 16.49% allocated to passive and 21.67% to active comparison conditions were reported as dropouts. CBT-IBIs that provided support and those that did not reported comparable dropouts, namely 22% to 23.93% in the treatment conditions. Only few studies provided information about the sociodemographic characteristics of the completers and dropouts (see table 5). Three studies reported no significant association of age with the dropout rate (Beyer, 2011; Knaevelsrud et al., 2015; Wang et al., 2013), but Kersting et al. (2013) and Lange et al. (2003) found that completers were significantly older than dropouts. However, Litz et al. (2007) found completers to be younger. A few studies have reported equality between dropouts and completers with

Table 5. Dropout analyses

2007

Author, year	Dropout rates intervention : control	Completers' characteristic in comparison to dropouts' characteristic			
Interventions base		vriting, passive comparison condition			
Winzelberg,	22.2% *:	- No differences on demographics (NOS)			
2003	16.7%	- No differences on psychopathology (NOS)			
Interventions base	ed on expressive w	vriting, active comparison condition			
Beyer, 2011 <sup>1</sup>	12.2%†/4.9%	- No differences on demographics (age, gender, ethnicity)			
	†/ 2.4 % * :	- No differences on psychopathology (functioning, PTSD, PTG			
	10%	physical health)			
Hirai, 2012	19.4% *:	- No differences on demographics (NOS)			
	24.2%	- Completers higher hyperarousal			
		- Completers higher avoidance			
Possemato,	4% *:13%	- No differences on demographics (NOS)			
2010		- Completers higher PTSD			
		- Completers lower quality of life			
Stockton,	45.7% *:	- No differences on demographics (NOS)			
2014	16.7%	- Completers higher intrusion			
Mean, EW AC	14.77% (range 2	2.4% – 45.7%) : 15.98% (range 10% – 24.2%)			
Mean, EW, †	8.55% (range 4.	9% – 12.2%) : 10%			
Mean, EW, *	18.74% (range 2	2.4% – 45.7%) : 16.12% (range 10% – 24.2%)			
Mean, EW	15.83% (range 2	2.4% – 45.7%) : 16.12% (range 10% – 24.2%)			
Interventions base	ed on cognitive be	havioral therapy, passive comparison condition			
Carpenter,	21.1% *:3.3%	- No differences on demographics (NOS)			
2014		- No differences on psychopathology (NOS)			
Hirai, 2005	27.8% *:	- No differences on demographics (NOS)			
	6.7%	- Not reported on psychopathology			
Kersting,	13.9% † :	- Completers older			
2013	11.5%	- Completers' loss occurred later during pregnancy			
		- Completers' time since pregnancy loss dates back longer			
		- No differences on psychopathology (NOS)			
Kersting,	28% † : 21%	- Completers' time since pregnancy loss dates back shorter			
2011		- No differences on psychopathology (PTSD, grief, overall menta			
		health, depression, somatization, anxiety)			
Knaevelsrud,	40.5% † :	- No differences (age, gender, education, marital status, profession)			
2015	41.2%	- No differences on the number of traumatic events/ the type of traum			
		- No differences on psychopathology (PTSD, anxiety, depression)			
Knaevelsrud,	16.3 % † : 2%	- Not reported on demographics			

-

Not reported on psychopathology

regard to gender (Beyer, 2011; Knaevelsrud et al., 2015; Litz et al., 2007; Wang et al., 2013), education (Knaevelsrud et al., 2015; Lange et al., 2003; Wang et al., 2013), ethnicity or minority status (Beyer, 2011; Litz et al., 2007), marital status (Knaevelsrud et al., 2015; Wang et al., 2013) or profession / income (Knaevelsrud et al., 2015; Wang et al., 2013). Only four studies provided information on trauma-related characteristics of the completers and dropouts (see table 5). One study reported no differences between completers and dropouts in the number of traumatic events and the trauma type (Knaevelsrud et al., 2015), and Lange et al. (2003) found no differences between completers and dropouts in the trauma occurred. However, Kersting et al. (2013) reported that the completers' traumatic event dates back longer, whereas Kersting et al. (2011) reported the opposite. Fourteen studies conducted analyses of baseline psychopathology, and four reported higher baseline PTSD-associated symptoms for completers compared to dropouts (Hirai et al., 2012; Lange et al., 2001; Possemato et al., 2010; Stockton et al., 2014). Importantly, all other studies did not present any results for dropout characteristics.

## 3.12. Publication bias

Publication bias analyses were applicable for three data sets at post assessment, namely for the subgroup investigating CBT-IBIs compared to passive comparison conditions on the PTSD global symptom score after the removal of the outlier study, as well as the subgroups regarding avoidance and intrusion. As can be seen in appendix C, for the PTSD sum data set Begg and Mazumdar's test was significant, but neither Egger's regression nor trim-and-fill indicated missing studies. For the avoidance data set, neither Begg and Mazumdar's rank correlation nor Egger's regression indicated publication bias. Trim-and-fill imputed two missing studies, but the adjusted effect size did not differ significantly from the original effect. For the intrusions data set, both Begg and Mazumdar and Egger indicated bias, and trim-andfill found four missing studies, but the reduction in effect size again was not significant. Thus, we can conclude that despite a minor tendency towards bias, this has no significant effect on the efficacy of CBT in the data sets under scrutiny.

### 4. Discussion

The findings of this meta-analysis provide support for the efficacy of CBT-IBIs in treating PTSD. Moderate to large effect sizes were found for PTSD global symptom severity as well as for the subscales for avoidance, intrusion, and hyperarousal, when compared to passive control conditions. These findings are in line with a recent meta-analysis that demonstrated a large effect of telehealth interventions for PTSD compared to passive conditions (Sloan et al., 2011). Internet-based treatments also resulted in moderate to large effects for other disorders such as anxiety (Cuijpers et al., 2009; Reger & Gahm, 2009; Tulbure, 2011) and small to moderate ones for depression (Andersson & Cuijpers, 2009; Cowpertwait & Clarke, 2013; Richards & Richardson, 2012; So et al., 2013). Meta-analyses investigating TF-CBT for PTSD delivered face-to-face resulted in larger effects (Bisson et al., 2013; Bisson et al., 2007; Bradley et al., 2014; Butler, Chapman, Forman, & Beck, 2006; Ehring et al., 2014; Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010), but as the evidence is based on different samples, it is not directly comparable with the current findings, and RCTs investigating face-to-face and internetdelivered TF-CBT for PTSD are entirely lacking. Therefore, we conclude that the evidence for IBIs is very encouraging, but the next step of direct comparisons to face-to-face therapy is still pending.

When compared to active control conditions such as psychoeducation or control writing tasks, no significant evidence was found for the superiority of either CBT or EW-IBIs in the reduction of PTSD symptoms. This is a common effect that has also been found in telehealth intervention (Sloan et al., 2011) and face-to-face treatment research for PTSD (Bisson et al., 2013; Bisson et al., 2007; Bradley et al., 2014; Butler et al., 2006; Ehring et al., 2014; Powers et al., 2010), as well as for internet-assisted interventions for other disorders (Andersson &

Cuijpers, 2009; Cheng & Dizon, 2012; Cowpertwait & Clarke, 2013; Grist & Cavanagh, 2013; Macea, Gajos, Calil, & Fregni, 2010; Reger & Gahm, 2009; So et al., 2013; Spek et al., 2007; van Beugen et al., 2014; Webb, Joseph, Yardley, & Michie, 2010). The effect sizes reported in the literature for comparisons to active control groups all varied between non-significant and small; if larger effects were reported, they were accompanied by wide confidence intervals, restricting the interpretation of the underlying true effect size. However, a likely reason for the null results found in the current meta-analysis is the low number of studies on which the comparisons of IBIs to active control groups were based. According to Cohen (1992), the sample sizes for comparisons to active treatments are set at N = 26 for a power of 0.80 (p <0.05). As a significant number of active control studies in our data sets included small samples, and moreover the respective data sets themselves comprised only few studies, the current testing of efficacy was underpowered. Some of the meta-analyses cited above likewise discuss underpowered testing as a presumptive explanation for their null results (e.g. Sloan et al., 2011).

Dropout rates were found to be 23.23% for CBT and 15.83% for EW, indicating that dropout is almost one third higher in CBT. One can only speculate whether this is due to potentially more distressing tasks, such as exposure, or the longer duration of CBT treatments. It should be noted that the dropout rates for CBT in the current meta-analysis were comparable to those found in face-to-face therapy, e.g. Bradley et al. (2014) reported in a recent meta-analysis that 21.1% of participants did not complete treatment. Moreover, we found that dropouts for CBT with therapeutic support (22%) were hardly different from CBT without support (23.93%). By contrast, EW treatment with support has a dropout rate of 8.55%, about half that of EW treatment without support (18.74%). However, the results for this EW comparison are based on a very small number of studies. Finally, the dropout rates in the current meta-analysis between EW and the control groups (15.89 - 16.7%) hardly differed, but dropout in the active comparisons applied in the RCTs investigating CBT was somewhat higher (21.67%) and closer to dropout under CBT treatment. All in all, the results nevertheless indicate

a good acceptance of the internet-based programs. Regrettably, the data base about differences in sociodemographic and psychopathological characteristics between dropouts and completers was rather incomplete due to the lack of comprehensive reporting in the primary studies. Furthermore, the available results were mixed. Therefore, as the degree to which these results can be generalized is limited, we refrain from any overall conclusions.

Few studies in the current meta-analysis reported follow-up results. CBT was of large efficacy at post-test, but after the removal of one outlier only two studies reported follow-up data and the combined effect was not significant. For EW also only two studies reported follow-up results with significant effects, even though EW was not efficacious at post-treatment. However, these comparisons were underpowered and different numbers of studies were included in the post compared to the follow-up assessments. Moreover, the follow-up time intervals in the included studies were rather short with a maximum of 24 weeks. Recently, large effects have been found in two non-randomized studies for CBT-IBIs after a period of 1.5 years (Knaevelsrud & Maercker, 2010; Wagner & Maercker, 2007). Therefore, we consider the current evidence base as inconclusive and preliminary and recommend more research to be conducted before any firm conclusions about the long-term efficacy of IBIs for PTSD can be drawn.

Moreover, we aimed at investigating the impact of specific program components on the overall efficacy of IBIs. However, EW and CBT based IBIs differed substantially with regard to study and program characteristics. All CBT-IBIs were manual-based and comprised at least six sessions, whereas all but one of the EW-IBIs were much shorter, not manual-based and without therapeutic support. Because of the substantial confounding and overlap with certain program components for EW, the small number of studies, and the fact that it was mainly compared to active control conditions and resulted in non-significant effects, an investigation of the impact of specific program characteristics was impossible for EW. Therefore, we focused

on the contribution of such components to the overall efficacy of CBT. Here, all comparisons were made to passive control groups.

The relevance of therapeutic support delivered via the internet was of particular interest. CBT-IBIs that provided support resulted in a large effect, whereas a medium effect was obtained without support. However, given that the difference between the effects was not significant in our analysis, no conclusion concerning the impact of the provision of therapeutic support on the efficacy of CBT-IBIs can be made to date. On the one hand, the effect sizes agree with earlier meta-analyses on the efficacy of internet and computer-based treatments in depressive and anxious samples, which reported higher effect sizes if support was provided than for self-guided treatments (Andersson & Cuijpers, 2009; Cowpertwait & Clarke, 2013; Grist & Cavanagh, 2013; Richards & Richardson, 2012; Spek et al., 2007). On the other hand, it is speculative to conjecture about the impact of therapeutic support on the efficacy of CBT-IBIs. Future research needs to examine this important program component systematically.

The duration of treatment was also of interest with respect to dose-response effects. We found that the provision of more treatment sessions was beneficial and resulted in a large effect after the removal of the outlier study, whereas CBT with fewer than ten sessions resulted in a medium effect. However, the difference between both conditions was once more not significant, precluding any definite conclusions with regard to the optimal length of treatment.

Finally, we were interested in investigating the impact of two setting-specific technical components linked to the mode of delivery of treatment via the internet. Our meta-analysis provides preliminary evidence that the provision of reminders and multimedia is not associated with higher efficacy of treatment. Whereas CBT without reminders resulted in a medium effect size, no significant effect was found for CBT including reminders. The efficacy of CBT without multimedia is large and with multimedia moderate, after the removal of the outlier study. However, these differences were not significant.

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Overall, we conclude that based on the current evidence no definite recommendations for an optimal program design can be drawn yet. First, the number of studies in each comparison was restricted. The null results between the different variants of program characteristics might stem from insufficiently powered comparisons, and a broader data base is necessary to test for differences. Second, the programs under comparison not only differed in the respective component, but also on a number of other characteristics that likely influenced the results over and above the components we intended to focus on. Specific variations of single components within otherwise identical treatments are necessary in future research to produce valid evidence for the specific treatment characteristics. Furthermore, not only were very different samples and trauma types included in the studies under comparison, the CBT-programs also differed slightly, as some included additional modules such as stress management, for example. Moreover, some of the studies were included in more than one comparison, for instance the same study might be included in the comparison for therapeutic support versus self-help and also in the comparison for multimedia components. In summary, we therefore refrain from any speculative interpretations. Future research must rely on high quality clinical trials that carefully disentangle the role of different program components for the efficacy. Furthermore, since faceto-face research suggests tailoring of CBT treatment components with respect to particular needs and specific topics associated with the trauma of the patients (Difede, Olden, & Cukor, 2014), this might be true for IBIs as well.

In a number of subgroup-analyses significant heterogeneity affected the interpretation of the effect size obtained. However, by applying sensitivity analysis we were able to identify one outlier study (Carpenter et al., 2014) that affected all heterogeneous data sets, and after the removal of this particular study heterogeneity was reduced to non-significance overall. Therefore, conducting subgroup and sensitivity analyses overall resulted in homogeneous data sets. We analyzed Carpenter et al. (2014) with regard to study quality, characteristics of the

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study design, or specific treatment components, but we found no deviations. The only noteworthy aspect was a very high baseline score on PTSD symptoms in this sample.

We were able to investigate publication bias in three data sets, because an inappropriate application of the methods to detect publication bias was avoided by restricting the analysis to homogeneous data sets including at least six primary studies (Egger et al., 1997; Ioannidis & Trikalinos, 2007). A small tendency toward selective reporting of positive outcomes was present, as indicated in two cases by Begg and Mazumdar's rank correlation method and once by Egger's regression analysis, but publication bias did not invalidate the results, as the two adjusted effect sizes provided by trim-and-fill with the imputed missing studies in these data sets did not differ significantly from the original effects.

## 4.1. Limitations

Even though the quality of the primary studies was overall sufficient, a couple of reporting and methodological limitations across the data base are apparent. First, as already mentioned above, a number of the studies included in this meta-analysis may have been underpowered to adequately test the null hypothesis. Second, 75% of the studies reported insufficiently on the samples' clinical status. Therefore, we had to refrain from categorizing the clinical levels of the study samples and consequently no subgroup analyses evaluating the efficacy of IBIs for subclinical and clinical samples were applicable. Furthermore, the samples varied with respect to the trauma type, both across and within studies, limiting the applicability of subgroup analyses testing the relevance of the traumatic event itself for the treatment outcome. Admittedly, this provides empirical evidence for the external efficacy of IBIs across a range of trauma samples.

With regard to the quality of the meta-analysis, the results of the subgroup analyses should be interpreted with caution given that most of the computations were based on a limited number of studies, and thus not adequately powered. The small number of studies mirrors the

limited empirical evidence from RCTs available, and future research with sufficient power is necessary. Furthermore, we were confronted with a significant amount of confounding of the theoretical approaches with particular program and study design characteristics. The heterogeneity and limited quality of the primary studies is associated with the reliability of the results of the meta-analysis. This and the concomitant small number of includable studies restricted the number and impeded the implementation of clean subgroup analyses for single program components. Furthermore, it is likely that sample characteristics affected outcome findings, but we were unable to examine trauma type as a moderator of treatment outcome because of the limited number of studies and the variability that existed between the samples. Finally, the data base also impeded a direct comparison of the efficacy of CBT versus EW based IBIs. In conclusion, although there are methodological limitations of the studies included in our meta-analysis, these shortcomings reflect the developmental infancy of the field of IBIs for PTSD.

## 4.2. Implications for future research

Although the findings for internet-based interventions for individuals with PTSD-related symptoms are encouraging, work in this area is still in its early stages. Future large-scale clinical trials are necessary, most appropriately conceptualized as active control studies, since with increased sample size also small effect sizes that can be of clinical relevance are detectable, and the superiority over another active treatment is more meaningful than superiority over a waiting list condition. Future studies should also carefully consider the target sample's clinical status and traumatic events and systematically manipulate particular program components to test for their efficacy, such as therapeutic support and number of treatment sessions. The next step is to identify *who* profits the most under *which* circumstances from *which* internet-based treatment concept. Finally, given the rapid development of different technology-assisted presentation modes on other devices such as tablets and smartphones to utilize various applications, research

on IBIs needs to broaden its view to the efficacy and potential of mobile devices. We see particular potential in the development of blended approaches, such as combining face-to-face treatment and also internet-based approaches with mobile applications. They may be particularly indicated for patients with pronounced deficits in emotion regulation or problems with changing dysfunctional coping patterns, as the practice of new skills can be prompted both in everyday life and as required to help these patients cope with either negative emotions, distress or maybe even dissociation. We are aware of two research groups that assess the efficacy of mobile phone applications for the treatment of PTSD (Kuhn et al., 2014; Reger et al., 2013). However, such blended approaches of face-to-face interventions or IBIs with smartphone applications still need to be systematically investigated in order to examine whether they promote incremental efficacy.

## 4.3. Conclusion

Our meta-analysis provides promising initial evidence for the efficacy of CBT-IBIs in the treatment of PTSD. IBIs have the potential to add new and beneficial options for interventions to mental health care and may address challenges associated with the provision of conventional psychotherapy. CBT-based IBIs in particular significantly reduce PTSD symptoms, and dropout rates indicate that treatment through the internet is well accepted among participants with various trauma types. Our findings are an initial step that highlights the overall promising avenues for internet-based programs for the treatment of PTSD, but more systematic research is necessary to strengthen the evidence and disentangle the impact of particular program characteristics, in order to increase the knowledge about the optimal internet-based delivery of treatment.

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# **CHAPTER 4 – STUDY 3**

Attentional bias in German Armed Forces veterans with and without posttraumatic stress symptoms – An eye-tracking investigation and group comparison.

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## Abstract

Background and objectives: Most eye tracking based paradigms evidence patterns of sustained attention on threat coupled with low evidence for vigilance to or avoidance of threat in posttraumatic stress symptoms (PTSS). Still, eye tracking data on attention bias is particularly limited for military population. This eye tracking study investigated attentional bias in PTSS in a sample of German Armed Forces veterans. Methods: Veterans with deployment-related PTSS (N = 24), veterans with deployment-related traumatization without PTSS (N = 28), and neverdeployed healthy veterans (N = 18) were presented with pairs of combat and neutral pictures, pairs of general threat and neutral pictures, and pairs of emotional and neutral faces. Their eye gazes were tracked during a free viewing task. 3 x 3 x 2 mixed general linear model analyses were conducted. Internal consistency of attention bias indicators was calculated for the entire sample and within groups. Results: Veterans with PTSS dwelled longer on general threat AOIs in contrast to non-exposed controls and shorter on general threat and combat associated neutral AOIs in contrast to both control groups. Veterans with PTSS entered faster to general threat AOIs than non-exposed controls. Veterans with PTSS showed circumscribed higher attention fluctuation in contrast to controls. Internal consistency varied across attention bias indicators. Limitations: Statistical power was reduced due to recruitment difficulties. Conclusions: Evidence is provided for the maintenance hypothesis in PTSS. No robust evidence is provided for hypervigilant behavior in PTSS. Findings on attention bias variability remain unclear, calling for more investigations in this field.

# Highlights

- Evidence is provided for the maintenance hypothesis in PTSS
- No robust evidence is provided for hypervigilant behavior in PTSS
- No conclusion can be drawn regarding attention bias variability
- This study was first to examine attention bias variability via eye tracking
- Internal consistency varied across indicators of attention bias and stimulus types

## Key Words:

posttraumatic stress; eye tracking; attentional bias; veterans; hypervigilance; maintenance

# **CHAPTER 5 – STUDY 4**

Attentional bias in veterans with deployment-related posttraumatic stress disorder before and after internet-based cognitive behavioral therapy – An eyetracking investigation

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## Abstract

Background: Veterans with posttraumatic stress disorder (PTSD) often exhibit an attentional bias towards trauma-relevant or generally threatening and negative stimuli. Internet-based cognitive behavioral therapy (ICBT) has been demonstrated to be efficacious in the treatment of PTSD. However, a previous study by our own group failed to find a symptom reduction following ICBT in a sample of traumatized veterans. No previous studies have examined the usefulness of ICBT in terms of modifying attentional bias in PTSD. Methods: In an eyetracking experiment, veterans with deployment-related PTSD were presented with combatrelated pictures and general threat-related pictures. These target stimuli were simultaneously displayed with neutral pictures. Additionally, participants were presented with pairs of emotional and neutral faces. Participants received ICBT, and attentional bias was examined pre- and post-intervention and at three-month follow-up. Results: No significant changes in attentional bias were observed, either from pre- to post-intervention or at follow-up. Conclusion: The findings suggest that attentional bias reduction is associated with, rather than being separable from, overall PTSD symptom improvement. The present eve-tracking study was the first longitudinal investigation to examine the effect of ICBT on PTSD-related attentional bias in a sample of veterans. More research is needed to gain a deeper understanding of the underlying mechanisms of attentional bias in PTSD and its modifiability.

## Highlights

- An IB-CBT did not modify PTSD related attentional bias significantly
- No changes emerged either from pre- to post-intervention or at follow-up
- Attentional bias modifiability seems to be associated with overall symptom change
- This eye-tracking study was the first longitudinal investigation of this kind
- Research is needed to gain a deeper understanding of the modifiability of attentional bias in PTSD

**Keywords:** posttraumatic stress disorder; eye tracking; attentional bias; combat-related PTSD; attentional bias modification; internet-based intervention

## **1.** Introduction<sup>1</sup>

Posttraumatic stress disorder (PTSD) can develop following exposure to a traumatic event, such as witnessing, experiencing, or being confronted with incidents of actual or threatened death or injury (Breslau et al., 1998). Patients often experience symptoms of intrusive thoughts or memories, hypervigilance, and avoidance of situations, places, and objects that are associated with the traumatic event (American Psychiatric Association, 2013). Due to their highly frequent exposure to potentially traumatizing events, military veterans are at increased risk of PTSD (Ramchand et al., 2010; Richardson, Frueh, & Acierno, 2010). Attentional bias is a phenomenon that is often experienced by trauma survivors (Weber, 2008). It is characterized by abnormal information processing, including increased sensitivity to trauma-related, generally threatening, or generally negative information, and it is assumed to be part of a larger mental network of fear structures, resulting in a vicious cycle of PTSD symptom persistence and amplification (Birrer & Michael, 2011; Foa, Feske, Murdock, Kozak, & McCarthy, 1991; Lissek, 2012; Michael, Halligan, Clark, & Ehlers, 2007; Pineles, Shipherd, Mostoufi, Abramovitz, & Yovel, 2009; Steil & Ehlers, 2000). There are two mechanisms which may jointly underlie the attentional bias in PTSD (Cisler & Koster, 2010; Fox, Russo, Bowles, & Dutton, 2001; Weierich, Treat, & Hollingworth, 2008). On the one hand, a pre-conscious and bottom-up-generated hyper-awareness of potentially threatening stimuli may lead to increased and facilitated detection of threat, resulting in an orienting bias (Corbetta & Shulman, 2002; LeDoux, 2000; Vuilleumier, 2005). On the other hand, top-down-regulated difficulties in willingly disengaging and moving attention away from threat may lead to an increased maintenance of attention on potential hazard, also called a maintenance bias (Fox et al., 2001). In their meta-analysis, Armstrong and Olatunji (2012) summarized that individuals with PTSD

<sup>&</sup>lt;sup>1</sup> Abbreviations: PTSD, posttraumatic stress disorder; GAF, German Armed Forces; ABM, attention bias modification; ICBT, internet-based cognitive behavior therapy; EMDR, eye movement desensitization and reprocessing; AOI, area of interest; WL, wait-list group; IT, immediate treatment group

exhibit an orienting bias insofar as they initially orient more often and faster to threatening stimuli compared to healthy individuals. At the same time, they also show a maintenance bias by maintaining their gaze on threatening or trauma-related stimuli to a greater extent compared to healthy controls (Armstrong & Olatunji, 2012).

Research over the last few decades has led to improved experimental paradigms to measure attentional processes. Eye tracking is a convenient experimental approach to obtain continuous recordings of participants' gazes and glances on certain areas of interest (AOI) that function as indicators of attention. This recording of eye gazes is separate from reaction time-based responses and does not rely on participants' conscious decision making. As such, eye-tracking paradigms can be seen as superior to tasks like the dot-probe task, visual search tasks, or the emotional Stroop task (Armstrong & Olatunji, 2012). The initial orienting, that is the location and speed of the initial fixation, is indicative of early attentional processes (e.g., Caseras, Garner, Bradley, & Mogg, 2007; Duque & Vázquez, 2015; Garner, Mogg, & Bradley, 2006; Giel et al., 2011). In contrast, the time spent gazing at a stimulus, also called dwell time, is indicative of a maintained attention on stimuli (e.g., Green, Williams, & Davidson, 2003; Horley, Williams, Gonsalvez, & Gordon, 2004; Lazarov, Abend, & Bar-Haim, 2016; Schofield, Johnson, Inhoff, & Coles, 2012).

Regarding the population of war veterans, previous study findings have suggested an interplay of pre- and peri-deployment gaze preferences and war zone stressors on the pathway from combat traumatization to PTSD and associated attentional bias (Beevers, Lee, Wells, Ellis, & Telch, 2011; Iacoviello et al., 2014; Wald et al., 2013). Wald et al. (2013) reported that whilst an increased vigilance to threat at the time of recruitment was associated with post-combat PTSD, an increased avoidance of threat shortly before deployment was also associated with post-combat PTSD. Moreover, the authors found that an increased vigilance to threat during deployment interacted with combat exposure during deployment to predict subsequent

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risk of PTSD. In line with these findings, Beevers et al. (2011) revealed that avoidance of fearful stimuli before deployment interacted with war zone stressors and predicted higher PTSD scores at post-deployment. Thus, attentional bias not only appears to be related to PTSD symptom maintenance, but also affects the risk of developing PTSD in trauma-exposed populations. In turn, the modifiability of attentional bias might also be relevant in the context of PTSD treatment and prevention following traumatization (Wald et al., 2017; Wald et al., 2016). Furthermore, previous research reported moderating or mediating effects of attention-related cognitive abilities such as attentional control on the prediction and course of PTSD and attentional bias (Badura-Brack et al., 2015; Bardeen & Orcutt, 2011; El Khoury-Malhame et al., 2011; MacLeod & Clarke, 2015; Schoorl, Putman, Van Der Werff, & Van Der Does, 2014). It is possible that attentional processes and attentional bias can be considered as early indicators of change in PTSD, which play a role in moderating, initiating, or smoothing the way for PTSD symptom changes. However, literature addressing the disentanglement of attentional processes or attentional bias and PTSD symptoms is lacking.

Recently, attention bias modification (ABM) programs for PTSD and anxiety disorders have been established. ABM treatments are related to treatments of cognitive behavioral therapy regarding the idea that biases in cognition can cause diverse pathological symptoms such as overly anxious thoughts, rumination, or depressive mood (Hakamata et al., 2010). ABM programs aim to bring about an overall symptom improvement by systematically and gradually reducing the attentional bias. This can be efficaciously done by enabling the individual to willingly shift the attention away from negative stimuli, and by training to focus on positive stimuli. Systematic reviews have reported that ABM seems to be a promising tool for treating attentional bias in PTSD and anxiety disorders, with small (Emmelkamp, 2012; Hallion & Ruscio, 2011; Mogoaşe, David, & Koster, 2014) to moderate effect sizes (Bar-Haim, 2010; Beard, 2011; Hakamata et al., 2010; MacLeod & Clarke, 2015). Most investigations to

date have compared symptom severity from pre- to post-intervention and assessed attentional bias using reaction time-based measures. We are aware of only one investigation that utilized eye tracking to estimate the effect of an ABM program in a sample of participants with subsyndromal depression (Wadlinger & Isaacowitz, 2008). During the experimental task, first, subjects were presented with negative affective pictures, serving as stressors. During a subsequent single session of attentional training treatment, subjects were either trained to selectively attend to a positive or to a neutral word. The training utilized a visual dot probe paradigm. After completion of the attentional training, subjects were exposed to another stress condition run. Negative images were presented, and subjects' eyes were tracked. The authors reported that participants who were trained to willingly attend to positive information looked significantly less to negative areas of presented aversive images compared to participants who were less trained to willingly shift their attention (Wadlinger & Isaacowitz, 2008). Whereas ABM programs are generally conceptualized as brief interventions to augment psychotherapeutic treatment, to the best of our knowledge, only one study has investigated the effect of a psychotherapeutic intervention on attentional bias in PTSD (El Khoury-Malhame et al., 2011). An emotional Stroop and a visual search task were administered to measure attentional bias, and patients with PTSD underwent eye movement desensitization and reprocessing (EMDR). Before treatment, patients showed a maintenance bias compared to a healthy control group. After the intervention and in association with significant symptom reduction, patients and healthy controls no longer differed from each other.

To our knowledge, no other study has investigated the effect of a psychotherapeutic treatment on attentional bias in participants with PTSD, and there are no previous investigations examining changes in attentional bias after internet-based cognitive behavioral therapy (ICBT). Notably, there is a large body of research demonstrating the efficacy of ICBT for symptom reduction in a range of psychiatric disorders (Andersson & Cuijpers, 2009;

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Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Barak, Hen, Boniel-Nissim, & Shapira, 2008; Kuester, Niemeyer, & Knaevelsrud, 2016; Richards & Richardson, 2012; Spek et al., 2007) and demonstrating patients' acceptance and satisfaction with the therapeutic alliance in ICBT (Baumeister, Reichler, Munzinger, & Lin, 2014; Cook & Doyle, 2002; Christine Knaevelsrud & Maercker, 2007; Melville, Casey, & Kavanagh, 2010; Preschl, Maercker, & Wagner, 2011; Wagner, Brand, Schulz, & Knaevelsrud, 2012). However, literature examining the efficacy and acceptance of ICBT in traumatized veterans is scarce; the few available results indicate only limited effects of ICBT on veterans' PTSD symptoms and low acceptance of ICBT in veteran populations (Hobfoll, Blais, Stevens, Walt, & Gengler, 2016; Litz, Engel, Bryant, & Papa, 2007).

### 1.1. Study aim and hypotheses

In an earlier investigation of pre-intervention characteristics of the same sample, we found that veterans with PTSD showed an orienting bias and a maintenance bias towards trauma-relevant and generally threatening stimuli compared to two healthy veteran control groups (STUDY 3). The previous and the current investigation were part of a larger randomized waitlist-controlled intervention study examining the effectiveness and acceptance of an ICBT program for PTSD symptom reduction in veterans (Niemeyer et al., 2020). This randomized controlled trial did not find a significant PTSD symptom improvement either from pre- to post-treatment or after a three-month follow-up period. Moreover, it reported limited treatment utilization, considerable dropout rates, and a low acceptance of the ICBT in the sample of traumatized veterans. Therefore, the main aim of the current examination was to explore whether an ICBT program can lead to a significant reduction in attentional bias in veterans with PTSD from pre- to post-intervention and at three-month follow up, despite the fact that no PTSD symptom improvement was identified in the sample of veterans.

## 2. Method

## 2.1. Participants

Participants were current or former members of the Bundeswehr (German Armed Forces, GAF). They were recruited in collaboration with unit commanders of the GAF via flyers, websites of the GAF and health service centers of the GAF, study announcement in military journals and military-related web blogs, as well as via mailing lists distributed among GAF doctors, GAF psychologists, and GAF social workers. Data were collected between May 2016 and July 2018. All participants were informed about the study content, the voluntary nature of participation, the principles of confidentiality and anonymity, and their right to discontinue participation at any time. Written informed consent was provided by all participants. The study was approved by the Freie Universität Berlin Institutional Review Board [85/2014] and registered at the Australian Clinical Trials Registry [ACTRN1216000956404].

Inclusion criteria for all participants of the current study were: have been deployed abroad, have been confronted with one or more deployment-related traumatic events, and have endorsed symptoms of PTSD within the last month according to the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5; Weathers et al., 2017). In a telephone interview conducted by a licensed psychotherapist, we screened for the following exclusion criteria: report of a neurological disorder, current or lifetime psychotic disorder, substance abuse or substance dependence disorder, current suicidality, and current psychotherapy or participation in any other psychological support or intervention program. Of 89 individuals that were screened, 41 met all inclusion criteria to take part in the intervention study that is described in detail in Niemeyer et al. (2020). In the present sample, we had to additionally exclude 13 individuals because they reported a traumatic head or brain injury during their lifetime. Importantly for the

current study, participants were free of medication affecting the oculomotor system, such as benzodiazepines, methadone, barbiturates, or lithium (Griffiths, Marshall, & Richens, 1984).

Twenty-four participants provided data at the time of the pre-intervention assessment. Of these, six were no-shows, meaning that they did not begin the ICBT. A further four participants terminated the ICBT early, meaning that they completed the first writing assignment but dropped out at some point before all writing assignments had been completed. Thus, 14 participants completed the ICBT and provided eye-tracking data at the post-treatment assessment. Of these, one participant dropped out during the follow-up interval, leaving 13 participants at the time of the three-month follow-up assessment. Three eye-tracking data sets had to be excluded at post-treatment and two eye-tracking data sets were excluded at the follow-up assessment, due to errors or difficulties in obtaining eye-tracking data (i.e., hardware/recording/ data-saving or uploading errors, difficulties in the calibration procedure, excessive blinking, droopy eyelids, excessive looking away from the screen). Therefore, a final sample of 11 participants at post-treatment and a slightly different sample of 11 participants at follow-up assessment were entered into the analyses (see Fig.1). Sociodemographic information and psychiatric conditions are displayed in Table 1.

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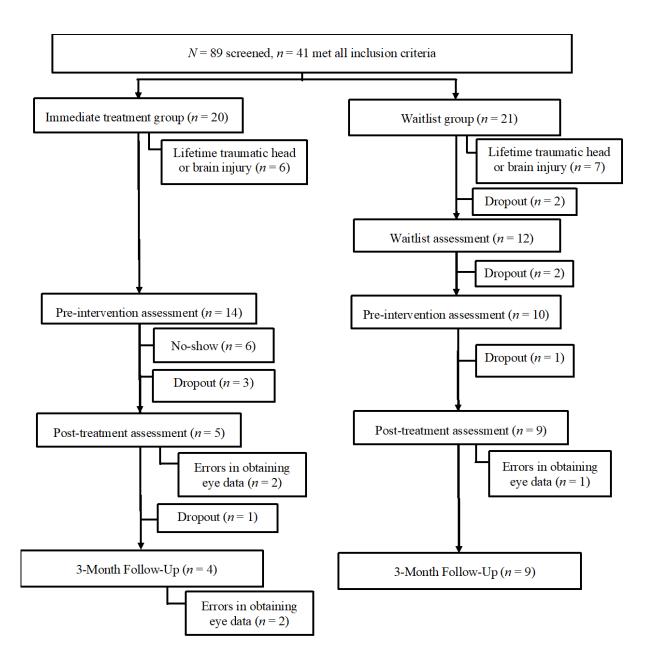


Fig. 1. Participants flow chart and flow of data collection.

	Full sample <sup>0</sup>	Non-completers <sup>1</sup>	Treatment completers		Comparison <sup>4</sup>	
			pre-to post <sup>2</sup>	pre- to follow up <sup>3</sup>	Non-completers to treatment	Non-completers to treatment
					completers pre-to-post	completers pre-to-follow up
Age, $M$ (SD) <sup>B</sup>	38.26 (10.86)	40.46 (12.27)	35.40 (8.45)	39.30 (13.61)	<i>Z</i> =40, <i>p</i> = .686	<i>Z</i> = -1.49, <i>p</i> = .136
Military status, $N(\%)^{A, B}$						
Soldier on time	11 (45.8)	6 (46.2)	5 (45.5)	5 (45.5)		
Professional military	4 (16.7)	2 (15.4)	2 (18.2)	2 (18.2)		
Voluntary conscripts	2 (8.3)	1 (7.7)	1 (9.1)	1 (9.1)		
Branches of armed forces, $N(\%)^{A, B}$						
Army	13 (54.2)	5 (38.5)	8 (72.7)	7 (63.6)		
Joint support service	3 (12.5)	1 (7.7)	2 (18.2)	2 (18.2)		
Air force	4 (16.7)	4 (30.8)	-	-		
Military rank, $N(\%)^{A, B}$						
Corporal	9 (37.5)	5 (38.5)	4 (36.4)	4 (36.4)		
Sergeant	9 (37.5)	6 (46.2)	3 (27.3)	3 (27.3)		
Staff officer	4 (16.7)	1 (7.7)	3 (27.3)	3 (27.3)		

*Table 1.* Sociodemographic information and psychiatric conditions of the study sample, N = 24.

Table 1 continues following page.

Continuation of Table 1.

	Full sample <sup>0</sup>	Non-completers <sup>1</sup>	Treatment completers		Comparison <sup>4</sup>	
			pre-to post <sup>2</sup>	pre- to follow up <sup>3</sup>	Non-completers to treatment	Non-completers to treatment
					completers pre-to-post	completers pre-to-follow up
Deployments, M (SD) <sup>A, B</sup>						
Total number	3.0 (3.69)	3.93 (4.70)	1.80 (1.03)	2.20 (1.40)	<i>Z</i> =13, <i>p</i> = .899	Z = -1.08, p = .280
Total duration in days	434.95 (441.13)	594.50 (577.46)	275.40 (144.16)	318.90 (170.39)	<i>Z</i> =38, <i>p</i> = .705	<i>Z</i> = -1.44, <i>p</i> = .151
Last deployment duration in days	142.95 (48.28)	141.60 (47.60)	144.44 (51.87)	139.44 (51.81)	<i>Z</i> =04, p = .967	<i>Z</i> =46, <i>p</i> = .649
Trauma exposure / military stressors,						
<i>M</i> ( <i>SD</i> ) <sup>A, B</sup>						
LEC-5	8.50 (3.32)	7.75 (3.74)	8.73 (2.28)	9.09 (1.92)	<i>Z</i> =87, p = .383	<i>Z</i> =44, <i>p</i> = .663
LMHAT	14.00 (8.01)	22.92 (7.21)	12.54 (7.27)	12.36 (7.12)	<i>Z</i> = -2.85, p = .004	Z = -2.70, p = .007
Psychopathology, M (SD)						
CAPS-5 at pre- treatment	32.37 (12.54)	33.67 (10.92)	27.00 (14.18)	24.45 (11.26)	<i>Z</i> = -2.25, p = .024	<i>Z</i> = -1.45, <i>p</i> = .147
CAPS-5 at post- treatment	-	-	27.82 (17.31)	-		
CAPS-5 at 3-month- follow up	-	-	-	25.45 (16.50)		
DSS-acute at pre- treatment	1.38 (1.10)	1.34 (1.45)	1.40 (0.92)	1.70 (1.15)	<i>Z</i> = -1.57, p = .117	<i>Z</i> =70, <i>p</i> = .487
DSS-acute at post-treatment	-	-	1.79 (1.12)	-		
DSS-acute at 3-month- follow up	-	-	-	1.36 (1.01)		

Table 1 continues on following page.

Continuation of Table 1.

	Full sample <sup>0</sup>	Non-completers <sup>1</sup>	Treatment completers		Comparison <sup>4</sup>	
			pre-to post <sup>2</sup>	pre- to follow up <sup>3</sup>	Non-completers to treatment	Non-completers to treatment
					completers pre-to-post	completers pre-to-follow up
Psychopathology, $N(\%)^{B}$						
Comorbid axis-I disorder	16 (66.67)	9 (69.23)	7 (63.6)	6 (54.55)	<i>Z</i> = .00, <i>p</i> = .999	<i>Z</i> = .00, <i>p</i> = .999
Intake of psychotropic medication	10 (41.67)	7 (53.85)	3 (27.27)	3 (27.27)	<i>Z</i> = -1.29, <i>p</i> = .198	<i>Z</i> = -1.29, <i>p</i> = .198

*Note*<sup>0</sup>, full-sample at pre-treatment assessment, N = 24; <sup>1</sup>, non-completers at pre-treatment assessment included all participants that provided data at pre-treatment assessment only, N = 13; <sup>2</sup>, treatment completers pre-to post included all participants that provided data at pre-treatment and at post-treatment assessment, N = 11; <sup>3</sup>, treatment completers pre-to follow up included all participants that provided data at pre-treatment and at three-months follow up assessment, N = 11; DSS acute, <sup>4</sup>, comparison between groups based on results of the Mann-Whitney U test with a Bonferroni corrected level of statistical significance set at p < .002; Dissociation Tension Scale acute; LEC-5, Life Events Checklist for DSM-5; LMHAT, List of Mental Health Advisory Team; CAPS-5, Clinical Administered PTSD Scale for DSM-5; <sup>A</sup>, due to missing information of some participants number (frequencies) do not sum up to total N (100%) in all categories; <sup>B</sup>, displayed are responses at time of pre-treatment assessment.

# 2.2. Study Procedure

Participants were randomized to either the waitlist (WL) or to the immediate treatment (IT) group. Randomization was based on a computer-generated randomization list. Participants who were randomized to the WL were invited to the laboratory four times: for the pre-waiting time assessment, pre-treatment assessment, post-treatment assessment, and three-month follow-up assessment. Participants who were randomized to the IT were invited to the laboratory three times: for the pre-treatment assessment, post-treatment assessment, and three-month follow-up assessment. After the pre-waiting time assessment, participants in the WL did not receive any kind of control intervention, but rather waited and were re-invited for pre-treatment assessment six weeks later. After the pre-treatment assessment, all participants received the same ICBT, which took approximately five weeks to be completed. The ICBT began within one week following the pre-treatment assessment, and participants were re-invited within one week after treatment completion to the post-treatment assessment. The follow-up assessment took place three months after the post-treatment assessment.

The diagnostic assessments were conducted by clinical psychologists or graduate students on a master's level of psychology. All assessors were specifically trained in assessing the diagnostic measurements and in conducting the experimental tasks. Assessors were not blinded to group allocation, but they did not serve as study therapists in order to avoid potential bias. Each of the assessments took place in the German Armed Forces Military Hospital in Berlin and took one or two days to be completed, depending on the participant's time of arrival at the laboratory. All assessments comprised the same examinations, which are listed in detail in Niemeyer et al. (2020). The eye-tracking experiment took place between 09.00 am and 10.00 am in the case of a one-day assessment, or between 01.00 pm and 02.00 pm on the first day of a two-day assessment. Prior to the eye-tracking task, participants completed the Life Events Checklist for DSM-5 (LEC-5; Krüger-Gottschalk et al., 2017; F. Weathers et al., 2013) and the

List of the Mental Health Advisory Team (LMHAT; Zimmermann et al., 2014). Next, participants underwent the eye-tracking experiment, which took approximately 15 minutes, and then completed the Dissociation-Tension-Scale-acute (DSS-acute; Stiglmayr, Braakmann, Haaf, Stieglitz, & Bohus, 2003). Following this, they were debriefed, and the assessment was paused. Subsequently, participants were interviewed by Master's-level psychologists or a psychology PhD student, who had been trained to administer the CAPS-5 (Weathers et al., 2017) and the Mini International Neuropsychiatric Interview German Version 5.0 (M.I.N.I.; Sheehan et al., 1998). In the afternoon of a one-day assessment (or the morning of the second day of a two-day assessment), participants were again presented with the same stimuli of the eye-tracking experiment. This time, they were asked to rate the picture stimuli with respect to valence and arousal and to identify the emotion for the presented facial expression, by way of a manipulation check.

# 2.3. Intervention

The ICBT created for the purpose of this study was a therapist-guided writing intervention that was adapted from treatment protocols from evidence-based treatments for PTSD (Knaevelsrud et al., 2017; Lange, Van De Ven, & Schrieken, 2003). The ICBT consisted of three treatment phases, namely biographical reconstruction, prolonged exposure, and cognitive restructuring. The entire treatment took five weeks and participants had to complete two writing assignments per week, with each assignment requiring approximately 45 minutes of writing. Licensed psychotherapists who had been specially trained to administer this treatment provided written feedback on the participants' text within one working day and encouraged the participant throughout the process. Allocation to study therapists was based on a computer-generated randomization list. The intervention is described in greater detail in Niemeyer et al. (2020).

# 2.4. Measures

Symptom severity of PTSD was assessed with the German translation of the CAPS-5 (German version: Schnyder, 2013; Weathers et al., 2017), a 30-item structured clinical interview. After verifying criterion A, the CAPS-5 examines the severity of each of the PTSD subscale symptoms according to DSM-5. Referring to the past month, each item asks respondents to state the frequency (how often during the past month?) and severity of each of the 20 symptoms on a 5-point Likert scale ranging from 0 (not present) to 4 (extremely/ incapacitating). Each PTSD subscale can be rated by summing up the respective severity responses (criterion B items 1-5; criterion C items 6-7; criterion D items 8-14; criterion E items 15-20). The total PTSD score is calculated by summing up the severity ratings of all 20 items, resulting in an overall symptom severity score ranging from 0 to 80. According to Weathers et al. (2017), the CAPS-5 shows very good psychometric properties, with high interrater reliability, test-retest reliability, and convergence with the CAPS for DSM-IV. In the current sample, Cronbach's alphas were  $\alpha = .89$ ,  $\alpha = .92$ , and  $\alpha = .92$  for the total severity score at pre-, post-, and follow-up assessment, respectively, and Gutmann's split half coefficient amounted to r = .87, r = .91, and r = .90 for the total severity score at pre-, post-, and follow-up assessment, respectively.

Traumatic events were assessed using the Life Events Checklist for DSM-5 (Krüger-Gottschalk et al., 2017; F. Weathers et al., 2013) and the List of the Mental Health Advisory Team (Zimmermann et al., 2014). The LEC-5 is a well-established self-rating trauma list which is used to screen for potentially traumatizing events during the lifetime. It consists of 16 traumatic events (e.g., *severe accident, natural disaster, traffic accident, severe physical injury, sudden death of a loved one*), and provides additional space to insert any event that is not listed but has been experienced. Participants indicate the level of exposure to the experienced events on a 6-point scale (*1, happened to me; 2, witnessed it; 3, learned about it; 4, part of my job; 5,* 

*not sure; 6, not experienced*). We summed the number of events that were rated as either *happened to me, witnessed it, learned about it,* or *part of my job.* Comprehensive analyses of the psychometric properties of the LEC-5 are pending, although previous versions of the LEC demonstrated satisfactory convergent validity, and as the changes of the LEC-5 from previous versions of the LEC are minimal, no major changes with respect to psychometric properties are expected (Weathers et al., 2013). The LMHAT is a list consisting of 33 military-specific, deployment- and combat-related stressors (e.g., *being shot, being wounded, witnessing a companion being shot, seeing bombed out villages, mine clearance*). Respondents indicate on a 5-point scale how often they have experienced the respective stressor (*0, never; 1, once; 2, 2 to 4 times; 3, 5 to 9 times; 4, 10 times or more*). We summed up the number of events that were rated as either *once, 2 to 4 times, 5 to 9 times*, or *10 times or more*.

The Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) is a structured clinician-administered diagnostic interview that checks for the diagnostic criteria of any axis I psychiatric disorder according to Diagnostic and Statistical Manual of Mental Disorders-IV (Wittchen, Wunderlich, Gruschwitz, & Zaudig, 1997) and International Classification of Diseases-10 (Dilling, Mombour, & Schmidt, 1991) and was applied in the current investigation to check for comorbidities. The M.I.N.I. has been frequently used in clinical research and psychometric evaluations across a variety of samples yielded satisfactory sensitivity and specificity indices for diagnosing and discriminating psychiatric conditions (Lecrubier et al., 1997; Sheehan et al., 1997).

The German Dissociation-Tension-Scale-acute (Stiglmayr et al., 2003), a 21-item selfrating scale, was used to check for the presence of dissociative symptoms during the experimental task. The scale asks about the experience of a range of psychological and somatoform dissociative symptoms on a 10-point Likert scale ranging from 0 (*not experienced*) to 9 (*very strong*) during the past 15 minutes. A mean score can be calculated, with higher

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scores indicating higher dissociative symptoms during the task. The authors report satisfactory internal consistency, and sufficient convergent, discriminant, and differential validity (Stiglmayr et al., 2003). In our sample, Cronbach's alphas were  $\alpha = .88$ ,  $\alpha = .85$ , and  $\alpha = .81$  at pre-, post-, and follow-up assessment, respectively, and Gutmann's split-half coefficient lay at r = .91, r = .74, and r = .82 at pre-, post-, and follow-up assessment, respectively.

## 2.5. Experimental set-up and procedure

Eye movements were recorded binocularly using a remote RED-m eye-tracking system (60 Hz sampling rate) from SensoMotoric Instruments (SMI Inc., 2016), which was connected to a Lenovo ThinkPad Typ X220 and a Dell monitor Ultrasharp 1907FPv. The experiment was written in Python (Version 2.7.10). Stimuli slides were prepared in Gimp (Version 2.8) and saved as JPG files for the experimental procedure. Participants were seated in a chair in front of the monitor with their eyes at 60 cm distance from the screen, as controlled by the study investigator. The monitor screen was 1280 pixels in width and 1024 pixels in height, and the experimental slides took up the entire screen. We presented all stimuli in black/white and gray shades against a white background. All stimuli within one condition had the same size. We prepared four different stimulus sets, one set for each assessment over the course of the longitudinal study. The order of sets over the course of the longitudinal investigation was generated randomly and prior to assessment. The order of conditions within the experimental set (condition I: pictures, condition II: faces) as well as the order of stimuli within conditions, was randomized for each participant at each point of assessment. Prior to the experiment, we calibrated the eye tracker by instructing the participant to follow a dot on the screen, moving between five different locations on the screen. We repeated the calibration procedure until it was considered satisfactory, defined as when a spatial accuracy below 0.4° was achieved for each eye recorded (Holmqvist et al., 2011, p. 132). The experiment investigator instructed the participants that during the following task, a slide show of photographic pictures and faces

would be presented and that eye movements would be recorded, making it necessary to keep their head still. We asked participants to stare at a fixation cross in the center of the screen, which appeared at the beginning of the experiment and between each new slide, ensuring a uniform starting point for the consecutive viewing task. Participants were instructed to look at the presented slides in any manner they wished, freely, and at whatever seemed interesting to them as soon as the stimuli slide appeared. To familiarize participants with the stimuli, they underwent six practice trials per condition. All stimuli slides remained on the screen for four seconds, each followed by the inter-stimulus interval presenting the fixation cross for one second before the next slide appeared on the screen.

At each time of assessment, participants were presented with two different stimulus conditions, a photographic pictures condition and a facial expression condition. The photographic pictures condition comprised 22 slides with pairs of photographs, with one scene on the right-hand side and one on the left-hand side. For combat-related slides (N = 12), the pair of photographs consisted of a combat-related scene versus a neutral scene (e.g. sports activity, urban street scene, leisure activity). We endeavored to match the simultaneously presented pictures with respect to figure posture, brightness, content of scene, and overall complexity. Thus, for example, a photograph of a woman standing in a bombed-out street was matched with a picture of a woman standing in a street in any non-destroyed city. For general threat-related slides (N = 10), the pair of photographs consisted of a general threat-related scene (e.g., motor vehicle accidents, physical aggression, injuries) versus a neutral scene. Again, we undertook to match the presented pictures regarding the aforementioned qualities, e.g. a picture presenting two emergency responders in front of a crashed car was paired with a picture displaying the same emergency responders in front of an intact car. General threat as well as neutral pictures were taken from the International Affective Picture System (Hamm, 2014; Lang, 2005) and combat-related photographs were collected from free online image databases.

We counterbalanced the side of presentation of the combat-related versus neutral pictures, such that the combat-related picture was presented on the left-hand side in 50% of slides and on the right-hand side in 50% of slides. The same applied for the presentation of the general threat versus neutral picture slides. The facial expression condition comprised 15 slides with pairs of facial expressions. Facial expressions were taken from 24 different actors divided evenly by gender and ethnicity. The pictures stemmed from the NimStim Set of Facial Expressions ("Research Network on early experiences and brain development. NimStim Face Stimulus Set. Online available at http://www.macbrain.org/resources.htm,") and were toned into oval shape and gray-scale. On each slide, one negative emotional facial expression (either anger, fear, or disgust) was paired with a neutral counterpart of the same actor. As in the photographic pictures condition, we counterbalanced the presentation of facial expressions such that half of the slides presented the emotional face on the left-hand side and the neutral counterpart on the right-hand side and vice versa.

#### 2.6. Data Analysis

Based on an a priori power analysis (power = 95%, alpha = 5%, two-tailed) using G-Power (Faul, Erdfelder, Buchner, & Lang, 2009) a minimum sample size of N = 100 was sought to detect a medium to large effect size. Issues in recruitment resulted in a final sample size of only n = 37 individuals. Due to this relatively small sample size and aiming to achieve an increased power for statistical analyses, participants of the WL and the IT group were collapsed into one larger sample. By doing so, investigating the attentional bias modifiability from preto post intervention was enabled. For this, we utilized all participants' data at pre-treatment assessment and contrasted them with participants' data at post-treatment and at follow-up assessment. The samples of the WL and IT condition did not differ significantly on any of the assessed sociodemographic and psychopathological characteristics at pre-treatment assessments, as analyzed by independent sample t-tests.

Analyses were conducted using BeGaze Version 3.7 (SMI Inc., 2016) to reduce eyetracking data and SPSS Version 22.0 (IBM Corporation, 2013) for all statistical analyses. Areas of interest (AOI) were predefined for the stimuli such that the whole photograph or face formed one AOI. Thus, on each slide, two comparative AOIs were set. A fixation was defined as a stable gaze within an area of 1 degree of visual angle for a period of at least 100 milliseconds, as defined using BeGaze prior to analysis. As an indicator of orienting bias, we examined the average entry time to the respective AOIs, i.e. the duration from the start of the trial to the first fixation on the AOI. As an indicator of maintenance bias, we analyzed average dwell time, average fixation duration, and average duration of initial fixation on every AOI. Average dwell time was defined as the sum of durations from all fixations and saccades that hit the AOI, i.e. dwell time starts at the moment the AOI is fixated for the first time and ends at the moment the last fixation on the AOI ends for each visit to the AOI (ref. to SMI Inc., 2016). For ease of interpretation, dwell time is reported in percentage rather than in milliseconds. Average fixation duration was calculated as the sum of duration of all fixations on the AOI divided by the number of fixations on the AOI (ref. to SMI Inc., 2016). Duration of initial fixation was the duration of the first fixation that hit the AOI. As dependent variables, speed of initial orienting, dwell time in percentage, average fixation duration, and initial fixation duration were considered.

Due to the small sample size, the dependent variables did not show a normal distribution; Non-parametric tests were therefore used for all analyses. Prior to the main analyses, we compared participants' ratings of valence and arousal of combat and of general threat-related pictures with their neutral matches and calculated the proportion of participants who correctly identified the presented facial expressions at each time of assessment (manipulation check). Subsequently, we tested for differences in the dependent variables at the time of pre-intervention assessment and between participants who completed the intervention

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versus participants who did not, using a Mann-Whitney U test. Next, we conducted a Wilcoxon signed-rank test to test for differences in the dependent variables between types of stimuli in order to verify the assumption of an existing attentional bias at pre-intervention across all participants who had been pre-assessed. Finally, to examine modifiability of attentional bias, we analyzed changes in the dependent variables from pre- to post-intervention assessment and from pre-treatment to three-month follow-up assessment. For this, we performed a completer analysis from pre- to post-intervention and from pre-intervention to three-month follow-up assessment using a Wilcoxon signed-rank test. Bonferroni correction was applied to correct for multiple testing. Thus, for all analyses on the manipulation check, statistical significance was set at p < .006; for all analyses on differences between participants who completed the intervention versus participants who did not, statistical significance was set at p < .002; and for all analyses on attentional bias modification from pre- to post-treatment assessment, statistical significance was set at p < .002; and for all analyses on attentional bias modification from pre- to post-treatment assessment and until follow-up assessment, statistical significance was set at p < .001.

# 3. Results

3. 1. Manipulation Check – Arousal and valence of pictures, perceptibility of emotional facial expressions.

As three participants failed to attend the second day of pre-treatment assessment, ratings were only available for 21 participants. At post-treatment and at follow-up assessment, ratings were available for all 11 participants in each case. As displayed in Table 2 (see Appendix A), valence of combat and of general threat pictures was rated as significantly less pleasant compared to neutral pictures at pre-intervention, post-intervention, and follow-up assessment. Arousal of combat and of general threat pictures was rated as significantly higher compared to neutral pictures at pre-intervention, post-intervention, and follow-up assessment. Most participants identified the correct emotional facial expression at each time of assessment (see Table 2, displayed as percentages, in Appendix A).

# 3.2. Differences between treatment completers versus non-completers at pre-intervention assessment.

The Mann-Whitney U test revealed that participants who provided data at posttreatment assessment and participants who provided data at follow-up assessment did not differ from participants who dropped out or did not begin the ICBT on any of the sociodemographic variables (see Table 1). Moreover, the groups did not differ on any of the tested dependent variables at pre-intervention assessment (see Tables 3 and 4, Appendix A).

# 3.3. Orienting bias at pre-intervention assessment – entry time.

Wilcoxon signed-rank tests revealed that mean entry times to combat-related and to general threat-related pictures were significantly lower than entry times to their neutral matches (Z = -3.09, p = .002; Z = -3.43, p = .001, respectively). No significant effects emerged in any of the comparisons between emotional facial expressions and neutral faces (Z fear vs. neutral-to-fear = -.91, p = .361; Z disgust vs. neutral-to-disgust = -1.31, p = .189; Z anger vs. neutral-to-anger = -2.89, p = .004).

# *3.4. Maintenance bias at pre-intervention assessment – mean dwell time.*

Wilcoxon signed-rank tests revealed that participants spent significantly more time on the AOIs of combat-related and of general threat pictures than on neutral matches (Z = -4.11, p < .001; Z = -3.91, p < .001, respectively). No significant effects emerged in any of the comparisons between emotional facial expressions and neutral faces (Z fear vs. neutral-to-fear = -.89, p = .376; Z disgust vs. neutral-to-disgust = -1.40, p = .162; Z anger vs. neutral-to-anger = -1.28, p = .209).

# 3.5. Maintenance bias at pre-intervention assessment – average fixation duration.

A Wilcoxon signed-rank test revealed that participants' average fixation was significantly longer on the AOIs of combat-related pictures compared to neutral matches (Z =

-3.71, p < .001). No significant effects were found, either on general threat pictures compared to neutral pictures (Z = -2.54, p = .011), or on any of the emotional facial expressions compared to neutral faces (Z fear vs. neutral-to-fear = -.66, p = .511; Z disgust vs. neutral-to-disgust = -.91, p = .361; Z anger vs. neutral-to-anger = -.31, p = .753).

## 3.6. Maintenance bias at pre-intervention assessment – initial fixation duration.

Wilcoxon signed-rank tests revealed no significant effects, either on any of the photographic pictures' conditions (Z combat related vs. neutral-to-combat related = -2.77, p = .006; Z general threat vs. neutral-to-general threat = -.51, p = .607), or on any of the emotional facial expressions when compared with neutral matches (Z fear vs. neutral-to-fear = -1.00, p = .317; Z disgust vs. neutral-to-disgust = -.26, p = .797; Z anger vs. neutral-to-anger = -1.71, p = .086).

# 3.7. Modifiability of attentional bias from pre- to post-intervention assessment.

Wilcoxon signed-rank tests yielded no significant effects, either on any of the dependent variables (i.e. entry time, mean dwell time, average fixation duration, and initial fixation duration) or on any of the different stimulus types (i.e. combat pictures, general threat pictures, angry faces, disgusted faces, fearful faces) from pre- to post-intervention. Descriptive and inferential statistical results are depicted in Tables 5 to 8 (see Appendix A).

3.8. Modifiability of attentional bias from pre-intervention to three-month follow-up assessment.

According to the Wilcoxon signed-rank test, there were no significant effects on any of the dependent variables (i.e. entry time, mean dwell time, average fixation duration, and initial fixation duration) or on any of the different stimulus types (i.e. combat pictures, general threat pictures, angry faces, disgusted faces, fearful faces) from pre-treatment to three-month followup assessment. Descriptive and inferential statistical results are depicted in Tables 5 to 8 (see Appendix A).

# 4. Discussion

The aim of the current investigation was to ascertain whether attentional bias can be modified in veterans with PTSD, even though a previous study found no significant improvement in PTSD symptoms following an ICBT program. In line with expectation, entry time to AOIs of combat and of general threat pictures was significantly shorter than entry time to the AOIs of the neutral counterparts at the pre-intervention assessment. These findings support the assumed existence of an orienting bias, based on our earlier examination (STUDY 3) and are in line with previous research (Bryant, Harvey, Gordon, & Barry, 1995; Felmingham, Rennie, Manor, & Bryant, 2011; Kimble, Fleming, Bandy, Kim, & Zambetti, 2010; Lee & Lee, 2012). Likewise, and also in accordance with expectation, the mean dwell time on AOIs of combat and of general threat pictures was significantly longer than that on AOIs of neutral matches. The same applied for average fixation duration on AOIs of combat pictures. These results indicate the assumed maintenance bias based on our earlier investigation (STUDY 3) and correspond to previous research findings (Armstrong, Bilsky, Zhao, & Olatunji, 2013; Kimble et al., 2010; Lee & Lee, 2012; Lee & Lee, 2014; Thomas, Goegan, Newman, Arndt, & Sears, 2013).

After receiving the ICBT, no significant changes in attentional bias were found in the current investigation, either from pre- to post-treatment or at the three-month follow-up assessment. At the same time, the larger intervention study, of which the present investigation forms part, did not find a significant treatment effect on PTSD symptom severity (Niemeyer et al., 2020). Therefore, the present examination did not find evidence that the ICBT was effective in significantly reducing attentional bias in the absence of a significant PTSD symptom reduction in a military sample with PTSD. It is reasonable to assume that the lack of significant treatment effect on overall PTSD symptoms in the larger investigation. Systematic reviews

have summarized that in effective ABM programs, changes in attentional bias were accompanied by overall symptom improvement (Beard, 2011; Hakamata et al., 2010; Hallion & Ruscio, 2011). Likewise, El Khoury-Malhame et al. (2011) provided PTSD patients with sessions of EMDR and reported a significantly reduced maintenance bias, which was associated with a significant PTSD symptom reduction. In contrast, Schoorl, Putman, and Van Der Does (2013) reported no superiority of an ABM program over a control condition regarding PTSD symptom reduction. At the same time, and in accordance with our findings, the latter authors reported no changes in attentional bias in either condition (Schoorl et al., 2013). Similarly, Schoorl, Putman, Mooren, Van Der Werff, and Van Der Does (2014) reported no significant effects of an individualized ABM program on PTSD symptoms or on attentional bias in a sample of traumatized Dutch veterans, which is also in line with our present findings.

In summary, our results support the assumption that changes in attentional bias in PTSD are associated with, rather than being separable from, overall PTSD symptom reduction. At this point, we wish to emphasize the specific sample of war veterans examined. First, although ICBT has been demonstrated to be effective for the treatment of a range of psychiatric disorders (Andersson & Cuijpers, 2009; Andersson et al., 2014; Andrews et al., 2010; Barak et al., 2008; Kuester et al., 2016; Richards & Richardson, 2012; Spek et al., 2007), previous research examining the efficacy of ICBT for the treatment of PTSD in war veterans reported only limited treatment effects (Hobfoll et al., 2016; Litz et al., 2007). These latter findings are in line with the restricted treatment effect that was found in our larger intervention study(Niemeyer et al., 2020). Notably, even conventional face-to-face psychotherapy has been found to be less effective in military samples than in non-military samples, as demonstrated in meta-analytical investigations (Bradley, Greene, Russ, Dutra, & Westen, 2005; Goodson et al., 2011; Haagen, Smid, Knipscheer, & Kleber, 2015; Steenkamp, Litz, Hoge, & Marmar, 2015). Second, according to the literature, ABM programs have some potential for changing attentional bias

in stress- and anxiety-related disorders (Bar-Haim, 2010; Beard, 2011; Emmelkamp, 2012; Hakamata et al., 2010; Hallion & Ruscio, 2011; MacLeod & Clarke, 2015; Mogoase et al., 2014). However, little is known about the independence of and disentanglement between attentional processes or attentional bias and PTSD symptoms. With the exception of the study by Schoorl, Putman, Mooren, et al. (2014), examinations of changes in attentional bias have hitherto been lacking. The results of the present investigation confirmed the study results reported by Schoorl, Putman, Mooren, et al. (2014), who also did not find a treatment effect on veterans' attentional bias. Thus, the question arises of whether military samples might show some specific characteristics that may render them less responsive to PTSD treatments in general and to attentional bias modification in particular, as might be assumed based on the present findings. With respect to the general population, and regarding the specific population of war veterans, far too little is known about subliminal processing stages in PTSD, interplaying variables, and mechanisms related to attentional bias. More investigations in this field of research are therefore warranted. Especially further studies that present larger sample sizes will be useful to control for potential effects of the chronicity of PTSD in study participants and outcome.

# 4.1. Limitations

The present investigation shows some restrictions that need to be discussed. First, the sample size was comparatively small. Although a sample size of N = 100 was required, issues in recruitment ensued a final sample size of only n = 37 individuals. Of these, we had to exclude 13 participants who reported a lifetime traumatic head or brain injury in order to meet the specific prerequisites associated with eye-tracking experiments. At the same time, the study participants' struggles with treatment and assessment adherence resulted in a reduced final sample size at post- and three-months follow up assessments. The reduced sample size limited the statistical power of analyses and impeded data interpretation, making it a necessity to utilize

Non-parametric methods for most analyses. Due to multiple testing, we had to apply Bonferroni correction to control for alpha error accumulation, resulting in corrected levels of significance set at p < .006, p < .002, and p < .001, respectively. To reach statistical significance, an effect of our ICBT on attentional bias would have needed to be very large. Second, we decided to examine effects of the ICBT on attentional bias in the overall sample by collapsing the WL and the IT group into one overall sample. It is possible that participants who were allocated to the WL were already familiar with the experimental setting at the time of pre-intervention assessment whereas participants allocated to the IT group were not. To reduce familiarity effects and to ensure that every stimulus was presented only once to each participant, we created different sets of stimuli for each assessment over the course of the longitudinal study. Third, the authors cannot preclude a sampling bias in the present investigation. Recruitment was realized in collaboration with unit commanders of the GAF and announcements for study participance were spread via multiple channels. However, most of the time, the authors experienced that participants were successfully included because of face-to-face contacts, for instance based on a recommendation of a comrade or a suggestion of the attending GAF doctor. At this point, we need to take into consideration that the present study sample may be a selfselected convenience sample.

Sampling and recruitment issues that this investigation was confronted with can be found in earlier investigations, as well. Notably, the population of (traumatized) military personnel may display characteristics and needs that differ from other (clinical) populations in some respect. First, traumatic head or brain injury is a rather common problem found in research targeting samples of military personnel (Brenner et al., 2010; Cernak & Noble-Haeusslein, 2010; Hoge et al., 2008; Scott, Vanderploeg, Belanger, & Scholten, 2005). Second, in PTSD, early treatment termination occurs in around 20% of all initiated treatments across samples and treatment programs (Hembree et al., 2003; Imel, Laska, Jakupcak, & Simpson,

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2013). Of note, dropout is even more frequent in samples of military personnel, ranging from 22% to 68% (Britt, Jennings, Cheung, Pury, & Zinzow, 2015; Garcia, Kelley, Rentz, & Lee, 2011; Hoge et al., 2014; Murphy et al., 2015). This is in line with the rates of early treatment termination and failure to begin treatment in the present investigation. Third, psychological research relies upon voluntary subject participation, confronting investigators with the risk of sampling bias at all time (Bornstein, Jager, & Putnick, 2013; Nielsen, Haun, Kärtner, & Legare, 2017) and across disorders and populations (Cheung, Peter, Smit, de Vries, & Pieterse, 2017; de Winter et al., 2005; Juster, Heimberg, & Engelberg, 1995). Populations of traumatized military personnel report accentuated fear of stigmatization, concerns regarding confidentiality, and skepticism concerning treatment effects (Blais & Renshaw, 2013; Hoge et al., 2004; Hoge et al., 2014). It is possible that a self-selection bias may be notably pronounced in samples of traumatized military personnel.

# 4.2. Implications

The present findings add knowledge and extend earlier investigations on attentional bias modification in PTSD. First, in contrast to ABM programs, the ICBT in the present study was not explicitly designed with the aim of ameliorating attentional bias. Rather, it aimed at reintegrating, restructuring, and reappraising the traumatic event into the trauma survivors' biography in order to reduce overall PTSD symptom severity (Niemeyer et al., 2020). The present authors are aware of only one previous study that investigated the effect of a psychotherapeutic intervention, namely EMDR, on attentional bias in a non-military sample of PTSD patients (El Khoury-Malhame et al., 2011). As investigations on the efficacy of ICBT on attentional bias in PTSD were hitherto lacking, the present investigation can be seen as innovative pioneering work. Second, we aimed to treat the specific population of traumatized veterans with PTSD. To our knowledge, only one previous investigation has examined the efficacy of an ABM program on attentional bias in a military sample (Schoorl, Putman,

Mooren, et al., 2014). Keeping in mind the specific needs of traumatized veterans and the difficulties in providing treatment for this vulnerable population, we wish to emphasize the need for future research to add greater knowledge and to extend the current findings. Third, our investigation utilized an eye-tracking paradigm. Eye-tracking paradigms are regarded as superior to reaction time-based methods due to their independence from participants' behavioral responses (Armstrong & Olatunji, 2012). With the exception of one investigation, which measured attentional bias in subclinical depression by utilizing eye-tracking techniques (Wadlinger & Isaacowitz, 2008), previous investigations applied emotional Stroop and visual search tasks (El Khoury-Malhame et al., 2011), or dot-probe paradigms (Schoorl, Putman, Mooren, et al., 2014; Schoorl et al., 2013) to assess attentional bias in PTSD.

The present study is the first longitudinal investigation to examine the effect of ICBT on PTSD-associated attentional bias in a clinical sample of veterans by utilizing eye-tracking techniques. With its innovative research approach, including a longitudinal design, a comprehensive assessment, thorough procedures, and sophisticated technical endeavors, the present study aimed at initiating a new branch of PTSD treatment research. We hope that our findings will encourage further experimental investigations of PTSD and its associated attentional, cognitive, autonomic, emotional, and epigenetic correlates. Such an integration can be achieved by applying paradigms that cover different methods, for instance eye-tracking, heart rate measures, skin conductance measures, brain studies, or investigations of stress systems.

# 4.3.Conclusion

The present eye-tracking-based study was the first longitudinal investigation to examine the effect of ICBT on PTSD-related attentional bias. The study adds an innovative experimental approach to the existing literature and presented a comprehensive assessment procedure to measure PTSD-related attentional bias and the ability to modify this bias. No significant change

in attentional bias was observed, either from pre- to post-treatment or at three-month followup. These findings suggest that attentional bias is associated with, rather than being separable from, overall PTSD symptom change. Further investigations are warranted to extend the knowledge and the methodological approaches used to examine the ability to modify attentional bias in (military-associated) PTSD using ICBT and other psychotherapeutic interventions for PTSD treatment. To achieve this, more cross-sectional studies as well as larger longitudinal studies are essential. The findings of such studies could help to foster a deeper understanding of the mechanisms and processes of change in PTSD, which are highly relevant for the development and enhancement of treatment.

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# **CHAPTER 6: Discussion, outlook, and conclusion**

# 6.1. STUDY 1

STUDY 1 provided data on the concordance or discordance of PTSD prevalence rates when moving between the diagnostic systems of the DSM-IV, DSM-5, ICD-10, and proposed ICD-11. All four systems were applied in military personnel of the GAF.

# 6.1.1. Summary of core findings

There was no difference in the PTSD prevalence rates when the DSM-IV was contrasted with the DSM-5, and the level of agreement was satisfactory ( $\kappa = .55$ , p < .001). A substantial increase in PTSD diagnostic cases was found when moving from the ICD-10 to the proposed ICD-11, and the level of agreement was low ( $\kappa = .228$ , p = .014). When comparing the DSM-5 to the proposed ICD-11, no differences emerged, and the level of agreement was convincing ( $\kappa$ = .801, p < .001). Table 1 presents the results in detail.

		Concordance with		Discordance with	
		DSM-5	ICD-11	DSM-5	ICD-11
	N (%)	N (%)	N (%)	N (%)	N (%)
DSM-IV					
Diagnosis given	56 (56.0)	45 (80.4)	n.a.	11 (19.6)	n.a.
Diagnosis not given	44 (44.0)	33 (75.0)	n.a.	11 (25.0)	n.a.
DSM-5					
Diagnosis given	56 (56.0)	./.	47 (83.9)	./.	9 (16.1)
Diagnosis not given	44 (44.0)	./.	43 (97.7)	./.	1 (2.3)
ICD-10					
Diagnosis given	30 (30.0)	n.a.	20 (66.7)	n.a.	10 (33.3)
Diagnosis not given	70 (70.0)	n.a.	42 (60.0)	n.a.	28 (40.0)
ICD-11					
Diagnosis given	48 (48.0)	47 (83.9)	./.	1 (2.3)	./.
Diagnosis not given	52 (52.0)	43 (97.7)	./.	9 (16.1)	./.

*Table 1.* PTSD prevalence rates under the diagnostic criteria of the DSM-IV, DSM-5, ICD-10, ICD-11, *N* = 100.

*Note.* PTSD, posttraumatic stress disorder; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Diseases and Related Health Problems; n.a., not applied.

# 6.1.2. The present findings of STUDY 1 and recent research findings

PTSD prevalence rates according to the DSM-IV and the DSM-5. STUDY 1 found equal rates of PTSD diagnostic status under the DSM-IV and the DSM-5, and a high agreement between the two versions. These findings are in line with investigations in samples of war veterans (Gentes et al., 2014; Miller et al., 2013), various trauma populations (Carmassi et al., 2013; Elhai et al., 2009; Elhai et al., 2012; Kilpatrick et al., 2013; O'Donnell et al., 2014; Stein et al., 2014), detained adolescents aged 13-19 years (Modrowski, Bennett, Chaplo, & Kerig, 2017), samples of 8-18-year-old children and adolescents who attended emergency departments after a single trauma event (Meiser-Stedman et al., 2017), samples of parents and caregivers of children with epilepsy (Carmassi et al., 2017), samples of 7-11-year-old children who were exposed to Hurricane Ike or Hurricane Charley (Danzi & La Greca, 2016), and samples of Japanese citizens who experienced various traumatic events (Oe, Ito, Takebayashi, Katayanagi, & Horikoshi, 2020). By contrast, one investigation in a sample of traumatized sexual minority women found significantly more PTSD cases under the DSM-5 compared to the DSM-IV (Kaysen et al., 2019) and another investigation reported lower PTSD prevalence rates under the DSM-5 in contrast to the DSM-IV in survivors of a traumatic injury (Forbes et al., 2011).

Changes to the Trauma Criterion (A1: what kind of event, what mode of exposure; A2: the trauma survivor's direct response to the event) are strongly discussed in the literature (Larsen & Berenbaum, 2017; Larsen & Pacella, 2016; Weathers, 2017). First, discussions are ongoing about how changes to the A1 Criterion may lead to a 'broadened' versus 'narrowed' definition of 'traumatization' (Larsen & Berenbaum, 2017). The occurrence of PTSS/ PTSD after a variety of stressful life events that do not meet the definition of 'trauma' conforming to the A1 Criterion is well documented (Boals & Schuettler, 2009; Larsen & Berenbaum, 2017; Mol et al., 2005; Mulder, Fergusson, & Horwood, 2013; Rumball, Happé, & Grey, 2020; van den Berg, Tollenaar, Spinhoven, Penninx, & Elzinga, 2017; Weathers, 2017). Although meta-analytical evidence supports the assumption that events conforming to the A1 Criterion are

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associated with higher rates of PTSD prevalence and increased symptom severity compared to 'stressor events', the between-group effect sizes are small (Larsen & Pacella, 2016). Second, the deletion of the A2 Criterion allows for diverse responses to trauma, acknowledging that every individual may respond differently when confronted with an acute situation of threat or horror. This may be of particular interest regarding the population of military personnel, who commonly do not show or report immediate reactions of horror, intense fear, or helplessness when confronted with traumatizing events during a military mission (Guina, Welton, Broderick, Correll, & Peirson, 2016). The deletion of the A2 Criterion might facilitate the access to psychotherapy, insofar as (reportable) responses of 'fear or horror' are no longer a prerequisite for a PTSD diagnosis (Adler, Wright, Bliese, Eckford, & Hoge, 2008; Boals & Schuettler, 2009; Brewin, Andrews, & Rose, 2000).

**PTSD prevalence rates according to the ICD-10 and the proposed ICD-11.** STUDY 1 found increased rates of PTSD diagnostic status under the proposed ICD-11 compared to the ICD-10, along with an unsatisfactory level of agreement. These findings conflict with earlier (Glück, Knefel, Tran, & Lueger-Schuster, 2016; Knefel & Lueger-Schuster, 2013; O'Donnell et al., 2014; Stein et al., 2014; Wisco et al., 2016) and more recent research (Barbano et al., 2019; Elliott et al., 2020; Møller, Augsburger, Elklit, Søgaard, & Simonsen, 2020; Oe et al., 2020). For instance, significantly reduced rates of PTSD under the proposed ICD-11 in contrast to the ICD-10 have been reported in samples of elderly survivors of childhood traumatization (Glück et al., 2016), survivors of various traumatic events (Barbano et al., 2019; Oe et al., 2020), samples of Danish psychiatric outpatients (Møller et al., 2020), samples of Finnish adolescents and young adults who were exposed to school mass shooting incidents (Haravuori, Kiviruusu, Suomalainen, & Marttunen, 2016), and samples of children and adolescents who attended an emergency department following a single traumatic event (Elliott et al., 2020).

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Delayed-onset PTSD is a common phenomenon, particularly in (military) populations who have been exposed to war or combat (Andrews, Brewin, Philpott, & Stewart, 2007; Eekhout, Reijnen, Vermetten, & Geuze, 2016; O'Toole, Catts, Outram, Pierse, & Cockburn, 2009; Rona et al., 2016; Sepahvand, Mokhtari Hashtjini, Salesi, Sahraei, & Pirzad Jahromi, 2019; Shoval-Zuckerman, Dekel, Cohen, & Levi, 2019; Smid, Mooren, van der Mast, Gersons, & Kleber, 2009; Solomon & Mikulincer, 2006; Utzon-Frank et al., 2014; Williamson, Stevelink, Greenberg, & Greenberg, 2018). This supports the deletion of the ICD-10-associated time criterion ('symptom onset within six months after the traumatic event'; World Health Organization, 1992) in the proposed ICD-11. STUDY 1 explicitly examined the inclusion versus exclusion of the time criterion according to the ICD-10 and proposed ICD-11, respectively. Receiving a PTSD diagnosis after moving from the ICD-10 to the proposed ICD-11 was attributable to the deletion of the time criterion in 85.7% of these status changes. One might assume that if STUDY 1 had referred to the symptom criteria only, the level of agreement and the transition rates of the PTSD diagnostic cases would have differed.

**PTSD** prevalence rates according to the DSM-5 and the proposed ICD-11. STUDY 1 found equal PTSD prevalence rates under the proposed ICD-11 and the DSM-5, along with a high level of agreement between the two systems. This high level of the agreement indicates that the two systems identified quite similar groups of PTSD cases, with about 90% of subjects retaining their diagnostic status when transiting between the systems. A great deal of research has been added to this field in recent years. There is a body of evidence showing reduced PTSD rates under the proposed ICD-11 compared to the DSM-5 and a poor agreement between the two systems, including investigations in samples of parents of Norwegian students who survived the school shooting attacks in 2011 (Hafstad, Thoresen, Wentzel-Larsen, Maercker, & Dyb, 2017), trauma exposed (foster) children (Bruckmann, Haselgruber, Sölva, & Lueger-Schuster, 2020; La Greca, Danzi, & Chan, 2017; Sachser et al., 2018; Vasileva, Haag, Landolt, & Petermann, 2018), diverse samples of survivors of various traumatic events (Bondjers, Willebrand, & Arnberg, 2018; Fox, Hyland, McHugh Power, & Coogan, 2020; Oe et al., 2020; Schellong et al., 2019), survivors of child sexual abuse or physical assault (Hyland, Shevlin, Fyvie, & Karatzias, 2018; Hyland et al., 2016), samples of internationally displaced persons or refugees (Heeke, O'Donald, Stammel, & Böttche, 2020; Hyland, Shevlin, Makhashvili, et al., 2017; Shevlin, Hyland, Vallières, et al., 2018), and US American military veterans (Wisco et al., 2017). Two studies found reduced PTSD rates under the DSM-5 in contrast to the proposed ICD-11 (Cao et al., 2020; Stein et al., 2014). Interestingly, Hansen et al. (2017) reported increased PTSD rates under the DSM-5 compared to the proposed ICD-11 in survivors of road traffic accidents, survivors of incest, and traumatized university students, but in line with STUDY 1, found equal rates between the two systems in samples of bereaved parents, sufferers of paraplegia, victims of physical assault, (female) victims of sexual assault, chronic pain patients, and deployed military personnel (Hansen et al., 2017). Likewise, equal PTSD rates under the proposed ICD-11 and the DSM-5 were found in samples of directly trauma-exposed Norwegian students (Hafstad et al., 2017), in children who were exposed to Hurricanes Ike or Charley (Danzi & La Greca, 2016), in children and adolescents who experienced a single traumatic event (Elliott et al., 2020), and in returning veterans (Green et al., 2017). As a limitation, some of these investigations reported only low (Danzi & La Greca, 2016) to moderate (Hafstad et al., 2017; Hansen et al., 2017) levels of agreement between the two systems. One must assume that equal numbers of PTSD cases under two competing systems, along with a limited level of agreement between these systems, may indicate mismatches between the systems concerning the identified cases. In STUDY 1, the DSM-5 and the proposed ICD-11 showed a high level of agreement on the identified PTSD cases. Interestingly, Hansen, Hyland, Armour, Shevlin, and Elklit (2015) indicated that the extent of agreement seems to vary depending on the type of traumatization.

# 6.1.3. Specific limitations of STUDY 1

First, at the time of conceptualization of STUDY 1, no instrument was available to assess ICD-11-related PTSD. STUDY 1 therefore derived the ICD-11 criteria from available instruments assessing the ICD-10-related PTSD diagnosis, in line with earlier investigations (Elliott et al., 2020; Glück et al., 2016; Knefel & Lueger-Schuster, 2013; Oe et al., 2020). Meanwhile, the ICD-11 International Trauma Questionnaire (ITQ; Cloitre, Roberts, Bisson, & Brewin, 2015; Cloitre et al., 2018) and the International Trauma Interview for ICD-11 PTSD and complex PTSD (Roberts, Cloitre, Bisson, & Brewin, 2018) have been established. Preliminary validations report satisfactory psychometric properties and a convincing clinical utility of the ITQ to measure and distinguish PTSD and complex PTSD (Cloitre et al., 2018; Haselgruber, Sölva, & Lueger-Schuster, 2020; Ho et al., 2019; Karatzias et al., 2017; Murphy et al., 2020; Owczarek et al., 2020; Rocha et al., 2019; Shevlin, Hyland, Roberts, et al., 2018; Vallières et al., 2018). Nevertheless, STUDY 1 was able to utilize an instrument that was established to assess DSM-5-related PTSD, whilst most previous investigations adapted instruments that were based on the DSM-IV (Cao et al., 2020; Danzi & La Greca, 2016; Elliott et al., 2020; Green et al., 2017; Hafstad et al., 2017; Hansen et al., 2015; Heeke et al., 2020; La Greca et al., 2017; O'Donnell et al., 2014; Oe et al., 2020; Sachser et al., 2018; Stein et al., 2014; Vasileva et al., 2018; Wisco et al., 2017).

Second, STUDY 1 utilized self-report questionnaires only, thus limiting the PTSD status to a 'provisional' diagnostic status in this study. Clinician-administered interviews are considered the gold-standard method for diagnosing PTSD (Ehring, Kleim, Clark, Foa, & Ehlers, 2007; Shalev, Freedman, Peri, Brandes, & Sahar, 1997). The literature suggests that respondents should be presented with multiple modes of assessment (Cody, Jones, Woodward, Simmons, & Gayle Beck, 2015; Grant et al., 2020; Woodward et al., 2018), but also demonstrates that self-report questionnaires can be as reliable as clinician-administered interviews for diagnosing PTSD (Dell'Osso et al., 2009; So, Choi, Chung, Kim, & Kang, 2016).

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Moreover, self-report measures represent an important component in clinical practice and research (Griffin, Uhlmansiek, Resick, & Mechanic, 2004; Parker-Guilbert, Moshier, Marx, & Keane, 2018). Wilson and Keane (2004) showed that the PDS (Foa, 1995) can be regarded as an excellent instrument to assess the diagnostic status and symptom severity of PTSD, with a high internal consistency and a convincing agreement with the SCID-I (First, Spitzer, Gibbon, & Williams, 1997). At the same time, Wilson and Keane (2004) reported that earlier versions of the PCL demonstrated excellent specificity and sensitivity with the SCID-I (First et al., 1997) and with earlier versions of the Clinician-Administered PTSD Scale (CAPS; Blake, Weathers, & Nagy, 1990). However, caution is warranted regarding the generalization of an instrument's psychometric properties when moving from one generation to the next (Wilson & Keane, 2004).

Third, STUDY 1 comprised a comparatively small sample size of N = 100, which consisted of self-referring members of the GAF. One cannot rule out that the study was underpowered and recruiting a convenience sample may limit the generalizability of the present findings (Etikan, Musa, & Alkassim, 2016). However, the larger-scale investigations available to date are predominantly restricted to the assessment of US American military samples (Green et al., 2017; Wisco et al., 2017; 2016). Investigations in the European area are still underrepresented, and the available studies that recruited veterans in Denmark (Hansen et al., 2017) and in Great Britain (Morina et al., 2014) reported sample sizes that are comparable with the sample size of STUDY 1.

# 6.1.4. Implications and future directions

First, the development and validation of reliable diagnostic instruments that assess the current diagnostic criteria will be of major importance for future research and practice. For the DSM-5, several questionnaires are available so far. The PCL-5 (Blevins, Weathers, Davis, Witte, & Domino, 2015) has been translated into various languages and is available in a short and long form; evaluations conducted to date show satisfactory psychometric properties across

different ethnic populations and trauma samples (Blevins et al., 2015; Bovin et al., 2016; Ibrahim, Ertl, Catani, Ismail, & Neuner, 2018; Krüger-Gottschalk et al., 2017; Pereira-Lima, Loureiro, Bolsoni, Apolinario da Silva, & Osório, 2019; Van Praag, Fardzadeh, Covic, Maas, & von Steinbüchel, 2020; Wortmann et al., 2016). The PDS-5 (Foa et al., 2016) demonstrates good psychometric properties with convincing levels of internal consistency, test-retest reliability, and convergent/discriminant validity (Alghamdi & Hunt, 2020; Foa et al., 2016; Su, Kung, Hung, & Chen, 2020). The clinician-administered CAPS-5 (Weathers et al., 2018) has been translated into several languages and shows satisfactory psychometric properties (Boeschoten et al., 2018; Boysan et al., 2017; Oliveira-Watanabe, Ramos-Lima, Santos, Mello, & Mello, 2019; Ramírez, Villarán-Landolt, Gargurevich, & Quiroz, 2020; Weathers et al., 2018; Zaman, Urouj, & Irfan, 2020). Concerning the ICD-11 criteria, future research is called for to develop additional instruments and to examine their psychometric properties. To date, the ITQ (Cloitre et al., 2018) and the International Trauma Interview for ICD-11 (Roberts, Cloitre, Bisson, & Brewin, 2018) are available and preliminary validations of their psychometric properties are promising (Cloitre et al., 2018; Ho et al., 2019; Hyland, Shevlin, Brewin, et al., 2017; Vallières et al., 2018). More validation studies on the psychometric properties of these instruments are needed. Moreover, the ICD-11 diagnosis of complex PTSD needs to be considered extensively in future clinical research (Ben-Ezra et al., 2018; Cloitre, 2021; Karatzias et al., 2017; Karatzias, Hyland, et al., 2019; Karatzias, Murphy, et al., 2019; Simon, Roberts, Lewis, van Gelderen, & Bisson, 2019).

Second, the DSM-5 and the ICD-11 suggest quite different conceptualizations of PTSD (Hansen et al., 2017). The ICD-11 minimizes the diagnostic criteria of PTSD, suggesting six qualifying symptoms across three symptom clusters, of which one symptom in each cluster must be met. The ICD-11 working group sought to identify a parsimonious set of PTSD 'core' symptoms that are intended to be of clinical utility to identify PTSD and to differentiate PTSD from other psychiatric disorders (Brewin et al., 2017; Cloitre et al., 2013; Maercker et al., 2013).

The ICD-11 aims at providing the practitioner with a brief and reliable diagnostic assessment of PTSD while relieving the trauma survivor of extensive diagnostic assessments. At the same time, one may argue that the ICD-11 seems to represent a comparably restrictive diagnostic system in which the responder needs to fulfill at least half of the qualifying items. By contrast, the DSM-5 maximizes the qualifiers, covering 20 potential symptoms across four clusters; from two clusters, one symptom from each must be met, and from the other two clusters, two symptoms from each must be met. This allows for various symptom combinations, and individuals who report quite different qualities of symptom experiences can be equally likely to be diagnosed with PTSD (Brewin, Lanius, Novac, Schnyder, & Galea, 2009; Friedman, Resick, Bryant, & Brewin, 2011; Weathers & Keane, 2007). Barbano et al. (2019) expect that in the future, a proportion of trauma survivors will meet the diagnostic criteria under earlier systems and the DSM-5 but will not fulfill the ICD-11 criteria. This speculation is of particular interest since the ICD-11 is of the highest relevance for the (mental) health care system in Germany and beyond. In line with Barbano et al. (2019) assumption, one may hypothesize that an increasing number of trauma survivors who are in need of treatment will not 'fit' into the six core symptoms of the ICD-11 (i.e., do not fulfill the ICD-11 criteria for PTSD), in turn complicating their access to adequate psychotherapy or psychiatric/ medical treatment. Indeed, although in contrast to the findings of STUDY 1, most earlier investigations found substantially decreased PTSD prevalence rates under the proposed ICD-11 as compared to the ICD-10 (Barbano et al., 2019; Elliott et al., 2020; Glück et al., 2016; Haravuori et al., 2016; Knefel & Lueger-Schuster, 2013; Møller et al., 2020; O'Donnell et al., 2014; Oe et al., 2020; Wisco et al., 2016). This gives rise to concerns about the potential risk of increasing numbers of un-/misdiagnosed (i.e., untreated, or not appropriately treated) trauma survivors in the future. Concurrently, meta-analytical evidence shows that 12% to 15% of trauma survivors display subthreshold PTSS (Brancu et al., 2016), and this proportion rises to 22% in military veterans (Bergman et al., 2017; El-Gabalawy et al., 2018; Fink et al., 2018). Although functional

impairment and overall (co-)morbidities are highest in full-PTSD samples, trauma survivors with subthreshold PTSS nevertheless show lower levels of functioning and quality of life, and an increased risk of suicidality, hopelessness, aggression, and secondary adverse (mental) health outcomes compared to healthy trauma survivors (Bergman et al., 2017; Brancu et al., 2016; Kim, Oh, Park, Min, & Kim, 2020; Morgan-López et al., 2020). Such findings highlight that trauma survivors with subthreshold (or 'atypical') PTSS may require access to adequate psychotherapeutic treatment opportunities and psychiatric medication. Accordingly, a crucial task for the future will be to provide trauma survivors who need psychotherapeutic intervention with access to adequate (trauma-focused) psychotherapy – even when they do not satisfy the ICD-11 diagnostic criteria of PTSD.

Third, diagnostic changes to the ICD (and the DSM) may have diverse implications for the diagnostic status and treatment provision in military personnel. A military service member's physical and mental fitness influences his or her military career path. For instance, fitness may be linked to a gain or loss of financial benefits and to acquiring further qualifications for foreign deployments, certain military posts, and higher career positions. Accordingly, psychiatric disorders such as PTSD are assumed to interfere with a veteran's overall fitness and can severely impede his or her career. The assessment of physical and mental fitness in military personnel – potentially bringing about, or ruling out, a diagnosis such as PTSD – can be of major concern for the further career of an individual member, for that member's task force, and even for national and international safety (Guina et al., 2016). Furthermore, military cohorts have been found to differ in terms of which trauma symptoms are reported and how they are reported, depending on several factors such as ethnicity, country of military service employment, and country of deployment (Gelernter et al., 2019; Schaper, Mackintosh, Willis, Liu, & White, 2020; Wall, Convoy, & Braybrook, 2019). Studies have revealed that ethnic and cultural characteristics impact on a patient's symptom reporting and attributional style, which can in turn affect the diagnostic procedure and assessments, diagnostic rating, and diagnostic

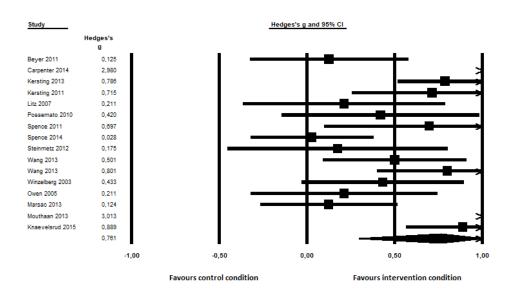
outcome (Asnaani & Hall-Clark, 2017; Hall-Clark et al., 2017). Future research is therefore needed to deepen the understanding of the impact of cultural and ethnic variables on the diagnostic process and to examine the role of these variables in the therapeutic process. Finally, it is well documented that there are diverse subtypes of military-related PTSD, including internalizing and externalizing types of PTSD (Miller, Greif, & Smith, 2003; Miller, Kaloupek, Dillon, & Keane, 2004), PTSD with pronounced dissociative features (Boyd et al., 2018; Tsai, Armour, Southwick, & Pietrzak, 2015; Wolf, Lunney, & Schnurr, 2016), PTSD with psychotic co-occurrences (Živić, Joković, Vranić, & Stojanović, 2020), and PTSD with severe somatic complaints (Graham et al., 2019). These military-related subtypes of PTSD need to be further explored and their implications for diagnosis and treatment provision need to be examined in greater depth.

# 6.2. STUDY 2

STUDY 2 provided a meta-analysis of the efficacy of IBI for PTSD. Subgroup analyses examined the impact of treatment components on overall treatment efficacy, and rates of early treatment termination along with completer characteristics were assessed on a descriptive level.

# 6.2.1. Summary of core findings

Twenty primary investigations were included (iCBT k = 15, iEW k = 5). ICBT was superior to waitlist at post-treatment assessment on the PTSD sum scale (k = 7, g = 0.72, p <.001, see Fig. 1) and on all subscales (intrusion: k = 7, g = 0.82, p < .001; avoidance: k = 7, g =0.83, p < .001; hyperarousal: k = 4, g = 0.66, p < .001). No superiority of iCBT was found compared to active control conditions and at follow-up. Moreover, no robust superiority of internet-based expressive writing (iEW) over control conditions was found. Subgroup analyses revealed no significant impact of any of the tested moderators (i.e., provision of therapeutic support, number of sessions, reminder function, multimedia components) on the effect sizes of iCBT. On average, 23.23% of participants terminated iCBT early and 15.83% terminated iEW early.



**Fig. 1.** Forest plots for the analyses of all included randomized controlled trials on the efficacy of internet-based interventions on PTSD sum scale from pre- to post-treatment assessment.

## 6.2.2. The present findings of STUDY 2 and recent research findings

Efficacy of IBI for PTSD. In line with STUDY 2, there is a body of available metaanalyses providing evidence for the efficacy of iCBT in terms of its superiority over passive control conditions, with effect sizes on measures of PTSD, anxiety, depression, grief, and quality of life ranging from small to large (Dawson et al., 2021; Etzelmueller et al., 2020; Fu, Burger, Arjadi, & Bockting, 2020; Lau, Htun, Wong, Tam, & Klainin-Yobas, 2017; Lewis, Roberts, Bethell, Robertson, & Bisson, 2018; Lewis, Roberts, Gibson, & Bisson, 2020; Lewis, Roberts, Simon, Bethell, & Bisson, 2019; Olthuis, Watt, et al., 2016; Sijbrandij et al., 2016; Simblett, Birch, Matcham, Yaguez, & Morris, 2017; Stefanopoulou, Lewis, Mughal, & Larkin, 2020; Taylor, Graham, Flatt, Waldherr, & Fitzsimmons-Craft, 2020; Wagner, Rosenberg, Hofmann, & Maass, 2020). However, the evidence regarding the superiority of iCBT when contrasted with active control conditions is heterogeneous. In line with STUDY 2, the working group of Lewis and colleagues found no significantly superior effects of iCBT compared to active control conditions (Lewis et al., 2018; Lewis et al., 2020; Lewis et al., 2019). By contrast, other meta-analyses reported small but significant effect sizes in favor of iCBT compared to active control groups (Sijbrandij et al., 2016; Simblett et al., 2017). Evidence demonstrating the equality (non-inferiority) of iCBT with other well-established interventions remains scarce. As such, it is crucial to investigate not only whether the treatment approach of IBI/ iCBT is superior to waitlist, but also whether superiority can be demonstrated over different active control conditions, and whether it can be established as non-inferior to the currently well-established and implemented (face-to-face) treatment options (D'Agostino Sr, Massaro, & Sullivan, 2003; Leichsenring et al., 2018).

Long-term efficacy of IBI for PTSD. STUDY 2 found no significant effects of IBI for PTSD in the longer term. Available data were scarce, and the follow-up periods reported in the primary studies were heterogeneous, thus limiting the statistical analyses and interpretation of findings. In line with STUDY 2, the working group of Lewis found that the significant effect sizes at post-treatment assessment were not sustained at the 3- and 6-month follow-up assessments (Lewis et al., 2018; Lewis et al., 2019). By contrast, other analyses reported small to large significant effects that were sustained at 3- or 6-month follow-ups in groups receiving IBI (Deng et al., 2019; Kuhn & Owen, 2020; Olthuis, Wozney, et al., 2016; Wagner et al., 2020). Primary investigations have yielded promising findings demonstrating a stable iCBTbased intervention effect of moderate to large scale for PTSD over a longer period of 12 to 18 months post-intervention (Knaevelsrud, Böttche, Pietrzak, Freyberger, & Kuwert, 2017; Knaevelsrud & Maercker, 2010; Sunjaya, Chris, & Novianti, 2020; Wagner & Maercker, 2007). More investigations with long-term follow-up periods are required to provide a sufficient pool of data to conduct meta-analyses on the long-term efficacy of IBI for PTSD.

Efficacy of IBI for PTSD in contrast to face-to-face treatments. Due to the lack of data, STUDY 2 was unable to provide findings on the comparison of IBI with face-to-face treatments for PTSD. To date, a limited number of meta-analyses and systematic reviews are

available that examined the non-inferiority of technology-/ internet-assisted interventions in contrast to conventional treatments (Kuhn & Owen, 2020; Norwood, Moghaddam, Malins, & Sabin-Farrell, 2018; Olthuis, Wozney, et al., 2016; Sunjaya et al., 2020). Notably, these analyses primarily examined the transfer of face-to-face CBT sessions to video-conferencing systems and compared the efficacy of these different delivery modes. The analyses yielded promising findings, indicating a non-inferiority of 'video telehealth CBT' compared to face-to-face CBT at post-treatment (Kuhn & Owen, 2020; Sunjaya et al., 2020). However, the therapeutic alliance in video-conferencing therapy was found to be inferior to the therapeutic alliance in conventional therapy (Norwood et al., 2018). Moreover, although the efficacy of therapist-assisted iCBT was found to be equal to that of face-to-face CBT at post-treatment, this equality of effect sizes was not sustained at a follow-up assessment of three to six months (Olthuis, Watt, et al., 2016). Therefore, future research is required to systematically contrast IBI/iCBT with well-established and frequently implemented face-to-face treatment options for PTSD, such as TF-CBT (Etzelmueller et al., 2020; Taylor et al., 2020).

Efficacy of other e-mental health treatments for PTSD. Although STUDY 2 did not include virtual reality (VR) treatments or smartphone applications for treating PTSD, a brief overview of the meta-analytical findings in this field is provided to emphasize their potential impact for the future. Overall, distance treatments (i.e., telephone interventions, emailing, video-conferencing) demonstrate medium to large within-group effect sizes on measures of PTSD and depression from pre- to post-treatment (Olthuis, Wozney, et al., 2016; Sunjaya et al., 2020). Video-conferencing interventions have significant between-group effects when compared to passive control conditions at post-treatment assessment (Kuhn & Owen, 2020). VR-based exposure therapy for PTSD was found to be superior to a waitlist control group but VR was not superior to active control conditions (Deng et al., 2019; Kothgassner et al., 2019). Although mobile applications were found to show significant small to moderate within-group effects on measures of PTSD and depression (Goreis, Felnhofer, Kafka, Probst, & Kothgassner, 2020), studies revealed no significant between-group effects in contrast to passive control groups (Goreis et al., 2020; Kuhn & Owen, 2020; Weisel et al., 2019). Although mobile, easily accessible, low-threshold, and user-friendly treatment applications may be of high relevance and utility for future mental health care, research needs to intensively engage in developing and evaluating smartphone applications for the treatment of PTSD in the future. Data privacy and protection need to be considered, examined, and enhanced (O'Loughlin, Neary, Adkins, & Schueller, 2019; Sander et al., 2020; Sucala et al., 2017; Terhorst, Rathner, Baumeister, & Sander, 2018). Moreover, concerns about the risk of iatrogenic side effects or deteriorating effects have been strongly discussed and need to be taken into serious consideration (Cuijpers & Schuurmans, 2007; Sander et al., 2020).

**Providing therapeutic support in iCBT.** In STUDY 2, iCBT with therapeutic support yielded large between-group effect sizes on measures of PTSD, while iCBT without therapeutic support yielded moderate effect sizes. The effect sizes did not significantly differ. By contrast, a larger body of earlier and recent meta-analyses and systematic reviews of internet- and computer-based treatments for mood and anxiety disorders reported significantly increased between-group effect sizes when support was provided in contrast to interventions without therapeutic contact (Andersson & Cuijpers, 2009; Cowpertwait & Clarke, 2013; Grist & Cavanagh, 2013; Lau et al., 2017; Lewis et al., 2019; Richards & Richardson, 2012; Sijbrandij et al., 2016; Simblett et al., 2017; Spek et al., 2007; Wagner et al., 2020). Some authors reported that unguided IBI/ iCBT is not effective in reducing PTSD and co-occurring mental health complaints (Lau et al., 2017; Simblett et al., 2017). To date, only two other investigations have found equal effect sizes between guided and unguided IBI (Fu et al., 2020; Stefanopoulou et al., 2020), in line with STUDY 2. Overall, the data provide robust evidence that the provision of therapeutic guidance plays a beneficial role in the overall treatment success of IBI. Positive

associations have been found between the provision of therapeutic guidance and patients' treatment satisfaction and adherence (Kaiser, Hanschmidt, & Kersting, 2021; Probst, Berger, & Flückiger, 2020; Simon, McGillivray, et al., 2019). Interestingly, it has been found that minimal-contact treatments become increasingly efficacious with an increasing extent of guidance in the treatment of obsessive-compulsive behavior (Pearcy, Anderson, Egan, & Rees, 2016), substance abuse and addiction disorders (Newman, Szkodny, Llera, & Przeworski, 2011), and anxiety disorders (Lewis, Pearce, & Bisson, 2012). Self-help programs without guidance seem to be most effective for motivated patients with anxiety symptoms and for clients with subthreshold mood disorders, whilst minimal-contact and guided therapies are assumed to reach a broader variety of less motivated patients as well as patients who report higher overall symptom burden (Farrand & Woodford, 2013; Newman, Erickson, Przeworski, & Dzus, 2003). Discussions are currently ongoing about whether there is an 'optimal' dose, mode, and time of contact in IBI (Etzelmueller et al., 2020; Farrand & Woodford, 2013; Lewis et al., 2012; Newman et al., 2003; Pearcy et al., 2016; Simblett et al., 2017; Stefanopoulou et al., 2020). Preliminary findings suggest that neither the mode of support (e.g., email, chat, telephone), the time point of support (e.g., on-demand versus scheduled), nor the type of support (e.g., tailored versus automated feedback) modify the overall efficacy of guided IBI/ iCBT programs (Etzelmueller et al., 2020; Simblett et al., 2017; Stefanopoulou et al., 2020). Future research needs to systematically manipulate different characteristics of the therapeutic contact in IBI to deepen the understanding in this field. Moreover, patients' characteristics need to be taken into consideration as another potentially influencing factor. In terms of providing tailored IBI programs, this may help to further increase the 'fit' between the patient's needs and the program's characteristics, which in turn can be expected to positively influence the patient's acceptance of, adherence to, and satisfaction with the program (Lewis et al., 2018).

Number of treatment sessions and other program components in iCBT. STUDY 2 found that the provision of ten treatment sessions or more was associated with a large betweengroup effect and the provision of less than ten sessions was associated with a moderate betweengroup effect. This difference was not statistically significant. Recent analyses reported significantly increased between-group effects of iCBT (Sijbrandij et al., 2016; Wagner et al., 2020) and of VR (Deng et al., 2019) with an increasing number of therapeutic sessions. Etzelmueller et al. (2020) found significantly reduced treatment effect sizes of iCBT for anxiety disorders (including PTSD) when the treatment duration was between nine to 13 weeks as compared to less than nine weeks or more than 13 weeks. The question of dose-response versus good-enough dynamics in conventional psychotherapy (Holmes et al., 2019) has also been discussed in the literature. According to Robinson, Delgadillo, and Kellett (2020), the optimal dose of face-to-face psychotherapy ranges between four and 26 sessions, and varies depending on the concept of treatment, setting, clinical population, and outcome measures. As yet, the question of whether the overall treatment efficacy in IBI may follow a dose-response relationship or a dynamic of good-enough effects remains unresolved, and more research is needed to foster our understanding of this aspect.

**Early treatment termination in IBI.** In STUDY 2, on average, 23.23% of participants dropped out of iCBT and 15.83% dropped out of iEW. There were no differences between iCBT without therapeutic support versus iCBT with therapeutic support. Recent analyses reported an overall broad range of iCBT dropout rates, from 8.69% to 62.5%, with an average of one in four participants terminating iCBT early (Simon, McGillivray, et al., 2019; Wagner et al., 2020). No differences were apparent between iCBT versus i-non-CBT programs (Lewis et al., 2018; Lewis et al., 2019; Simon, McGillivray, et al., 2019). Non-uptake of treatment (i.e., declining study participation after enrollment and prior to the first module) was found to range between 15.22% and 18.6% in iCBT and between 0% and 14.63% in control conditions (Simon,

McGillivray, et al., 2019). Wagner et al. (2020) found no differences between early terminators and treatment completers in iCBT when examining demographic, trauma-related, and symptom-related variables. Notably, the mean dropout rates of around 25% reported for iCBT are equal to those for conventional therapy (Bradley, Greene, Russ, Dutra, & Westen, 2014; Dixon & Linardon, 2020; Garcia, Kelley, Rentz, & Lee, 2011; Gersh et al., 2017; Hembree et al., 2003; Imel, Laska, Jakupcak, & Simpson, 2013; Lewis et al., 2020; Linardon, Fitzsimmons-Craft, Brennan, Barillaro, & Wilfley, 2019; Sharf, Primavera, & Diener, 2010; Stubbs et al., 2016; Vancampfort et al., 2016).

Therapeutic alliance and treatment acceptance in IBI. Although STUDY 2 cannot provide data on acceptance, satisfaction, and the therapeutic alliance in IBI, a brief overview of recent analyses targeting these questions is provided. ICBT has been found to be moderately to largely acceptable, based on patients' willingness to recommend the treatment to others, their feedback regarding treatment satisfaction, and high levels of treatment adherence (Etzelmueller et al., 2020; Simon et al., 2019; Sunjaya et al., 2020). Most participants rate the therapeutic alliance as strong and satisfactory (Etzelmueller et al., 2020; Kaiser et al., 2021; Simon, McGillivray, et al., 2019; Simon, Roberts, et al., 2019; Sunjaya et al., 2020). Therapeutic alliance and treatment efficacy in IBI were found to correlate substantially, supporting the assumption that a strong alliance can be of high value for the overall treatment success (Kaiser et al., 2021). Furthermore, the therapeutic alliance was found to account for about 6% of the variability of treatment outcomes in IBI for a variety of psychiatric conditions, including PTSD (Probst, Berger, & Flückiger, 2020). Concerning conventional interventions, a strong therapeutic alliance has been found to diminish the risk of dropout (Sharf et al., 2010) and to improve the outcome (Del Re, Flückiger, Horvath, Symonds, & Wampold, 2012; Martin, Garske, & Davis, 2000). Future research is necessary to further examine and systematically assess predictors of treatment adherence, therapeutic alliance, and treatment acceptance in IBI in order to improve its efficacy and to reduce dropout rates (Lewis et al., 2018; Taylor et al., 2020).

Symptom deterioration, non-response, recovery, and remission rates in IBI. The risk of symptom deterioration has been found to be significantly reduced in IBI in contrast to control conditions across various psychiatric disorders, including anxiety disorders, mood disorders, and PTSD (Ebert et al., 2016; Etzelmueller et al., 2020; Rozental, Magnusson, Boettcher, Andersson, & Carlbring, 2017). Higher symptom severity, being in a relationship, a higher educational level, and older age were associated with a reduced risk of symptom deterioration in subjects in a treatment (Rozental et al., 2017). In terms of non-response, between 11.3% and 26.8% of all patients (PTSD: 9.7% - 19.4%) can be expected to be classified as non-responders (Rozental, Andersson, & Carlbring, 2019). Higher symptom severity, male gender, and primarily reporting an anxiety disorder (including PTSD) were found to increase the odds of non-response to iCBT (Rozental et al., 2019). In terms of recovery and remission rates in iCBT, recovery rates range from 12.1% - 92.3% and remission rates range from 0% - 82% across different mental health conditions. On average, it can be expected that 69.9% of all patients (PTSD: 75%) are classified as recovered, and 35.2% of all patients (PTSD: 39.3%) as remitted (Andersson, Carlbring, & Rozental, 2019). Higher symptom severity and female gender increase the odds ratio for recovery, but higher symptom severity reduces the odds ratio for remission, and receiving treatment for an anxiety disorder (including PTSD) lowers the odds ratio for recovery and remission (Andersson et al., 2019). With respect to faceto-face treatments, it is well documented that patients with different psychiatric disorders respond with differing levels of success to different treatment options, and substantial proportions of patients do not reach full or lasting recovery or remission in response to psychotherapy or pharmacotherapy (Carpenter et al., 2018; Cuijpers et al., 2014; Cuijpers, Reijnders, Karyotaki, de Wit, & Ebert, 2018; de Maat, Dekker, Schoevers, & de Jonghe, 2007; Eddy, Dutra, Bradley, & Westen, 2004; Olatunji, Davis, Powers, & Smits, 2013; Thompson-Brenner, Glass, & Westen, 2003). The systematic and consistent assessment of indices of symptom deterioration, recovery, and remission in IBI should be a scope for future research (Simon, McGillivray, et al., 2019).

## 6.2.3. Specific limitations of STUDY 2

First, only k = 20 primary investigations were included in STUDY 2. Although the number of studies examining the efficacy of IBI/ iCBT to treat PTSD has been growing in recent years, only a small proportion of the identified and screened studies were eligible for inclusion in STUDY 2. Most recent meta-analyses on IBI for PTSD included between k = 6 (Goreis et al., 2020) and k = 12 primary studies (Sijbrandij et al., 2016), rising to k = 29 when a wider range of mental disorders was included (Andersson et al., 2019; Rozental et al., 2019) and up to k = 33 when the included treatment options were more heterogeneous (Simblett et al., 2017). By contrast, meta-analyses on conventional treatment options easily include  $k \ge 100$  RCT (e.g., Lewis, Roberts, Andrews, et al., 2020; Lewis, Roberts, Gibson, et al., 2020). The comparably small number of trials eligible for inclusion in STUDY 2 may reflect the still limited amount of research in this area.

Second, although the quality of the primary studies that were included in STUDY 2 was overall sufficient, several weaknesses regarding the methodological approaches or reporting of results in some of the studies need to be acknowledged. Small sample sizes reduce primary studies' statistical power to detect a 'true' effect in the respective population being tested. It might be assumed that larger effect sizes or significant between-group differences could have emerged in STUDY 2 if a larger pool of primary investigations with larger sample sizes had been available. Moreover, some of the included studies lack appropriate descriptions of sample characteristics, including clinical status/ level of symptom severity of the participants, which may have increased the heterogeneity of the data included in STUDY 2. Likewise, the reported

follow-up assessment periods were quite heterogeneous across the primary trials, and in particular, follow-up periods of more than 6 months were lacking. The findings of STUDY 2 thus refer to limited follow-up intervals and the statistical power of these analyses is substantially reduced. However, it should be noted that most recent meta-analyses were faced with comparable constraints of the primary investigations, underlining the need for continuous enhancements regarding the reporting of methods, design, inclusion criteria, sampling, and results in the primary investigations.

Third, the implementation of subgroup analyses in STUDY 2 was confined to iCBT. Most of the subgroup analyses were based on a very limited number of studies (2 < k < 5), meaning that the statistical power was presumably limited. This may have contributed to the overall lack of significant between-group differences across the subgroup analyses. Again, most recent meta-analyses were subject to comparable constraints regarding the subgroup analyses, underscoring the presumably still limited state of research in this field to date.

### 6.2.4. Implications and future directions

Distance-delivered interventions are set to play a significant role for the future mental health care system, particularly in regions with a limited psychotherapeutic infrastructure such as rural regions or low- to middle-income countries where psychotherapeutic support is lacking (Fu et al., 2020; Sunjaya et al., 2020). At the same time, during the COVID-19 pandemic, internet-based (mental-) health care programs have played a major role for (psycho-)therapy supply under exceptional circumstances such as conditions of social distancing and quarantine (Bäuerle et al., 2020; Brog, Hegy, Berger, & Znoj, 2021; Dantas, Barreto, & Ferreira, 2020; Fu et al., 2020; Racine, Hartwick, Collin-Vézina, & Madigan, 2020; van der Lee & Schellekens, 2020; Wang, Gao, Zhang, & Wu, 2020; Wei et al., 2020).

Nevertheless, the impact of population-/ patient-specific characteristics on treatment efficacy needs to be considered in greater depth within future investigations. Different groups

of patients, with different ethnicities, educational levels, socio-economic status, trauma history, and comorbidities, present with varying needs and respond with differing degrees of success to (internet-based) (psycho-)therapy (Bradley et al., 2005; Coventry et al., 2020; Lely, Smid, Jongedijk, Knipscheer, & Kleber, 2019; Schwartze, Barkowski, Strauss, Knaevelsrud, & Rosendahl, 2019). At this point, it is worth mentioning a study by Niemeyer et al. (2020), which was also part of the larger research project within which the current thesis is embedded. Niemeyer et al. (2020) assessed the efficacy and acceptability of an iCBT program in a treatment-seeking sample of GAF veterans with PTSD. The authors found no significant changes in PTSD symptoms following iCBT, along with a limited treatment adherence and a substantial rate of 32.2% of participants who dropped out from the treatment. Although veterans are expected to be generally receptive to mental health technologies (Erbes et al., 2014; Whealin et al., 2015), they have been found to benefit less from various conventional (psycho-)therapy options in comparison to other trauma populations (Haagen et al., 2015; Kitchiner et al., 2019; Kitchiner et al., 2012; Steenkamp et al., 2015; Straud et al., 2019). At the same time, veterans show a limited treatment adherence (Crocker et al., 2018; Eftekhari et al., 2020) and an increased probability of early treatment termination (Byllesby et al., 2019; Edwards-Stewart et al., 2021; Fischer et al., 2018; Gilmore et al., 2020; Hundt et al., 2020; Norona et al., 2020; Sciarrino et al., 2021). These findings highlight the need to develop IBI that are tailored to the specific needs of different (military) patient populations, and to evaluate the treatments' efficacy and acceptability in consideration of the individual patient's characteristics and needs. Research is required to systematically explore probable mechanisms of change in IBI and consequently enhance the possibilities to provide tailored, patient- and process-oriented IBI (Brakemeier & Herpertz, 2019; Captari et al., 2018; Gazzillo, Dazzi, Kealy, & Cuomo, 2020; Twomey, O'Reilly, Bültmann, & Meyer, 2020).

It is well documented that conventional treatments such as EMDR, (non-)traumafocused CBT, group therapy, and pharmacological therapy achieve varying effect sizes,

depending on the target population and context (Bradley et al., 2005; Coventry et al., 2020; Lely, Smid, Jongedijk, Knipscheer, & Kleber, 2019; Schwartze et al., 2019). In particular, populations of veterans, war survivors, and survivors of sexual assault, child maltreatment, and interpersonal (domestic) violence are found to benefit less from psychotherapeutic interventions than other patient populations – regardless of the mode, type, or theoretical framework of the respective intervention (Linde et al., 2020; Taylor et al., 2020). Presumably, these dynamics likewise apply to IBI. Future studies need to systematically assess the specific needs, barriers to care, and moderators of treatment success in IBI in order to reach varying populations on the one hand, and to assess limitations of IBI in terms of identifying populations that may not benefit from these approaches on the other (Linde et al., 2020; Taylor et al., 2020). It must be acknowledged that IBI do not unconditionally 'fit all' (Linde et al., 2020). It is necessary to increase the knowledge surrounding these questions to guide future research.

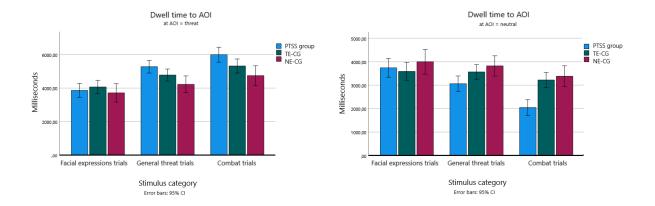
Finally, analyses of the cost-effectiveness of (guided) IBI or tele mental health interventions report substantial initial costs of e-mental health programs, such as investing in software and hardware, but that e-mental health programs seem to be cost-efficient in the longer term and potentially lead to mental health care cost savings in comparison to conventional therapy or when no treatment is provided (Kolovos et al., 2018; Sunjaya et al., 2020). However, such findings are limited by the fact that estimations of cost-effectiveness vary across investigations, and only a minority of primary investigations have reported data on a program's cost-effectiveness, thus impeding meta-analytical calculations and restricting the interpretation and generalizability of findings (Sunjaya et al., 2020; Tate, Finkelstein, Khavjou, & Gustafson, 2009). Therefore, consistent, and transparent indicators of cost-effectiveness in IBI need to be established in future research. Increasingly capturing and reporting reliable and consistent data on costs for developing, disseminating, and evaluating the treatment programs, as well as providing the reader with reliable cost-effectiveness ratios, can be considered as a major mission for future investigations in this field of research (Sunjaya et al., 2020; Tate et al., 2009).

# 6.3. STUDY 3

STUDY 3 provided a cross-sectional group comparison on baseline patterns of attentional bias to threat in a sample of GAF veterans with deployment-related traumatization with PTSS versus veterans with deployment-related traumatization without PTSS versus healthy non-exposed veterans. The reliability of eye-tracking-based indicators of attentional bias was examined from an exploratory perspective.

## 6.3.1. Summary of core findings

Regarding a maintenance bias, veterans with PTSS showed shorter dwell times on general threat-related neutral AOIs and on combat-related neutral AOIs compared to both control groups (see Fig. 2) and showed longer dwell times on general threat AOIs compared to non-exposed veterans. Regarding hypervigilant orienting, veterans with PTSS attended faster to general threat AOIs in contrast to non-exposed veterans. No effects were found on spatial orienting and average initial fixation duration. Regarding attentional bias variability, veterans with PTSS showed a greater fluctuation of attention compared to both control groups. Internal consistency regarding dwell time to threat AOIs was satisfactory.



**Fig. 2.** Average dwell time in milliseconds as a function of group and stimulus category by AOI. PTSS group, trauma-exposed group with PTSS; TE-CG, trauma-exposed healthy control group; NE-CG, non-exposed healthy control group; AOI, area of interest.

# 6.3.2. The present findings of STUDY 3 and recent research findings

Maintenance of attention. In STUDY 3, veterans with PTSS showed a maintenance bias to threat and to trauma-relevant cues in contrast to trauma-exposed and non-exposed healthy veterans, which is generally in line with earlier and more recent eye-tracking-based research (Armstrong et al., 2013; Armstrong & Olatunji, 2012; Clauss, Gorday, & Bardeen, 2022; Kimble et al., 2010; Lazarov, Suarez-Jimenez, Tamman, et al., 2019; Lazarov et al., 2021; Lee & Lee, 2012; Lee & Lee, 2014; Matlow, 2013; Thomas et al., 2013), with earlier investigations of visual search task paradigms (Pineles et al., 2009; Pineles, Shipherd, Welch, & Yovel, 2007), with a review on cognitive (i.e., memory, attention, interpretation) bias in military personnel with and without PTSD (Vyas, Murphy, & Greenberg, 2020), and with findings of a meta-analysis of emotional Stroop paradigms (Cisler et al., 2011). In a recent study by Lazarov et al. (2021), survivors of interpersonal violence with and without PTSD and a third study group of non-exposed healthy individuals were presented with matrices of threat-related and neutral facial expressions while their eye gazes were tracked. The authors found that participants with PTSD showed longer dwell times on threat cues than did participants of both control groups. Moreover, individuals with PTSD had shorter dwell times on neutral cues than did non-exposed healthy individuals, and subjects in the trauma control group had shorter dwell times on neutral cues than did healthy non-exposed individuals (Lazarov et al., 2021). These findings are broadly in line with the findings of STUDY 3.

**Hypervigilance and first fixation measures.** Although STUDY 3 found that veterans with PTSS show a reduced latency to general threat AOIs compared to non-exposed veterans, neither the examination of spatial orienting nor the examination of average initial fixation duration support the assumption of hypervigilant orienting to threat in PTSS or the assumption of difficulties in initial attentional disengagement in PTSS. These findings are largely consistent with the majority of previous eye-tracking-based research (Armstrong et al., 2013; Bryant et

al., 1995; Clauss et al., 2022; Corrigan, Hanna, & Dyer, 2020; Felmingham et al., 2011; Kimble et al., 2010; Lazarov, Suarez-Jimenez, Tamman, et al., 2019; Lazarov et al., 2021; Lee & Lee, 2012; Lee & Lee, 2014; Thomas et al., 2013). Likewise, a systematic review (Vyas et al., 2020) and a meta-analysis of behavioral task paradigms (Cisler et al., 2011) found no evidence of hypervigilant orienting in PTSS. In another systematic review, Lazarov, Suarez-Jimenez, Tamman, et al. (2019) reported no evidence of hypervigilance to threat in PTSS/ PTSD when analyzing eye-tracking-based first fixation measures. Notably, all primary studies that were included in the latter review and that utilized eye-tracking-based first fixation measures presented the study participants with directly trauma-relevant versus neutral cues. None of these studies included cues of a broader context beyond the individual's trauma history. By contrast, STUDY 3 included non-trauma-related cues of generally threatening/ ambiguous content as well as facial cues in addition to trauma-relevant cues.

Hypervigilance and the impact of trauma history. Although not of statistical relevance, a closer look at the descriptive values in STUDY 3 might be of interest. The descriptive values suggest only small differences in latency to combat AOIs and to general threat AOIs when comparing veterans with PTSS to trauma-exposed veterans without PTSS. By contrast, these measures reveal larger differences when either trauma-exposed group is compared with the non-exposed group of healthy veterans. Based on these descriptive observations, one might assume that traumatization itself contributes to patterns of hypervigilant orienting in the sample of STUDY 3. This assumption is supported by findings demonstrating behavioral hyperarousal, attentional alterations, and structural brain changes in trauma survivors who do not exhibit PTSS or PTSD (Covey, Shucard, Violanti, Lee, & Shucard, 2013; Gjini et al., 2013; Karl et al., 2006). Earlier eye-tracking-based investigations acknowledge that the extent of trauma exposure may be a more crucial factor with respect to alterations in information and attention processing, rather than the presence of PTSS or PTSD

(Felmingham et al., 2011; Kimble et al., 2010; Kimble, Fleming, & Bennion, 2013; Lee & Lee, 2012; Lee & Lee, 2014; Thomas et al., 2013). An investigation assessing event-related potentials in trauma survivors with and without PTSD and in non-exposed healthy subjects provides further support in this regard (Zukerman, Fostick, & Ben-Itzchak, 2018). The authors presented participants with acoustic stimuli and measured their brain wave activity at early information processing stages that are associated with attention processes (N1, P2, N2, P3, and N1-P2 complex amplitude; for an overview, please see Miller, Simmons, Whittle, Forbes, & Felmingham, 2021). The results revealed significant differences in N1-P2 complex amplitudes between the PTSD group and the non-exposed control group and in N1 amplitudes between the trauma-control group and the non-exposed control group. Furthermore, correlations emerged between PTSS severity scores, trauma history, and N1-P2 complex amplitudes within all groups. Zukerman et al. (2018) interpreted these findings as providing preliminary evidence of a generalized hyperarousal in trauma survivors – even in the absence of PTSD – that can be measured via brain wave activity at early stages of information processing. Finally, in another secondary analysis of the larger longitudinal investigation of which the present thesis is part, Schumacher et al. (2022) examined cross-sectional differences in hair cortisol concentrations between the three study groups of (non-) trauma-exposed veterans with and without PTSD. The results revealed significantly higher hair cortisol concentration in both traumatized groups compared to the non-exposed control group, along with no group differences between the group of traumatized veterans with PTSD versus the group of traumatized veterans without PTSD. Furthermore, hair cortisol concentration was not significantly correlated either with the level of perceived chronic stress or with the overall PTS symptom severity. Schumacher et al. (2022) concluded that trauma exposure seems to have a long-lasting effect on HPA axis activity, as indicated by the higher hair cortisol concentrations in all trauma survivors and given that these dysregulations persisted for several years post-trauma. Moreover, they suggested that increased hair cortisol concentration seems to be a psychobiological indicator of trauma exposure rather than of the presence of PTSD.

Hypervigilance and pupil dilation. In recent years, interest in research on pupil responses in PTSD has been growing and experimental paradigms have evolved (Cascardi et al., 2015; Felmingham et al., 2011; Ginton et al., 2021; Kimble et al., 2010; McKinnon, Gray, & Snowden, 2020; Rubin & Telch, 2021). Although some investigations report mixed findings (Felmingham et al., 2011; Ginton et al., 2021; Rubin & Telch, 2021), there is a body of evidence demonstrating that pupil diameter, and changes therein, differ between individuals with PTSD and healthy controls. Preliminary findings demonstrate that participants with PTSD show an increased pupil dilation when confronted with emotionally salient cues (e.g., threatening, fearinducing, happy content) compared to cues with neutral content (Cascardi et al., 2015), and in contrast to (traumatized) participants without PTSD (Cascardi et al., 2015; McKinnon et al., 2020) or with lower levels of PTSD (Kimble et al., 2010). The authors interpreted these findings as being indicative of decreased parasympathetic activity and increased sympathetic activity in subjects with PTSD compared to (non-)exposed healthy controls, supporting the assumption of a generalized hyperarousal and sensitivity to emotionally salient cues in PTSD (McKinnon et al., 2020). Henderson, Bradley, and Lang (2018) examined participants' pupil diameter and changes therein during emotional imagery and found that the pupil diameter was significantly enhanced shortly after beginning and throughout the imagery of emotional (pleasant and unpleasant) content. The authors interpreted these findings as suggesting the involvement of the autonomic nervous system during emotional imagery in general, highlighting its relevance for the assessment and treatment of PTSD.

Attentional bias variability. STUDY 3 is a pioneering eye-tracking-based investigation concerning the operationalization of ABV via eye-tracking-based indices. The findings of STUDY 3 can support the assumption of PTSD-associated within-subject

fluctuations of attentional engagement and disengagement to relevant cues over time (Bar-Haim et al., 2007; Zvielli et al., 2014). Earlier eye-tracking investigations examined participants' attention over time by subdividing the total presentation time into multiple sections of 500 up to 2000 milliseconds each, and by analyzing the gaze patterns in each of these sections (Armstrong et al., 2013; Lee & Lee, 2012; Lee & Lee, 2014; Matlow, 2013; Thomas et al., 2013). Others assessed the duration or number of subsequent fixations to the threat cues after the first fixation was exited (Felmingham et al., 2011; Kimble et al., 2010). Overall, findings were heterogeneous, and evidence of attentional fluctuation was weak. Only Thomas et al. (2013) and Matlow (2013) found that participants with PTSD showed a temporal sequence of heightened attention to trauma cues at the beginning of a trial, followed by a shift of attention away from trauma cues and a subsequent increase in attention at the end of the trial (engagement - disengagement - re-engagement). These patterns were absent in (non-)exposed healthy controls (Thomas et al., 2013). In their systematic review, Lazarov, Suarez-Jimenez, Tamman, et al. (2019) interpreted these findings as indicating a fluctuation of attention over time in PTSD in the sense of ABV. However, eye-tracking-based data on ABV in PTSD remain extremely scarce, and future research in this field is called far. As yet, it is not possible to draw any conclusions about the presence and nature of patterns of ABV in (military) participants with PTSS or PTSD.

The impact of mediating and moderating variables on attentional bias. In recent years, a growing body of research has examined the relevance of moderating and mediating variables on the pathway from PTSD to attentional bias. Although STUDY 3 did not assess mediating or moderating factors on the pathway from PTSS to attentional bias, some current findings in this field are presented here. First, disrupted abilities in attentional control (i.e., attention regulation and response inhibition) have been found to be associated with PTSS severity (Iacoviello et al., 2014; Naim et al., 2015; Swick & Ashley, 2017; Yuval et al., 2016)

and with attentional bias and ABV in PTSD (Bardeen & Daniel, 2017; Bardeen et al., 2020; Bardeen & Fergus, 2016; Clauss, Bardeen, Gordon, & Daniel, 2021; Naim et al., 2015). Moreover, impairments of attentional control have been found to act as moderators on the pathway from PTSS/ PTSD to attentional bias (Aupperle et al., 2012; Bar-Haim et al., 2007; Bardeen, Daniel, Gordon, Hinnant, & Weathers, 2020; Bardeen & Fergus, 2016; Bardeen, Fergus, & Orcutt, 2015; Bardeen, Tull, Daniel, Evenden, & Stevens, 2016; El Khoury-Malhame, Reynaud, et al., 2011; Iacoviello et al., 2014; Olatunji et al., 2013; Schoorl, Putman, Van Der Werff, et al., 2014; Yuval et al., 2016; Zvielli et al., 2014). Individuals with PTSD and a reduced attentional control ability were found to show increased patterns of attentional bias and ABV compared to individuals with PTSD and a relatively increased attentional control ability (Bardeen & Daniel, 2017; Bardeen et al., 2020; Bardeen & Fergus, 2016). It is assumed that individuals with relatively higher levels of attentional control can utilize these resources to manage the impairing effects of PTSS and when confronted with threat cues (Eysenck, Derakshan, Santos, & Calvo, 2007). Interestingly, Clauss et al. (2021) demonstrated the impact of cognitive load on this moderating effect of attentional control. The authors found a significant moderating effect of attentional control on the path between PTSS and ABV under a 'low cognitive load condition', but this moderating effect disappeared under a condition of 'higher cognitive load', indicating that the moderating effect of attentional control may vanish under conditions of increased strain (Clauss et al., 2021). Second, Mekawi et al. (2020) demonstrated an impact of negative affect on the association between PTSD and attentional bias. The authors found a significant association between PTSD and attentional bias to threatening cues that was mediated by negative trait affect, indicating that attentional bias to threat was more pronounced with increasing negative affect. Third, emotion dysregulation has been repeatedly found to significantly mediate the association between PTSS and ABV, insofar as individuals with PTSS and concurrently increased levels of emotion dysregulation exhibit greater levels of ABV when confronted with threat cues as compared to individuals with PTSS

and relatively lower levels of emotion dysregulation (Bardeen et al., 2017; Klanecky Earl et al., 2020).

Reliability of eye-tracking-based indicators of attentional bias. STUDY 3 was one of the first studies to examine the reliability of eye-tracking-based measures of attentional bias. Lazarov et al. (2021) were the first researchers to investigate reliability values for dwell time and first fixation duration. For the dwell time measures, the authors found overall satisfactory values on Cronbach's alpha and on test-retest reliability between and within groups, whilst the values for the first fixation measures were not acceptable (Lazarov et al., 2021). These findings are in line with the results of STUDY 3, which showed acceptable values for the internal consistencies of average dwell time but unacceptable values for the internal consistencies of initial fixation duration. As such, the results support the preliminary assumption that eyetracking-based measures of attention that are computed over a longer presentation duration demonstrate higher reliability scores than eye-tracking-based measures of attention that capture only brief (initial) presentation sequences (Lazarov, Suarez-Jimenez, Tamman, et al., 2019; Lazarov et al., 2021; Skinner et al., 2018; Waechter, Nelson, Wright, Hyatt, & Oakman, 2014; Wermes, Lincoln, & Helbig-Lang, 2017). Nevertheless, the low values of internal consistency for measures of initial fixation may be helpful for explaining the non-significant between-group effects on these measures (Lazarov et al., 2021). Although problems with reliability measures of various psychological tasks and experimental designs are intensively debated in the literature (Enkavi et al., 2019; Hedge, Powell, & Sumner, 2018; Kruijt, Field, & Fox, 2016; Parsons, Kruijt, & Fox, 2019), Hedge et al. (2018) pointed out that limited reliability scores in experimental paradigms do not necessarily imply that the measure, task, or paradigm needs to be questioned in terms of its validity or replicability. Rather, it is suggested to further explore the potential impact of different experimental and task-related factors on the effect sizes and reliabilities of the dependent measures and to continuously pay serious consideration to these potential influences when planning and conducting experimental investigations (Enkavi et al., 2019; Hedge et al., 2018; Parsons et al., 2019).

### 6.3.3. Specific limitations of STUDY 3

First, STUDY 3 did not include a non-military control group, at the expense of controlling for potential military-related effects on the participants' gaze patterns and attentional bias. Given the veterans' pre-deployment training, one might conceive of a 'trained' attentional bias to combat-relevant cues that may have been observable across the entire sample of military personnel in STUDY 3. It might be speculated that the entire sample of military personnel could show occupation-related 'trained' increases in dwell time to combat AOIs and 'trained' decreases in entry time to combat AOIs that would be absent in healthy non-military controls. Future studies should systematically include multiple military and non-military control groups to scrutinize probable 'trained' patterns of attentional bias versus traumatization- and PTSDrelated patterns of attentional bias.

Second, due to difficulties regarding the recruitment of participants, eye-tracking-specific exclusion criteria, and errors in obtaining eye-tracking data, the final sample size was meaningfully reduced in STUDY 3, which consequently resulted in a substantially reduced statistical power. Thus, one cannot definitively rule out the existence of 'true' between-group effects that were not detectable in STUDY 3 due a limited statistical power. Nevertheless, with N = 70, this is one of the larger eye-tracking studies on attentional bias to date (Lazarov, Suarez-Jimenez, Tamman, et al., 2019).

Third, STUDY 3 did not include positive stimuli such as positive scenes or happy facial expressions, in contrast to some earlier investigations (Armstrong et al., 2013; Lee & Lee, 2012; Lee & Lee, 2014; Thomas et al., 2013). Rather, STUDY 3 was interested in comparing traumarelated and generally threatening/ ambiguous stimuli to neutral stimuli, in line with other investigations (Bryant et al., 1995; Felmingham et al., 2011; Kimble et al., 2010; Lazarov et al.,

2021). Whereas previous investigations utilized either words (Bryant et al., 1995; Felmingham et al., 2011), faces (Armstrong et al., 2013; Beevers et al., 2011; Disner et al., 2013; Lazarov et al., 2021; Lee & Lee, 2014), or pictures (Kimble et al., 2010; Lee & Lee, 2012; Thomas et al., 2013), STUDY 3 was the first to include more than one stimulus condition. As such, STUDY 3 was able to demonstrate that the reliability of the eye-tracking-based indicators of attentional bias varied between the different stimulus types and AOIs within and across study groups, extending the findings of Lazarov et al. (2021).

Fourth, STUDY 3 did not include an additional experimental manipulation, such as inducing a cognitive load, masking stimuli, or stimulus onset asynchrony. Eye-tracking-based investigations demonstrated that in healthy subjects, masked emotionally salient information was capable of provoking automated processes, such as facilitated orientation to the relevant information (Bodenschatz, Kersting, & Suslow, 2018; Terburg, Hooiveld, Aarts, Kenemans, & van Honk, 2011). However, in their meta-analysis, Bar-Haim et al. (2007) found no differences between the pooled between-group effect sizes in studies that used subliminal exposure times versus studies that used supraliminal exposure times for stimulus presentation. Bar-Haim et al. (2007) concluded that patterns of anxiety- and stress-related attentional bias to threat can be observed under either experimental condition in eye-tracking-based paradigms. Based on these verdicts, STUDY 3 specified no need for additional experimental manipulations to assess group differences in attentional bias to threat under the current paradigm and in the present sample.

Finally, given the lack of eye-tracking paradigms that operationalized ABV, its operationalization in STUDY 3 was grounded on approaches stemming from reaction timebased paradigms that were adapted and modified according to the eye-tracking-specific outcome measures in STUDY 3. Thus, it needs to be emphasized that the operationalization and measurement of ABV in STUDY 3 is exploratory in nature and as yet, no conclusive interpretations concerning the presence or absence of ABV in PTSD can be drawn. Kruijt et al. (2016) pointed out the eminent difficulties that seem to be associated with current operationalizations of ABV based on behavioral/ reaction time-based parameters and formulas. When analyzing randomly generated datasets in a simulation study, the authors found that the examined outcome parameters demonstrated a crucial sensitivity to increases in the standard deviation at the reaction time level and to increases in the overall mean reaction time – but in the absence of a true bias in the data – thus producing false-positive group differences (Kruijt et al., 2016). According to the authors, it remains unclear what 'real' underlying constructs or processes may be measured and may thus be represented by the currently implemented operators in the empirical research to date. Kruijt et al. (2016) called for more fundamental research and a generally cautious attitude concerning the implementation of innovative operators in attention research.

## 6.3.4. Implications and future directions

First of all, the findings of STUDY 3 generally support the assumption that after an automated and bottom-up-generated threat detection, top-down-regulated neuronal processes lead to a maintenance of attention on cues that have been identified as being of particular relevance (Fox et al., 2001; Theeuwes, Godijn, & Pratt, 2004; Vuilleumier, 2005). The increased dwell times on threat-relevant cues support the notion that motivation-driven processes of higher neuronal order evaluate these cues as being of high relevance for the individual and in turn contribute to a sustaining of attention on these cues in PTSD (Foa et al., 1991; Fox et al., 2001; Katsuki & Constantinidis, 2013; Lissek, 2012; Pineles et al., 2009). These findings underscore the central role played by a vicious cycle of cognitive and emotional processes in maintaining PTSD (Birrer & Michael, 2011; Michael, Halligan, Clark, & Ehlers, 2007; Steil & Ehlers, 2000).

No evidence of avoidance of threat-related cues was observable in the current sample in STUDY 3, which is in line with available meta-analyses and systematic reviews on attentional bias in PTSD (Armstrong & Olatunji, 2012; Clauss et al., 2022; Lazarov, Suarez-Jimenez,

Tamman, et al., 2019). Moreover, it supports earlier notions raised by Michael et al. (2007) and Steil and Ehlers (2000), who pointed out that anxiety disorders, particularly specific phobias, are characterized by continuous efforts to avoid threat-associated cues, and this can be evidenced via eye-tracking technology (Armstrong & Olatunji, 2012). In contrast to these patterns of avoidance in phobias, the authors assumed that maintaining attention on threat in PTSD can be indicative of ruminative features of this disorder. Furthermore, PTSD may include ruminative features that resemble the ruminative symptoms known in the context of obsessivecompulsive disorder (OCD) and depressive disorder (Michael et al., 2007; Steil & Ehlers, 2000), as well as generalized anxiety disorder (Yang et al., 2014). Such interpretations may further support the diagnostic changes that have been made to the DSM, that is removing OCD and PTSD from the category of anxiety disorders and transferring them to newly developed, distinct categories of obsessive-compulsive spectrum disorders and of trauma- and stressorrelated disorders, respectively (American Psychiatric Association, 2013).

In view of the veterans' pre-deployment training and a speculated 'trained' attentional maintenance bias to combat cues across the entire sample of military personnel, the question arises of whether maintaining one's attention on relevant (i.e., combat-related) cues plays an adaptive or rather maladaptive role in the context of foreign deployment and exposure to battlefield action. Due to the cross-sectional design of STUDY 3 and based on the present data, no inference can be drawn about this question. Noteworthy in this regard are a limited number of longitudinal investigations examining the prospective impact of pre-deployment patterns of gaze and attentional bias on the subsequent development of post-deployment PTSD. These findings provide preliminary evidence for the assumption that pre-deployment attentional bias (towards and away) from threat interacts with the number of intermediate traumatizing events on the path to post-deployment PTSD (Schäfer et al., 2016; Wald et al. 2013). Furthermore, veterans who shift their attention away from threat during an acute situation of stress exposure have been found to show higher symptom scores on subsequent PTSD measures (Wald, Lubin,

et al., 2011; Wald, Shechner et al., 2011). These preliminary findings highlight the need for future longitudinal investigations in this field to further examine the predictive value of preand peri-deployment attentional bias for the development and course of post-deployment PTSD. This will be of high clinical relevance with respect to the development and evaluation of primary prevention programs for this high-risk population of military veterans. Moreover, research in this field of interest might have a major impact for further populations at high risk of developing occupation-related PTSD, such as firefighters, first responders, and police officers.

While the investigation in the present thesis found no support for the assumption of hypervigilant orienting to threat in PTSS, future (eye-tracking) research exploring this field of PTSD-related symptom characteristics and their assessment would be worthwhile. For instance, and Waters (2019) conducted a systematic review although Hyde, Ryan, of psychophysiological parameters of anxiety- and stress-related disorders, they did not discuss findings from pupillometry in PTSD, highlighting the current lack of and future need for investigations in this field. Future interest should also focus on the association between reporting a lifetime traumatization and hypervigilance versus the association between reporting PTSD and hypervigilance. Zukerman et al. (2018) provided preliminary evidence for the assumption that trauma exposure per se can lead to alterations in early stages of information processing, potentially contributing to patterns of hypervigilance across trauma survivors, regardless of the presence of PTSD. Likewise, preliminary psychobiological evidence suggests that (cumulative) trauma exposure itself - rather than reporting PTSD - is associated with longlasting alterations or dysregulations of HPA axis activity, as evidenced by higher hair cortisol concentrations in trauma survivors with and without PTSD (Castro-Vale et al., 2020; Schumacher et al., 2022). Future studies should systemically account and control for effects attributable to the traumatization itself versus effects that are associated with symptoms of PTSD. Furthermore, research on attentional, biological, and behavioral patterns of

hypervigilance in trauma survivors with and without PTSD would be helpful in yielding a clearer differentiation between the impact of traumatization and of PTSD. Moreover, future research should incorporate the experimental presentation of a broader variety of stimulus content. Hyperarousal and hypervigilant behavior are not exclusively directed at trauma cues, but show a substantial tendency to generalize to cues of a broader, non-trauma-related context (American Psychiatric Association, 2013). Cascardi et al. (2015) demonstrated that trauma survivors with and without PTSD do not differ in hypervigilant orienting to trauma-relevant cues, whilst hypervigilance was generalized to non-trauma-related cues in participants with PTSD only. Future studies should pursue these lines of research and systemically investigate differences between traumatized samples with and without PTSD and non-traumatized samples regarding their attentional patterns to trauma cues and to cues beyond the individual trauma context.

Existing research on mediating and moderating factors on the path from traumatization to PTSD and the associated attentional bias provides a strong basis to corroborate the assumption that neither traumatization itself nor PTSD itself leads to differing patterns of attentional bias in traumatized individuals with and without PTSD. Rather, one must assume that trauma history and severity of PTSS relate to each other and to further interindividual differences regarding several emotion- and cognition-related factors, to contextual factors, and to further variables that have not yet been in the scope of research. Future investigations are needed to further explore and identify these and further interactional processes over the course of traumatization, development, and maintenance of PTSD, and the associated attentional bias. Such findings would also be of particular interest for PTSD intervention research. For instance, preliminary findings support the premise that interventions aiming to increase conscious emotion regulation and attentional control may be promising for the treatment of PTSD and the associated attentional bias (Bardeen et al., 2020; Barkus, 2020; Renna, Fresco, & Mennin, 2020; Tull & Kimbrel, 2020).

Finally, the findings of STUDY 3 concerning the reliability of eye-tracking-based measures of attentional bias need to be viewed in light of the fact that the work was pioneering, preliminary and exploratory in nature, along with the pioneering investigation by Lazarov et al. (2021). A gap in the literature can be observed between the reporting of reliability indices of self-report or interview measures versus the reporting of reliability indices of experimental or behavioral measures (Enkavi et al., 2019). Researchers have repeatedly called for empirical clinical research to commonly report reliability indices of the utilized experimental/behavioral task measures (Drost, 2011; Kimberlin & Winterstein, 2008; Lazarov, Suarez-Jimenez, Tamman, et al., 2019; Lilienfeld & Strother, 2020; Parsons et al., 2019). There is a strong need for future eye-tracking-based investigations to systematically investigate the reliability of their utilized eye-tracking-based measures of attentional bias.

## 6.4. STUDY 4

STUDY 4 examined the modifiability of patterns of attentional bias in a national sample of treatment-seeking GAF veterans with PTSS. A stand-alone iCBT program was provided and modifications of patterns of attentional bias were recorded from pre- to post-treatment assessment and at three-month follow-up.

### 6.4.1. Summary of core findings

Wilcoxon signed-rank tests revealed no significant effects of the iCBT program on any of the measures of attentional bias (see Table 2). STUDY 4 provides no support for the efficacy of an iCBT program to modify patterns of attentional bias in veterans with PTSS.

	Comparison pre- to post-treatment <sup>1</sup>	Comparison pre- to follow up <sup>2</sup>
Mean dwell time in %		
Combat (neutral)	Z = -2.13, p = .033 (Z = -1.96, p = .050)	Z = -2.40, p = .016 (Z =62, p = .534)
General threat (neutral)	Z =98, p = .328 (Z =09, p = .929)	Z =27, p = .790 (Z =53, p = .594)
Average fixation duration in ms		
Combat (neutral)	Z =09, p = .929 (Z = -1.60, p = .110)	Z = -1.07, p = .286 (Z =18, p = .859)
General threat (neutral)	Z =45, p = .657 (Z =18, p = .859)	Z =98, p = .328 (Z = -36, p = .722)
Mean entry time in ms		
Combat (neutral)	Z = -1.69, p = .091 (Z = -1.07, p = .286)	Z =09, p = .929 (Z = -1.16, p = .248)
General threat (neutral)	Z =27, p = .790 (Z = -1.51, p = .131)	Z = -1.60, p = .110 (Z = -1.42, p = .155)
Mean initial fixation duration in ms		
Combat (neutral)	Z =80, p = .424 (Z =09, p = .929)	Z =89, p = .374 (Z = -1.78, p = .075)
General threat (neutral)	Z =18, p = .859 (Z =89, p = .374)	Z = -1.51, p = .131 (Z =80, p = .424)

*Table 2.* Results of Wilcoxon signed-rank tests on modification of attentional bias by dependent variable and stimulus, N = 24.

*Note.* N = 24 is number of subjects at baseline; <sup>1</sup>, treatment completers at post-treatment assessment, N = 11; <sup>2</sup>, treatment completers at follow-up, N = 11; Bonferroni corrected level of statistical significance set at p < .001.

## 6.4.2. The present findings of STUDY 4 and recent research findings

**Modification of attentional bias through psychotherapeutic interventions.** STUDY 4 examined the efficacy of an iCBT program to modify baseline patterns of attentional bias in treatment-seeking veterans with PTSS. In contrast to attentional bias modification (ABM) programs (Fodor et al., 2020; Gober, Lazarov, & Bar-Haim, 2021; Hakamata et al., 2010; Hallion & Ruscio, 2011; Kuckertz & Amir, 2015; Mogg & Bradley, 2016; Mogg et al., 2017; Mogoaşe et al., 2014; Price et al., 2016) or attention control training (ACT) programs (Badura-Brack et al., 2015; Gober et al., 2021; Lazarov, Suarez-Jimenez, Abend, et al., 2019), the iCBT being tested did not include treatment components that particularly strive to modify patterns of attentional bias. Rather, it sought to reduce the overall PTSD symptom severity in terms of a trauma-focused iCBT manual (Niemeyer et al., 2020). Concerning ABM programs, the effect sizes for anxiety-related attentional bias range from small (Hallion & Ruscio, 2011; Mogoaşe et al., 2014) to medium (Fodor et al., 2020; Hakamata et al., 2010; Price et al., 2016), and it is

repeatedly found that PTSD-related attentional bias seems to be less responsive to ABM training compared to attentional bias that is related to other (anxiety) disorders (Fodor et al., 2020; Woud, Verwoerd, & Krans, 2017). To date, research examining the efficacy of 'general' interventions on measures of attentional bias is limited. Regarding psychiatric conditions other than PTSD, some investigations are available that analyzed the efficacy of traditional CBT to modify attentional bias, but the findings were disappointing (Babai, Sepavand, Nokani, Aghamohammadi, & Sheybani, 2016; Davis et al., 2016; Huppert et al., 2018; Kampmann, Emmelkamp, & Morina, 2018; Tobon, Ouimet, & Dozois, 2011). For instance, Huppert et al. (2018) found no significant effects of a CBT program on social anxiety disorder-related attentional bias, although the results did reveal significant effects on social anxiety symptoms. The authors assumed that their CBT may not have been sufficiently specific to adequately capture and modify patterns of attentional bias (Huppert et al., 2018). Possibly, this may account for the present iCBT as well. In terms of PTSD, there is promising preliminary evidence to support the efficacy of Eye Movement Desensitization and Reprocessing (EMDR) for symptom reduction and concurrent modification of attentional bias (El Khoury-Malhame, Lanteaume, et al., 2011; Ribchester, Yule, & Duncan, 2010). EMDR addresses and utilizes dynamic visual processes that activate neuronal networks, and discussions are ongoing regarding the degree to which EMDR itself may alter neuronal circuits and associated visual-attentional processes, potentially contributing to modifications of attentional bias (Coubard, 2012; Coubard, 2015; Coubard, 2016; Coubard & Kapoula, 2006; Kapoula, Yang, Bonnet, Bourtoire, & Sandretto, 2010). In contrast, the iCBT tested in STUDY 4 did not integrate EMDR or comparable techniques in the treatment protocol. Notably, these aforementioned investigations utilized behavioral- or reaction time-based paradigms and outcome measures. Available eye-trackingbased investigations that assessed the modifiability of attentional bias targeted subclinical depression or dysphoric mood (Möbius, Ferrari, van den Bergh, Becker, & Rinck, 2018; Wadlinger & Isaacowitz, 2008), major depressive disorder (Krejtz, Holas, Rusanowska, & Nezlek, 2018; Woolridge, Harrison, Best, & Bowie, 2021), tobacco use disorder (Mondino, Lenglos, Cinti, Renauld, & Fecteau, 2020), and anorexia nervosa (Mercado, Schmidt, O'Daly, Campbell, & Werthmann, 2020). Concerning PTSD, there are not yet any eye-tracking-based studies examining the pre- to post-intervention efficacy of an (i-)CBT or other general (psychotherapeutic) intervention to modify patterns of attentional bias. STUDY 4 constitutes a pioneering work in this area.

Modifiability of attentional bias in military populations. So far, investigations aiming to modify attentional bias in military personnel are scarce, and available findings are mixed. In line with the null-findings of STUDY 4, some investigations reported only limited or null effects of ABM training or ACT programs in samples of Dutch veterans (Schoorl, Putman, Mooren, Van Der Werff, & Van Der Does, 2014) and of Israeli and US American veterans (Badura-Brack et al., 2015). By contrast, promising findings were reported by Khanna et al. (2016), who provided a male sample of US American military personnel with PTSD with sessions of an ABM or ACT program. After program completion, symptoms of PTSD were significantly reduced under both competing intervention arms, the veterans' response latencies to combat cues no longer differed from their response latencies to neutral cues, and the response latencies to combat cues in the group of veterans with PTSD no longer differed from those in the group of healthy veterans (Khanna et al., 2016). Moreover, there are several studies examining the efficacy of preventive ABM and ACT programs that were delivered to members of the Israeli Defense Force before deployment (Wald et al., 2017; Wald et al., 2016). Remarkably, at 2-month post-combat assessment, the association between combat exposure and post-combat PTSD was significantly reduced in the group that received preventive ABM training (Wald et al., 2017). Moreover, at 4-month post-combat assessment, participants who received a preventive 4-session ABM training intervention showed significantly lower PTSD prevalence rates than those who received no training (Wald et al., 2016). It should be noted that the group of participants who received 8 sessions of the same ABM training and the group of participants who received an ACT program did not differ from the no-training control group (Wald et al., 2016). This inverse dose-response effect is in accordance with a meta-analysis of the efficacy of ABM training for social anxiety disorder (Price et al., 2017). In sum, the data available thus far on the modifiability of attentional bias in populations of military veterans is restricted to the evaluation of ABM and ACT programs. While some promising findings have been reported, the overall evidence is heterogeneous. STUDY 4 constitutes a pioneering work concerning the evaluation of a general psychotherapeutic intervention in this area.

Modifiability and change sensitivity of autonomic markers. Niemeyer et al. (2020) did not find a significant treatment effect of the provided iCBT on the level of overall PTSD symptom severity in the military sample. Referring to the larger project of which STUDY 4 was part, some additional publications may be of particular interest at this point. First, Schumacher et al. (2021) investigated changes on the level of salivary cortisol and on concentrations of alpha-amylase in response to the same iCBT in the same population as that investigated in STUDY 4 and by Niemeyer et al. (2020). The authors collected diurnal profiles of saliva samples for the analysis of salivary cortisol and alpha-amylase before and after treatment completion and at three-month follow-up. It was expected that the levels of cortisol would be increased and that the levels of alpha-amylase would be reduced after the treatment provision, indicating an improved balance of the stress systems in the study participants (Schumacher et al., 2021). Contrary to expectation, however, the salivary cortisol level and alpha-amylase concentration were not significantly changed after treatment provision, and there were no significant changes in PTSD symptom severity (Schumacher et al., 2021). Due to the non-significant findings regarding PTSD symptom changes from pre- to post-treatment assessment, the authors concluded that no inferences can be drawn about the change-sensitivity of cortisol and alpha-amylase markers within their psychotherapy research in veterans with

PTSS. Furthermore, Engel et al. (2021) and Engel et al. (2020) analyzed changes in oxytocin and vasopressin levels in response to the same iCBT in the same sample from Niemeyer et al. (2020) and STUDY 4. No significant treatment effects emerged, either on oxytocin levels or on vasopressin levels. These null-findings were present from pre- to post-treatment assessment and at three-month follow-up, and there were no significant changes in PTSD symptom severity during and after the treatment provision (Engel et al., 2021; Engel et al., 2020). The authors reported that both parameters, oxytocin level and vasopressin level, were not stable within individuals over time. The pre-treatment levels of neither one nor the other parameter were identified as useful markers to predict PTSD symptom change over time in response to the iCBT (Engel et al., 2021; Engel et al., 2020). As such, they inferred that in the present sample of veterans, PTSD symptom severity seemed to be rather unrelated to levels of vasopressin and oxytocin, and no feasible conclusions could be drawn concerning the change-sensitivity of vasopressin and oxytocin as autonomic markers of change (Engel et al., 2021; Engel et al., 2020). Therefore, it might be assumed that in the absence of significant changes in PTSD symptom severity in response to the iCBT, the observation and assessment of significant modifications of attentional bias was impeded in the sample under study, which was also the sample of STUDY 4. In the absence of significant symptom changes, no conclusions can presumably be drawn concerning the change-sensitivity of attentional bias in the present sample of veterans with PTSS and in response to receiving the current iCBT analyzed in STUDY 4.

### 6.4.3. Specific limitations of STUDY 4

A probable risk of sampling bias in STUDY 4 must be acknowledged. The included sample is likely to show characteristics of a self-referred convenience sample. Research investigators are confronted with the risk of sampling bias across all disciplines and at all times (Bornstein, Jager, & Putnick, 2013; Cheon, Melani, & Hong, 2020; Cheung, Peter, Smit, de Vries, & Pieterse, 2017; de Winter et al., 2005; Nielsen, Haun, Kärtner, & Legare, 2017; Pollet

& Saxton, 2019). Despite all efforts, feasible participants were most likely to be enrolled in the present intervention study in the aftermath of a face-to-face contact, such as based on a recommendation of a comrade or the GAF doctor. Traumatized military personnel report an increased fear of stigmatization, concerns regarding data confidentiality, skepticism about treatment effects, and fear of the treatment harming their reputation (Acosta et al., 2018; Blais & Renshaw, 2013; Hamilton, Coleman, & Davis, 2017; Hoge et al., 2004; Morgan et al., 2020; Nichter, Hill, Norman, Haller, & Pietrzak, 2020; Tanielian et al., 2016). A recommendation by a comrade or the attending GAF doctor may have fostered veterans' confidence in the announced study and their willingness to participate.

Nevertheless, it should also be acknowledged that the assessment procedure of the longitudinal intervention investigation was comparatively intense. Participating veterans were required to travel to the laboratory in Berlin for each of the multiple assessments of pre-, (waitlist), post-, and follow-up assessment, had to stay in Berlin overnight, had to provide several samples during the assessments (e.g., hair, blood, saliva), had to undergo the repeated pre- to post- to follow-up diagnostic assessments (i.e., assessing PTSD symptoms and further psychiatric symptoms), and had to take part in repeated experimental assessments (i.e., eye-tracking experiment and heart rate variability experiment). In sharp contrast to this intense in-person assessment procedure, the trauma-focused intervention was provided online, and the participating veterans received asynchronous written feedback on their writing assignments only (except for telephone calls in the case of technical problems and reminder telephone contacts). One must assume that this specific combination of a highly time-consuming assessment procedure along with an intense trauma-focused iCBT contributed to the experienced difficulties concerning the recruitment, high rates of dropout, and limited treatment adherence over time.

These limitations regarding recruitment and study adherence resulted in a substantially diminished sample size of N = 41 that was entered into the larger intervention trial (Niemeyer

et al., 2020). Of these, a substantial proportion of data sets were not suitable for the data analyses in STUDY 4, due to eye-tracking-specific exclusion criteria, software- and hardware-related data loss, and dropout. Nevertheless, the problem of small sample sizes is of general concern in this field of research and does not explicitly represent a specific problem of STUDY 4. In addition, data loss due to software and hardware errors in obtaining eye-tracking data is known to account for at least around 5% of overall data loss in eye-tracking investigations (Holmqvist et al., 2011). Thus, one must accept a highly reduced statistical power of the analyses in STUDY 4.

Finally, particularly concerning the limited treatment adherence and high rates of dropout reported by Niemeyer et al. (2020), one might speculate about the reasons why this iCBT was not acceptable in the present sample of GAF veterans. Besides acknowledging a potential 'misfit' between the provided iCBT and the present sample of veterans, in the case of PTSD, premature treatment termination occurs in around 20% of all initiated treatments and regardless of the content and type of treatment (Hembree et al., 2003; Imel et al., 2013; Kline, Baier, Klein, Feeny, & Zoellner, 2020; Lewis, Roberts, Gibson, et al., 2020; Zhou et al., 2020). Particularly in military samples, dropout rates can range up to 68% (Berke et al., 2019; Britt, Jennings, Cheung, Pury, & Zinzow, 2015; Edwards-Stewart et al., 2021; Eftekhari et al., 2020; Garcia et al., 2011; Hoge et al., 2014; Murphy et al., 2015; Steenkamp, Litz, & Marmar, 2020; Szafranski et al., 2017). Given this, the rates of dropout in STUDY 4 may be declared to lie in the normal range of the available empirical literature, including internet-based interventions (Livingston et al., 2020; Simon, McGillivray, et al., 2019; Vöhringer et al., 2020).

## 6.4.4. Implications and future directions

First, it remains to be discussed whether the non-significant changes in overall PTSD symptom severity reported by Niemeyer et al. (2020) might be mirrored by the lack of observable or measurable modifications of patterns of attentional bias in STUDY 4, and as

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discussed across the associated works from the larger research project (Engel et al., 2021; Engel et al., 2020; Schumacher et al., 2021). This assumption would echo earlier suggestions of a direct linkage between subjectively reportable and objectively measurable symptom changes (Beard, 2011). However, the assumption is called into doubt by meta-analyses of the efficacy of ABM training in anxiety, stress, mood, and addictive disorders. Rather, these meta-analyses provide evidence for an alternative assumption, namely that changes in the primary (that is, subjectively reported) symptom outcome can be detached from changes in automated or subconscious processes, and vice versa (Cristea, Kok, & Cuijpers, 2016; Hakamata et al., 2010; Hallion & Ruscio, 2011; Mogg et al., 2017). A detailed examination of (de-)linking 'subjective change' and 'objective change' will be of major relevance for future research and may contribute to a deeper understanding of the underlying processes of change in psychotherapy research. Future investigations should also apply objective measures of symptom change, in addition to the subjective level of symptom reporting in terms of questionnaires and clinicianconducted interviews. The use of objective measures such as eye gaze, heart rate (variability), muscle tone, skin conductance, neuronal activity, and saliva and blood concentrations of (stress) hormones will constitute an increasingly important part of future innovative psychotherapy research.

Second, future (longitudinal) investigations are essential to enrich the field of psychotraumatology in terms of efficacious, low-threshold, and acceptable intervention opportunities for (military) PTSD. Clinical research and practice need to develop, evaluate, and disseminate interventions that can meet the veterans' specific needs and demands, and that are acceptable in this specific population at high risk of PTSD. At the same time, future research needs to evaluate psychotherapeutic interventions systematically and recurrently by making use of multiple measurements of symptom change. Psychotherapy research might be further developed and enhanced by assessing subjective measures of symptom change, such as applying questionnaires and clinician-administered interviews, while concurrently assessing

objective markers of psychopathology, such as measuring physiological, autonomic, neuronal, and hormonal processes. One might speculate whether future psychotherapy research will be characterized by an increasing relevance of physiological and biological markers of symptom change, besides the conventional subjective symptom change outcomes. The examination of processes of change and of associated interrelations between subjective symptom reporting and objective markers of psychopathology must be seriously considered in future research. Such approaches will hopefully foster our understanding of underlying mechanisms of change in PTSD.

## 6.5. Overall conclusion

STUDY 1 assessed the concordance of the diagnostic systems DSM-IV, DSM-5, ICD-10, and the proposed ICD-11 in diagnosing PTSD in a sample of GAF veterans. In the light of current research, it is highlighted that a range of subtypes ('phenotypes') of PTSD might be described, which appear to vary between different trauma populations, and military PTSD seems to differ from other types of PTSD. Deeper knowledge regarding the specific needs of different military populations, considering their symptom presentation and sociodemographic, cultural, ethnical, and trauma history backgrounds, will be of key relevance for future clinical research and practice in this field. Additionally, future research needs to broaden the context in which diagnostic assessment takes place, for instance by assessing objective variables concurrently with subjectively reported symptom experiences. Multidimensional diagnostic assessments and treatment evaluation are highly relevant for future intervention research and evidence-based practice.

STUDY 2 extended the field of meta-analytical evidence on the efficacy of IBI for PTSD, explored the potential impact of treatment components on its efficacy, and descriptively assessed rates of early treatment termination and completer characteristics. In the light of current literature, the broad field of meta-analytical evidence provides overall encouraging

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findings on the efficacy, acceptance, and safety of iCBT to treat PTSD. Future research is essential to provide a robust database concerning the longer-term efficacy of iCBT, concerning potential moderators of its efficacy, and concerning its utility, acceptance, and safety for diverse patient populations under differing circumstances and contexts. In addition, the systematic and consistent assessment of adverse events and symptom deterioration is set to become increasingly relevant. Research focusing on the possibilities of tailoring IBI to patients' needs and characteristics will also play a major role. Such research may ultimately help to strengthen the overall efficacy of IBI, user satisfaction, and treatment adherence in different patient populations and in the longer term.

STUDY 3 investigated group differences between traumatized veterans with PTSS, traumatized veterans without PTSS, and non-traumatized healthy veterans in baseline attentional bias to threat. To date, evidence has revealed a maintenance bias to threat in PTSD. Future clinical research and practice will benefit from deeper investigations of the mediating and moderating variables on the path from individual risk factors and traumatization to PTSD and attentional bias. Moreover, future research needs to systematically and continuously examine diverse objective measures of symptoms and symptom change, including autonomic, physiological, neurological, and hormonal parameters, in addition to subjectively reported symptom severity. Finally, the consistent evaluation of the reliability and validity of respective measures will be highly important. In particular, the 'development' (operationalization) of an innovative behavioral or attentional measure needs to be carefully accomplished through a critical and repeated examination of its reliability and validity.

STUDY 4 examined the efficacy of a stand-alone iCBT program to modify patterns of attentional bias in treatment-seeking GAF veterans with PTSS. It augments the existing empirical literature by presenting an innovative experimental approach to measure PTSD-related attentional bias and to examine its modifiability in response to the provision of iCBT.

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Future research should deepen the understanding of the link between subjectively reportable symptom severity and symptom changes and objectively measurable symptom parameters and their modifiability in PTSD and other psychiatric conditions in response to the provision of a general psychotherapeutic treatment. Based on the current state of research, it remains largely unclear to what extent patterns of attentional bias and other objective parameters can be modified via general psychotherapeutic interventions or to what extent these may seem to be rather repellent to change. Systematic and ongoing efforts to increase our knowledge about the interplay of different autonomic, hormonal, physiological, and psychological variables in psychiatric conditions and in response to psychotherapy will be of key priority when conceiving of evidence-based practice in the future.

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# **APPENDICES**

## **STUDY 1 – Supplementary Material**

### LEC-5

Nachfolgend sind eine Anzahl schwieriger oder belastender Dinge aufgelistet, die Menschen manchmal zustoßen. Kreuzen Sie für jedes Ereignis eines oder mehrere Felder auf der rechten Seite an, um anzugeben, dass (a) es Ihnen persönlich zugestoßen ist; (b) Sie Zeuge davon waren, als es jemand anderem zugestoßen ist; (c) Sie davon erfahren haben, dass es einem nahen Angehörigen oder engen Freund zugestoßen ist; (d) Sie damit im Rahmen Ihres Berufes konfrontiert wurden (z.B. Rettungssanitäter, Polizist, Soldat oder anderer Ersthelfer); oder (e) Sie unsicher sind, ob es zutrifft.

Bitte achten Sie darauf, Ihr gesamtes Leben zu berücksichtigen (Kindheit/Jugend und Erwachsenenalter), wenn Sie die Liste der Ereignisse durchgehen.

	Ereignis	mir persönlich zugestoßen	Zeuge davon gewesen	davon erfahren	im Rahmen meines Berufs	unsicher
1.	Naturkatastrophe (z.B. Überschwemmung, Orkan, Tornado, Erdbeben)					
2.	Feuer oder Explosion					
3.	Verkehrsunfall (z.B. Autounfall, Schiffsunglück, Zugunglück, Flugzeugabsturz)					
4.	Schwerer Unfall bei der Arbeit, zuhause oder während einer Freizeitaktivität					
5.	Einem Schadstoff ausgesetzt sein (z.B. gefährliche Chemikalien, Strahlung)					
6.	Gewalttätiger Angriff (z.B. überfallen, geschlagen, getreten oder zusammengeschlagen werden)					
7.	Angriff mit einer Waffe (z.B. verletzt oder bedroht werden mit einer Schusswaffe, einem Messer oder einer Bombe)					
8.	Sexueller Übergriff (Vergewaltigung, versuchte Vergewaltigung, zu irgendeiner Art von sexueller Handlung durch Gewalt oder Androhung von Gewalt gezwungen werden)					
9.	Andere unerwünschte oder unangenehme sexuelle Erfahrung					
10.	Kampfhandlungen oder Aufenthalt in einem Kriegsgebiet (beim Militär oder als Zivilist)					
11.	Gefangenschaft (z.B. gekidnappt, entführt, als Geisel genommen werden, Kriegsgefangener)					
12.	Lebensbedrohliche Erkrankung oder Verletzung					
13.	Schweres menschliches Leid					
14.	Plötzlicher gewalttätiger Tod (z.B. Mord, Suizid)					
15.	Plötzlicher Unfalltod					
16.	Schwere Verletzung, Schaden oder Tod, die/den Sie jemand anderem zugefügt haben					
17.	Irgendein anderes sehr belastendes Ereignis oder Erlebnis					

### TEIL 2:

A. Falls Sie irgendetwas bei Nr. 17 in TEIL 1 angekreuzt haben, benennen Sie kurz das Ereignis, an das Sie gedacht haben:

B. Falls Sie mehr als eines der in TEIL 1 genannten Ereignisse erlebt haben, denken Sie bitte an das Ereignis, das Sie als das *schlimmste Ereignis* betrachten; das bedeutet für diesen Fragebogen das Ereignis, das Sie zurzeit am meisten belastet. Falls Sie nur eines der in TEIL 1 genannten Ereignisse erlebt haben, nehmen Sie dieses als das schlimmste Ereignis. Bitte beantworten Sie die folgenden Fragen in Bezug auf das schlimmste Ereignis (*kreuzen Sie alle Auswahlmöglichkeiten an, die zutreffen*):

1. Beschreiben Sie kurz das schlimmste Ereignis (z.B. was passierte, wer beteiligt war, usw.)

2. Wie lange ist es her? \_\_\_\_\_\_ (Bitte schätzen, falls Sie sich nicht sicher sind)

### 3. Auf welche Weise haben Sie es erlebt?

- \_\_\_ Es ist mir selbst passiert.
- \_\_\_ Ich habe es beobachtet
- \_\_\_ Ich habe erfahren, dass es einem nahen Angehörigen oder engen Freund passiert ist
- \_\_\_\_ Ich wurde im Rahmen meines Berufes wiederholt mit Details des Ereignisses konfrontiert (z.B.

### Rettungssanitäter,

- Polizist, Soldat oder anderer Ersthelfer)
- \_\_\_ Sonstiges, bitte beschreiben: \_\_\_\_\_

### 4. War jemand in Lebensgefahr?

- \_\_\_ Ja, ich
- \_\_\_\_ Ja, jemand anderes
- \_\_\_ Nein

### 5. Wurde jemand schwer verletzt oder getötet?

- \_\_\_\_ Ja, ich wurde schwer verletzt
- \_\_\_\_ Ja, jemand anderes wurde schwer verletzt oder getötet
- \_\_\_ Nein

### 6. Beinhaltete es sexuelle Gewalt? \_\_\_\_ Ja \_\_\_\_ Nein

# 7. Falls das Ereignis den Tod eines nahen Angehörigen oder engen Freundes beinhaltete, war das die Folge eines Unfalls oder von Gewalt, oder war es die Folge natürlicher Umstände?

- \_\_\_ Unfall oder Gewalt
- \_\_\_ Natürliche Umstände
- \_\_\_ Nicht zutreffend (Das Ereignis beinhaltete nicht den Tod eines nahen Angehörigen oder Freundes)

# 8. Wie häufig haben Sie insgesamt ein ähnliches Ereignis erlebt, das genauso belastend oder fast genauso belastend war wie das schlimmste Ereignis?

- \_\_\_ Nur einmal
- \_\_\_ Mehr als einmal (Bitte nennen oder schätzen Sie die Anzahl, wie häufig Sie dieses Erlebnis hatten: \_\_\_\_)

Teil 3: Nachfolgend sind Probleme aufgelistet, die Menschen manchmal als Reaktion auf ein sehr belastendes Erlebnis haben. Bitte lesen Sie jedes Problem sorgfältig, denken Sie dabei an Ihr schlimmstes Ereignis, und markieren Sie dann eine der Zahlen auf der rechten Seite, um anzugeben, wie stark Sie im letzten Monat durch dieses Problem belastet waren.

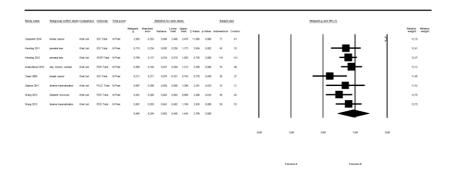
Im le	etzten Monat, wie sehr waren Sie belastet durch:	überhaupt nicht	ein wenig	ziemlich	stark	sehr stark
1.	Wiederholte, beunruhigende und ungewollte Erinnerungen an das belastende Erlebnis?	0	1	2	3	4
2.	Wiederholte, beunruhigende Träume von dem belastenden Erlebnis?	0	1	2	3	4
3.	Sich plötzlich fühlen oder sich verhalten, als ob das belastende Erlebnis tatsächlich wieder stattfinden würde ( <i>als</i> <i>ob Sie tatsächlich wieder dort wären und es wiedererleben</i> <i>würden</i> )?	0	1	2	3	4
4.	Sich emotional sehr belastet fühlen, wenn Sie etwas an das Erlebnis erinnert hat?	D	1	2	3	4
5.	Starke körperliche Reaktionen haben, wenn Sie etwas an das belastende Erlebnis erinnert hat (z.B. Herzklopfen, Schwierigkeiten beim Atmen, schwitzen)	0	1	2	3	4
6.	Vermeidung von Erinnerungen, Gedanken oder Gefühlen in Bezug auf das belastende Erlebnis?	0	1	2	3	4
7.	Vermeidung äußerer Auslöser für Erinnerungen an das belastende Erlebnis (z.B. Personen, Plätze, Gespräche, Aktivitäten, Gegenstände oder Situationen)?	0	1	2	3	4
8.	Schwierigkeiten, sich an wichtige Teile des belastenden Erlebnisses zu erinnern?	0	1	2	3	4
9.	Starke negative Überzeugungen über sich selbst, andere Menschen oder die Welt haben (z.B. Gedanken haben wie: Ich bin schlecht, mit mir stimmt ernsthaft etwas nicht, man kann niemandem vertrauen, die Welt ist absolut gefährlich)?	0	1	2	3	4
10.	Sich selbst oder jemand anderem Vorwürfe machen in Bezug auf das belastende Erlebnis oder was danach passiert ist?	0	1	2	3	4
11.	Starke negative Gefühle haben, wie zum Beispiel Angst, Schrecken, Ärger, Schuld oder Scham?	0	1	2	3	4
12.	Verlust von Interesse an Aktivitäten, die Ihnen früher Spaß gemacht haben?	0	1	2	3	4
13.	Sich von anderen Menschen entfernt oder wie abgeschnitten fühlen?	0	1	2	3	4
14.	Schwierigkeiten, positive Gefühle zu erleben (z.B. keine Freude empfinden können oder keine liebevollen Gefühle haben können gegenüber Menschen, die Ihnen nahestehen)?	0	1	2	3	4
15.	Reizbares Verhalten, Wutausbrüche oder aggressives Verhalten?	0	1	2	3	4
16.	Zu viele Risiken eingehen oder Dinge tun, die Ihnen Schaden zufügen könnten?	0	1	2	3	4
17.	In erhöhter Alarmbereitschaft, wachsam oder auf der Hut sein?	0	1	2	3	4
18.	Sich nervös oder schreckhaft fühlen?	0	1	2	3	4
19.	Konzentrationsschwierigkeiten haben?	0	1	2	3	4
20.	Schwierigkeiten, ein- oder durchzuschlafen?	0	1	2	3	4

### **STUDY 2 – Supplementary Material**

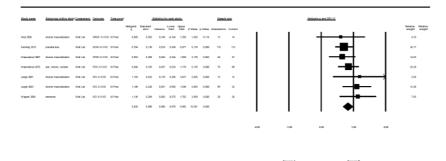
# Appendix A. Example of an electronical search strategy (SCOPUS, conducted on 24<sup>th</sup> of February 2015).

History Search Terms( (TITLE-ABS-KEY (internet intervention)) OR (TITLE-ABS-KEY (web intervention)) OR (TITLE-ABS-KEY ( online intervention ) ) OR ( TITLE-ABS-KEY (online psychotherapy)) OR (TITLE-ABS-KEY (web psychotherapy)) OR (TITLE-ABS-KEY (internet psychotherapy))) AND ((TITLE-ABS-KEY (post traumatic stress)) OR (TITLE-ABS-KEY (post traumatic stress symptoms)) OR (TITLE-ABS-KEY (post traumatic stress disorder)) OR (TITLE-ABS-KEY (trauma\*)) OR (TITLE-ABS-KEY (victim\*))) AND (LIMIT-15 TO (DOCTYPE, "ar")) AND (LIMIT-TO (SRCTYPE, "j")) 419 document results History Search Terms( (TITLE-ABS-KEY ( internet intervention ) ) OR ( TITLE-ABS-KEY (web intervention)) OR (TITLE-ABS-KEY (online intervention)) OR (TITLE-ABS-KEY (online psychotherapy)) OR (TITLE-ABS-KEY (web psychotherapy)) OR (TITLE-ABS-KEY (internet psychotherapy))) AND ((TITLE-ABS-KEY (post traumatic stress)) OR (TITLE-ABS-KEY ( post traumatic stress symptoms ) ) OR ( TITLE-ABS-KEY ( post traumatic stress disorder ) ) OR ( TITLE-ABS-14 KEY (trauma\*)) OR (TITLE-ABS-KEY (victim\*))) 675 document results History Search Terms( TITLE-ABS-KEY (post traumatic stress)) OR (TITLE-ABS-KEY ( post traumatic stress symptoms ) ) OR ( TITLE-ABS-KEY ( post traumatic stress disorder ) ) OR ( TITLE-ABS-13 KEY (trauma\*)) OR (TITLE-ABS-KEY (victim\*)) 466,219 document results History Search Terms( TITLE-ABS-KEY ( internet intervention ) ) OR ( TITLE-ABS-KEY (web intervention)) OR (TITLE-ABS-KEY ( online intervention ) ) OR ( TITLE-ABS-KEY (online psychotherapy)) OR (TITLE-ABS-KEY (web psychotherapy)) OR (TITLE-ABS-12 KEY (internet psychotherapy)) 18,938 document results 11 History Search TermsTITLE-ABS-KEY (victim\*) 80,587 document results 10 TITLE-ABS-KEY(trauma\*) 398,739 document results 9 TITLE-ABS-KEY(post traumatic stress disorder) 27,208 document results 8 TITLE-ABS-KEY(post traumatic stress symptoms) 11,203 document results 7 TITLE-ABS-KEY(post traumatic stress) 28,389 document results 6 TITLE-ABS-KEY(internet psychotherapy) 1,094 document results 5 TITLE-ABS-KEY(web psychotherapy) 395 document results 4 TITLE-ABS-KEY(online psychotherapy) 572 document results 3 TITLE-ABS-KEY(online intervention) 7,048 document results 3 TITLE-ABS-KEY(web intervention) 7,444 document results 2 TITLE-ABS-KEY(internet intervention) 8,550 document results

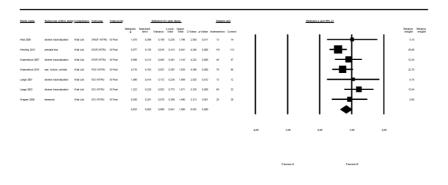
Appendix B. Forest plots for the analyses on CBT-IBIs for PTSD sum, avoidance, intrusion and hyperarousal scales at post assessments.



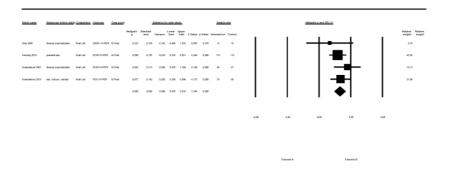
### 1. PTSD sum scale



#### 2. PTSD avoidance scale



### 3. PTSD intrusion scale



4. PTSD hyperarousal scale

# Appendix C.

k studies for	Begg and Mazumdar:	Egger's regression:	Trim and fill
publication	Kendall's tau with	β [95% CI],	Observed values
bias	continuity correction,	p (1-tailed)	Adjusted values
analyses	p (1-tailed)		k imputed studies
CBT-IBIs, PT	SD global sum scale, passiv	ve comparison conditio	m, post assessment, excluding one outlier
7	Tau = -0.57,	-2.21 [-5.57 – 1.15]	Obs: 0.72 [0.57 – 0.86]

 $\mathbf{k} = \mathbf{0}$ 

Table 1. Results of publication bias analyses.

p = .036

CBT-IBIs, PTSD avoidance scale, passive comparison condition, post assessment

7	Tau = 0.29,	1.16 [-1.34 – 3.66]	Obs: 0.83 [0.67 – 0.98]
	p = .184	p = .143	Adj: 0.78 [0.64 – 0.93]
			k = 2

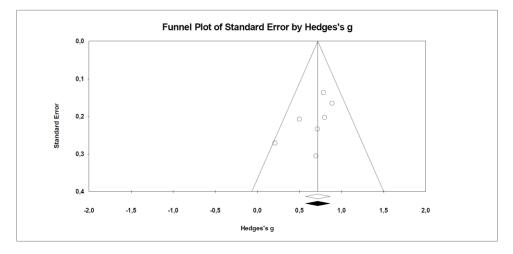
p = .076

CBT-IBIs, PTSD intrusion scale, passive comparison condition, post assessment

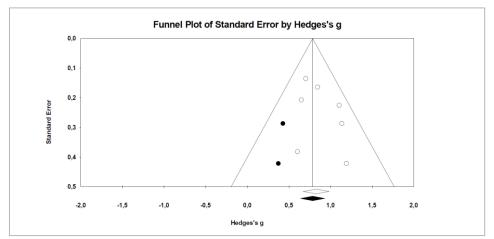
7	Tau = 0.57,	2.09 [-0.18 - 4.36]	Obs: 0.82 [0.64 – 1.01]
	p = .036	p = .032	Adj: 0.70 [0.50 – 0.89]
			k = 4

# Appendix D.

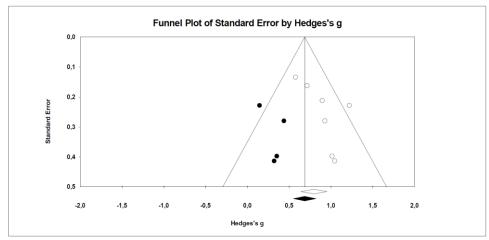
Funnel plots.



### 1. PTSD sum scale



2. PTSD avoidance scale.



3. PTSD intrusion scale.

## **STUDY 3 – Supplementary Material**

## Appendix A.

Α

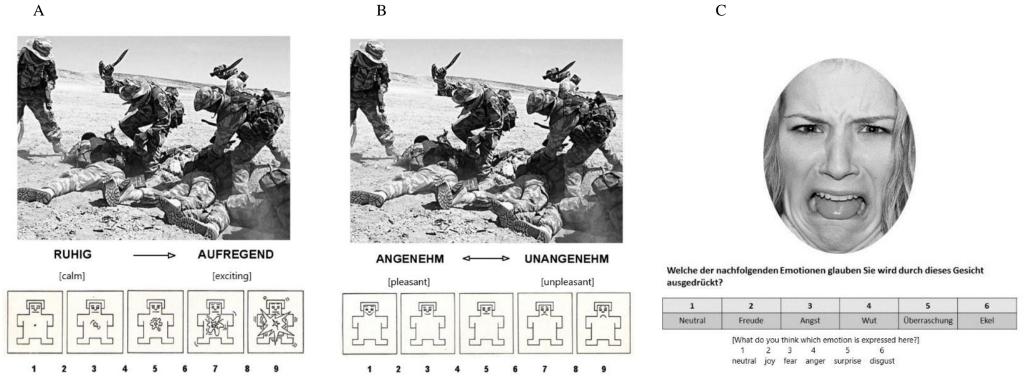


Fig. A1. Manipulation check. Exemplary slide and utilized scale on arousal (A); Exemplary slide and utilized scale on valence (B). Exemplary slide and utilized scale for indicating the identified emotional expression (C).

### *Results on Manipulation Check (original grouping according to main text)*

Valence of combat and of general threat AOIs were less pleasant compared to the related neutral AOIs ( $t_{(66)} = 17.04$ , p < .001;  $t_{(66)} = 20.12$ , p < .001, resp.). Arousal of combat and of general threat AOIs were higher compared to the related neutral AOIs ( $t_{(66)} = 10.89$ , p < .001;  $t_{(66)} = 11.64$ , p < .001, resp.). Combat and general threat AOIs did not differ on either scale ( $t_{(66)} = 1.11$ , p = .269;  $t_{(66)} = -.67$ , p = .506, resp.). Between-group differences were found on arousal of combat AOIs ( $F_{(2.64)} = 7.93$ , p = .001) and on valence of combat AOIs ( $F_{(2.64)} = 8.48$ , p = .037). The PTSS group rated combat AOIs higher on arousal in contrast to both control groups (both p < .004), and less pleasant in contrast to the NE-CG (p = .055). About the facial expressions, fearful faces were significantly less often identified correctly compared to neutral, angry, and disgusted faces, and neutral faces were significantly less often identified correctly in contrast to angry and disgusted faces (all  $p \le .001$ ). No group differences on emotion identification were found. Descriptive values are presented in the Table A1.

				~					
	Entire	sample	PTSS	-Group	TE	-CG	NE	-CG	
	М	SD	М	SD	М	SD	М	SD	
Valence									
Combat AOIs	6.34	1.60	7.03	1.41	6.10	1.41	5.84	1.88	
Combat neutral AOIs	3.23	1.26	3.15	1.24	3.09	1.17	3.54	1.43	
General threat AOIs	6.48	1.56	6.85	1.09	6.37	1.47	6.18	1.09	
General threat neutral AOIs	2.98	1.15	3.14	1.15	2.89	1.09	2.94	1.28	
Arousal									
Combat AOIs	4.94	2.30	6.39	2.03	4.27	1.02	4.16	2.28	
Combat neutral AOIs	2.51	1.36	2.61	1.41	2.33	1.09	2.68	1.69	
General threat AOIs	4.84	2.25	5.62	2.03	4.51	2.10	4.39	2.60	
General threat neutral AOIs	2.66	1.30	2.77	1.38	2.49	1.19	2.77	1.41	
Correct emotion identification, 9	%								
Neutral valence	81.29	19.33	79.12	17.04	84.96	20.00	78.45	21.10	
Negative valence	85.27	12.15	83.94	12.79	85.43	11.40	86.67	12.94	
Fearful faces	65.97	30.15	66.36	10.48	65.19	28.06	66.67	34.30	
Angry faces	95.22	11.06	94.55	12.62	96.30	9.67	94.44	11.49	
Disgusted faces	94.63	14.60	90.91	22.87	94.81	8.93	98.89	4.71	

Table A1. Ratings on valence and arousal of pictorial stimuli and emotion identification of face stimuli,  $N = 67^{11}$ 

*Note*. <sup>1</sup>, n = 3 missing due to now-show on the second day of assessment; PTSS group, trauma-exposed group with PTSS N = 22; TE-CG, trauma exposed healthy control group N = 27; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.

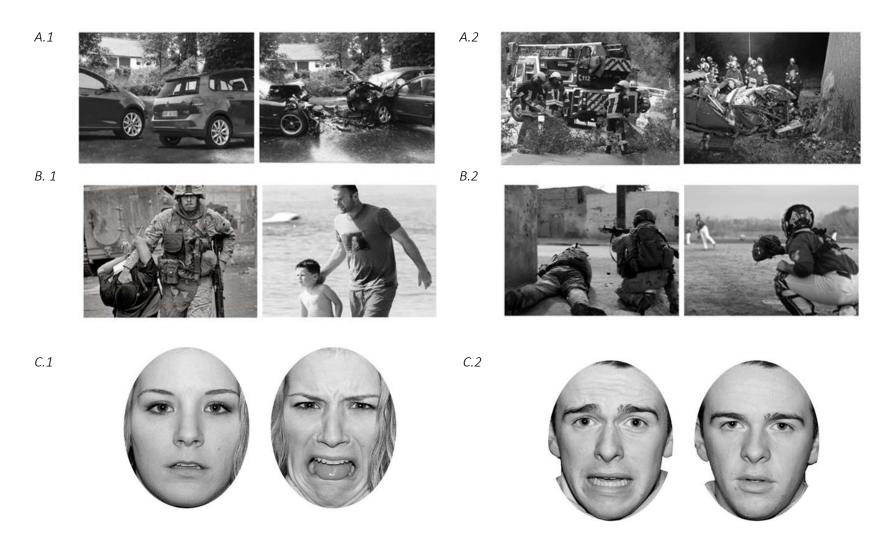
*Results on Manipulation Check (alternative grouping, according to Supplementary Material C)* 

Valence of combat and of general threat AOIs were less pleasant compared to the related neutral AOIs ( $t_{(66)} = 17.04$ , p < .001;  $t_{(66)} = 20.12$ , p < .001, resp.). Arousal of combat and of general threat AOIs were higher compared to the related neutral AOIs ( $t_{(66)} = 10.89$ , p < .001;  $t_{(66)} = 11.64$ , p < .001, resp.). Combat and general threat AOIs did not differ on either scale ( $t_{(66)}$ = 1.11, p = .269;  $t_{(66)} = -.67$ , p = .506, resp.). Between-group differences were found on arousal of combat AOIs ( $F_{(2,64)} = 7.81$ , p < .001) and on valence of combat AOIs ( $F_{(4,64)} = 12.24$ , p =.007). The PTSD group rated combat AOIs higher on arousal in contrast to both control groups (both p < .003), and less pleasant in contrast to the TE-PTSS group (p = .017) and the NE-CG (p = .010). About the facial expressions, fearful faces were significantly less often identified correctly than neutral, angry, and disgusted faces (all  $p \le .001$ ). No group differences on emotion identification were found. Descriptive values are presented in the Table A2.

	Entire sample		PTSD-Group		TE-PTSS Group		NE-CG	
	М	SD	М	SD	М	SD	М	SD
Valence								
Combat AOIs	6.34	1.60	7.49	1.09	6.13	1.44	5.84	1.88
Combat neutral AOIs	3.23	1.26	3.29	1.38	3.05	1.11	3.54	1.43
General threat AOIs	6.48	1.56	6.86	1.17	6.48	1.38	6.18	1.09
General threat neutral AOIs	2.98	1.15	3.18	1.38	2.93	1.00	2.94	1.28
Arousal								
Combat AOIs	4.94	2.30	6.88	1.81	4.56	2.11	4.16	2.28
Combat neutral AOIs	2.51	1.36	2.67	1.32	2.37	1.21	2.68	1.69
General threat AOIs	4.84	2.25	5.92	1.99	5.65	2.09	4.39	2.60
General threat neutral AOIs	2.66	1.30	2.77	1.44	2.55	1.22	2.77	1.41
Correct emotion identification,	%							
Neutral valence	81.29	19.33	74.73	18.02	85.38	18.43	78.45	21.10
Negative valence	85.27	12.15	82.38	14.22	85.71	10.98	86.67	12.94
Fearful faces	65.97	30.15	61.43	30.85	67.43	28.32	66.67	34.30
Angry faces	95.22	11.06	94.29	12.22	96.00	10.63	94.44	11.49
Disgusted faces	94.63	14.60	91.43	26.85	93.71	10.60	98.89	4.71

*Table A2.* Ratings on valence and arousal of pictorial stimuli and emotion identification of face stimuli,  $N = 67^{1}$ 

*Note*.  $^{1}n = 3$  missing due to now-show on the second day of assessment; PTSD group, trauma-exposed group with full diagnostic PTSD N = 14; TE-PTSS group, trauma exposed control group with subthreshold PTSS N = 35; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.



**Fig. A2**. Stimuli slides. Examples of general threat related pictures paired with neutral picture slides (A1/A2); Examples of combat related pictures paired with neutral picture slides (B1/B2); Examples of emotional facial expressions paired with neutral expression (C1/C2).

# Appendix B

*Table B1*. List of military related traumatic events of participants based on the LMHAT, N = 70.

				PTSS group	)				TE-CG		
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	never	one time	2-4 times	5-9 times	+10
	the LMHAT, $N(\%)$					times					times
1	Being attacked or ambushed	5 (20.8)	3 (12.5)	9 (37.5)	1 (4.2)	2 (8.3)	16 (57.1)	6 (21.4)	3 (10.7)	1 (3.6)	-
2	Seeing destroyed homes and villages	-	-	2 (8.3)	1 (4.2)	17 (70.8)	4 (14.3)	2 (7.1)	4 (14.3)	3 (10.7)	12 (42.9)
3	Receiving small arms fire	6 (25.0)	5 (20.8)	6 (25.0)	1 (4.2)	3 (12.5)	18 (64.3)	2 (7.1)	6 (21.4)	-	-
4	Seeing dead bodies or human remains	2 (8.3)	2 (8.3)	9 (37.5)	4 (16.7)	3 (12.5)	11 (39.3)	5 (17.9)	6 (21.4)	3 (10.7)	1 (3.6)
5	Handling of uncovering dead bodies	8 (33.3)	7 (29.2)	4 (16.7)	-	1 (4.2)	21 (75.0)	2 (7.1)	2 (7.1)	-	1 (3.6)
6	Witnessing an accident which results serious	6 (25.0)	3 (12.5)	9 (37.5)	1 (4.2)	2 (8.3)	11 (39.3)	8 (28.6)	6 (21.4)	1 (3.6)	-
	injury or death										
7	Witnessing violence within the local population	5 (20.8)	2 (8.3)	10 (41.7)	1 (4.2)	2 (8.3)	18 (64.3)	2 (7.1)	5 (17.9)	1 (3.6)	-
8	Seeing dead or seriously injured fellow soldiers	6 (25.0)	4 (16.7)	6 (25.0)	3 (12.5)	2 (8.3)	13 (46.4)	3 (10.7)	8 (28.6)	1 (3.6)	1 (3.6)
9	Knowing someone who was seriously injured or	4 (16.7)	8 (33.3)	6 (25.0)	3 (12.5)	-	15 (53.6)	7 (25.0)	4 (14.3)	-	-
	dead										

Continuation of Table B1 on the following page.

				PTSS group	)				TE-CG		
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	Never	one time	2-4 times	5-9 times	+10
	the LMHAT, $N(\%)$					times					times
10	Participating in demining operations	10 (41.7)	2 (8.3)	6 (25.0)	3 (12.5)	-	24 (85.7)	1 (3.6)	1 (3.6)	-	-
11	IED/ Booby trap exploded near you	5 (20.8)	8 (33.3)	5 (20.8)	1 (4.2)	2 (8.3	22 (78.6)	4 (14.3)	-	-	-
12	Working in areas that are mined or had IEDs	8 (33.3)	3 (12.5)	2 (8.3)	2 (8.3)	6 (25.0)	20 (71.4)	2 (7.1)	3 (10.7)	-	1 (3.6)
13	Having hostile reactions from civilians	5 (20.8)	-	5 (20.8)	4 (16.7)	7 (29.2)	9 (32.1)	6 (21.4)	8 (28.6)	3 (10.7)	-
14	Disarming civilians	9 (37.5)	4 (16.7)	5 (20.8)	1 (4.2)	2 (8.3)	22 (78.6)	2 (7.1)	-	2 (7.1)	-
15	Being in threatening situations where you were	12 (50.0)	-	5 (20.8)	3 (12.5)	1 (4.2)	23 (82.1)	2 (7.1)	1 (3.6)	-	-
	unable to respond because of the ROE										
16	Shooting or directing fire at the enemy	10 (41.7)	2 (8.3)	5 (20.8)	1 (4.2)	3 (12.5)	22 (78.6)	1 (3.6)	2 (7.1)	1 (3.6)	-
17	Calling in fire on the enemy	14 (58.3)	5 (20.8)	1 (4.2)	-	1 (4.2)	25 (89.3)	1 (3.6)	-	-	-
18	Being involved in close combat action	17 (70.8)	1 (4.2)	3 (12.5)	-	-	23 (82.1)	3 (10.7)	-	-	-
19	Clearing/ searching homes or buildings	13 (54.2)	1 (4.2)	5 (20.8)	2 (8.3)	-	23 (82.1)	1 (3.6)	1 (3.6)	-	1 (3.6)
20	Clearing/ searching caves or bunkers	14 (58.3)	3 (12.5)	3 (12.5)	1 (4.2)	-	25 (89.3)	-	1 (3.6)	-	-
21	Witnessing brutality/ mistreatment toward non-	15 (62.5)	2 (8.3)	4 (16.7)	-	-	23 (82.1)	1 (3.6)	2 (7.1)	-	-
	combatants										

Continuation of Table B1 on the following page.

Continuation of Table B1. List of military	y related traumatic events of p	participants based on the LMHAT, $N = 70$ .

		PTSS group						TE-CG				
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	never	one time	one time 2-4 times	5-9 times	+10	
	the LMHAT, $N(\%)$					times					times	
22	Being wounded	14 (58.3)	5 (20.8)	2 (8.3)	-	-	26 (92.9)	-	-	-	-	
23	Seeing ill/ wounded women and children who	7 (29.2)	5 (20.8)	5 (20.8)	2 (8.3)	2 (8.3)	18 (64.3)	2 (7.1)	2 (7.1)	2 (7.1)	2 (7.1)	
	you were unable to help											
24	Receiving incoming artillery, rocket, or mortar	8 (33.3)	2 (8.3)	4 (16.7)	1 (4.2)	6 (25.0)	17 (60.7)	2 (7.1)	3 (10.7)	2 (7.1)	2 (7.1)	
	fire											
25	Being directly responsible for the death of an	16 (66.7)	2 (8.3)	-	-	1 (4.2)	25 (89.3)	1 (3.6)	-	-	-	
	enemy combatant											
26	Observing violation of the Geneva Convention	17 (70.8)	2 (8.3)	1 (4.2)	-	-	25 (89.3)	-	1 (3.6)	-	-	
27	Being responsible for the serious injury or death	19 (79.2)	1 (4.2)	-	-	-	26 (92.9)	-	-	-	-	
	of a comrade											
28	Witnessing how a comrade got seriously injured	11 (45.8)	6 (25.0)	3 (12.5)	1 (4.2)	-	23 (82.1)	2 (7.1)	1 (3.6)	-	-	
29	Had a close call, dud landed near you	10 (41.7)	3 (12.5	6 (25.0)	1 (4.2)	1 (4.2)	23 (82.1)	3 (10.7)	-	-	-	
30	Had equipment being shot away from you	20 (83.3)	-	-	-	-	26 (92.9)	-	-	-	-	

Continuation of Table B1 on the following page.

Continuation of Table B1. List of military	y related traumatic events of p	participants based on the LMHAT, $N = 70$ .

		PTSS group					TE-CG				
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	never	one time	2-4 times	5-9 times	+10
	the LMHAT, $N(\%)$					times					times
31	Being shot but protective vest saved your life	20 (83.3)	1 (4.2)	-	-	-	26 (92.9)	-	-	-	
32	Had a comrade shot or hit who was near to you	17 (70.8)	3 (12.5)	1 (4.2)	-	-	26 (92.9)	-	-	-	-
33	Told a comrade about the death of another	13 (54.2)	5 (20.8)	1 (4.2	-	1 (4.2)	25 (89.3)	1 (3.6)	-	-	-
	comrade										

*Note.* PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma-exposed healthy control group N = 28; LMHAT, List of Mental Health Advisory Team; due to

missing information of some participants frequencies do not sum up to 100% in all categories.

*Table B2.* Dwell time in ms to AOI, N = 70.

	PTSS-Group		TE	E-CG	NE-CG	
	М	SD	М	SD	М	SD
Combat related pictures						
Combat related	5868.21	1275.97	5156.31	971.69	5172.89	1156.52
Neutral	2125.33	910.06	3322.34	745.12	3118.38	877.52
General threat pictures						
General threat	5211.06	1238.73	4692.03	761.09	4451.89	671.16
Neutral	3110.74	731.45	3626.19	878.75	3660.72	766.22
Emotional facial expressions						
Negative valence	3785.30	1046.26	3966.72	997.42	3979.22	1032.46
Neutral	3795.54	1012.09	3658.06	818.65	3815.71	1133.65

*Note*. PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma exposed healthy control group N = 28; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.

	PTSS-Group		TE-CG		NE-CG	
М	SD	М	SD	М	SD	
502.48	286.00	542.01	226.30	708.94	583.41	
920.42	512.51	994.48	383.21	1170.06	846.70	
518.03	278.65	588.98	249.64	827.26	468.57	
746.98	338.77	985.51	409.27	756.91	435.91	
s						
712.13	404.20	700.99	448.40	736.43	357.81	
871.13	329.14	992.96	439.56	1214.16	702.92	
	502.48 920.42 518.03 746.98 s 712.13	502.48 286.00 920.42 512.51 518.03 278.65 746.98 338.77 s 712.13 404.20	502.48       286.00       542.01         920.42       512.51       994.48         518.03       278.65       588.98         746.98       338.77       985.51         s       712.13       404.20       700.99	502.48       286.00       542.01       226.30         920.42       512.51       994.48       383.21         518.03       278.65       588.98       249.64         746.98       338.77       985.51       409.27         s       712.13       404.20       700.99       448.40	502.48       286.00       542.01       226.30       708.94         920.42       512.51       994.48       383.21       1170.06         518.03       278.65       588.98       249.64       827.26         746.98       338.77       985.51       409.27       756.91         s       712.13       404.20       700.99       448.40       736.43	

*Table B3.* Mean entry time in ms to AOI, N = 70.

*Note.* PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma exposed healthy control group N =

28; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.

	PT	SS-Group	r	TE-CG		NE-CG
	М	SD	М	SD	М	SD
Combat-related pictures						
Combat related	6.26	1.36	6.64	1.16	6.28	1.27
Neutral	5.74	1.36	5.36	1.16	5.72	1.27
General threat pictures						
General threat	5.09	1.35	5.29	1.33	4.83	0.92
Neutral	4.91	1.35	4.71	1.33	5.17	0.92
Emotional facial expressions						
Negative valence	2.62	0.65	2.83	0.49	2.74	0.54
Neutral	2.39	0.65	2.17	0.49	2.26	0.54

*Table B4.* Counts on location of initial fixation to AOI, N = 70.

*Note.* PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma exposed healthy control group N = 28; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.

	PTS	S-Group	T	TE-CG		E-CG
	М	SD	М	SD	М	SD
Combat related pictures						
Combat related	312.25	79.71	321.26	71.50	301.44	65.40
Neutral	272.10	60.46	306.91	66.72	275.17	60.84
General threat pictures						
General threat	295.82	99.93	295.25	72.57	278.72	59.12
Neutral	295.84	79.75	312.87	80.43	268.52	62.99
Emotional facial expressions						
Negative valence	316.80	168.80	288.71	69.94	290.29	84.93
Neutral	309.53	86.83	280.37	57.85	304.30	133.35

*Table B5.* Duration of initial fixation in ms to AOI, N = 70.

*Note*. PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma exposed healthy control group N = 28; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.

	PTSS-Group		TE-CG		NE-CG	
	М	SD	М	SD	М	SD
Combat-related pictures						
Combat-related	0.32	0.28	0.31	0.13	0.35	0.16
Neutral	0.61	0.29	0.48	0.24	0.55	0.22
General threat pictures						
General threat	0.45	0.23	0.34	0.15	0.33	0.14
Neutral	0.62	0.25	0.43	0.18	0.42	0.19
Emotional facial expressions						
Emotional valence	0.46	0.33	0.38	0.35	0.36	0.17
Neutral	0.46	0.29	0.34	0.28	0.43	0.41

*Table B6.* Indicator of attention bias variability to AOI, N = 70.

*Note.* PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma exposed healthy control group N = 28; NE-CG, non-exposed healthy control group N = 18; AOI, area of interest.

	Full sample	PTSS group	TE-CG	NE-CG
	Cronbach's a	Cronbach's α	Cronbach's α	Cronbach's o
Average dwell time				
Overall threat (overall neutral)	0.83 (0.74)	0.86 (0.77)	0.78 (0.26)	0.84 (0.84)
Combat pictures (neutral)	0.79 (0.74)	0.83 (0.81)	0.67 (0.38)	0.81 (0.65)
General related pictures (neutral)	0.60 (0.49)	0.64 (0.26)	0.41 (0.62)	0.52 (0.45)
Emotional faces (neutral)	0.79 (0.71)	0.80 (0.75)	0.77 (0.62)	0.80 (0.79)
Average duration of initial fixation				
Overall threat (overall neutral)	0.54 (0.55)	0.51 (0.62)	0.54 (0.67)	0.65 (0.42)
Combat pictures (neutral)	0.43 (0.53)	0.62 (0.61)	0.36 (0.45)	0.28 (0.58)
General related pictures (neutral)	0.45 (0.48)	0.49 (0.57)	0.47 (0.34)	0.32 (0.53)
Emotional faces (neutral)	0.31 (0.33)	0.40 (0.39)	-0.25 (0.56)	0.52 (0.25)
Latency				
Overall threat (overall neutral)	0.71 (0.67)	0.57 (0.27)	0.64 (0.55)	0.81 (0.82)
Combat pictures (neutral)	0.34 (0.51)	0.38 (0.29)	0.18 (0.19)	0.45 (0.74)
General related pictures (neutral)	0.43 (0.23)	0.17 (0.10)	0.10 (0.05)	0.46 (0.37)
Emotional faces (neutral)	0.67 (0.67)	0.66 (0.55)	0.72 (0.60)	0.64 (0.72)

*Table B7.* Internal consistency of dependent variables using Cronbach's alpha, N = 70.

*Note.* PTSS group, trauma-exposed group with PTSS N = 24; TE-CG, trauma-exposed healthy control group N = 28; NE-CG, non-exposed healthy control group, N = 18.

#### Appendix C

Given that 62.5% of the participants in the PTSS group met the full diagnostic criteria for DSM-5 PTSD, we conducted the main statistical analyses when using an 'alternative' re-grouping of the participants in terms of contrasting traumatized subjects with a full PTSD according to the DSM-5 criteria (PTSD group, N = 15) versus traumatized subjects with subthreshold PTSS (TE-PTSS group, N = 37) versus non-exposed healthy controls (NE-CG, N = 18).

#### ad 2.1. Participants

Inclusion criteria for the PTSD group were: Have had operational experience, have reported one or more lifetime deployment-related traumatic events, have met the full diagnostic criteria of current PTSD according to the DSM-5, and seeking to receive the i-CBT for treating their PTSD. Inclusion criteria for the group of trauma-exposed subjects with subthreshold PTSS (TE-PTSS group) were: Have had operational experience, have reported one or more lifetime deployment-related traumatic events, have reported subthreshold PTSS that do not fulfill the diagnostic criteria of a current PTSD according to the DSM-5, and were not treatment seeking for their PTSS. Inclusion criteria for never-exposed healthy controls (NE-CG) were: Have had no operational experience, have reported no lifetime traumatic events, have shown no psychiatric symptoms at all. Exclusion criteria for all subjects were: Have reported a neurological disorder, current or lifetime psychotic disorder, substance abuse or substance dependence disorder, current suicidality, or current psychotherapy.

#### ad 2.7.4. Statistical analyses

Analyses were conducted using SPSS v.22.0 (IBM Corporation, 2013). 3 x 3 x 2 mixed General Linear Model analyses (Analysis of Variance, ANOVA) were conducted. Group (PTSD group, TE-PTSS group, NE-CG) served as between-group factor and stimulus category (combat, general threat, faces) and AOI (threat, neutral) served as within-group factors. Age

was entered as covariate to all analyses. In case of a significant three-way-interaction effect, separate two-way ANOVAs (Group x AOI) were conducted, one for each stimulus category. Significant two-way interactions were followed up using simple effect analyses. All follow-up analyses were Bonferroni corrected. Based on Levene statistics and visual inspection of distribution, homogeneity of variance and normal distribution of dependent variables were assumed. Based on the Box-M-Test, homogeneity of covariances was assumed. Due to violated sphericity, Huynh-Feldt corrected test statistics were reported for all ANOVAs. The level of significance was set at p < .05.

### ad 3.1. Participant flow

We found a final sample size of N = 70 (PTSD group, n = 15, TE-PTSS group, n = 37, NE-CG n = 18).

#### ad 3.2. Sample characteristics

Sociodemographic and military information are displayed in Table C1, and psychiatric and trauma information are displayed in Table C2. Participants were on average 35.28 years old (SD = 10.08), the PTSD group and the TE-PTSS group were older than the NE-CG ( $F_{(2,66)} = 17.31$ , p < .001). Table C3 reports the military related traumatic events.

	PTSD Group	TE-PTSS Group	NE-CG
Age in years, M (SD)	35.73 (8.62)	39.70 (9.38)	25.78 (4.52)
Military status <sup>1</sup> , N (%)			
Professional military	3 (20.0)	19 (51.4)	-
Soldier on time	6 (40.0)	15 (40.5)	15 (83.3)
Voluntary conscripts	1 (6.7)	1 (2.7)	3 (16.7)
Branches of armed forces <sup>1</sup> , $N(\%)$			
Army	7 (46.7)	12 (32.4)	6 (33.3)
Joint support service	1 (6.7)	9 (24.3)	9 (50.0)
Air force	4 (46.7)	11 (29.7)	2 (11.1)
Military rank <sup>1</sup> , $N(\%)$			
Corporal	6 (40.0)	7 (18.9)	10 (55.6)
Sergeant	5 (33.3)	19 (51.4)	6 (33.3)
Staff officer	2 (13.3)	11 (29.7)	2 (11.1)
Deployments, M (SD)			
Total number	3.5 (4.59)	2.89 (2.57)	-
Total duration in days	538.64 (568.59)	401.62 (515.01)	-
Last deployment duration in days	141.45 (41.16)	116.44 (61.68)	-
Country of last deployment <sup>1</sup> , $N(\%)$			
Afghanistan	11 (73.3)	16 (43.2)	-
Kosovo	1 (6.7)	9 (24.3)	-
Mission of last deployment <sup>1</sup> , $N(\%)$			
ISAF	10 (66.7)	15 (40.5)	-
KFOR	1 (6.7)	7 (18.9)	-

*Table C1.* Sociodemographic and military related characteristics of participants, N = 70.

*Note.* PTSD group, trauma-exposed group with full PTSD N = 15; TE-PTSS group, trauma-exposed group with subthreshold levels of posttraumatic stress symptoms N = 37; NE-CG, non-exposed healthy control group, N = 18; <sup>1</sup>, due to missing information of some participants frequencies do not sum up to 100% in all categories.

Table C2. Trauma related and	psychiatric characteristics of	participants, $N = 70$ .

	PTSD Group	TE-PTSS Group	NE-CG
Deployment related military stressors, M (SD)			
LMHAT	15.93 (7.76)	7.57 (6.22)	-
Most frequent military related stressors, $N(\%)$			
Seeing destroyed homes and villages	13 (86.7)	9 (24.3)	-
Seeing dead bodies or human remains	12 (80.0)	21 (56.8)	-
Having hostile reactions from civilians	12 (80.0)	21 (56.8)	
Being attacked or ambushed	12 (80.0)	14 (37.8)	
IED/ Booby trap exploded near you	12 (80.0)	8 (21.6)	
Witnessing an accident which results serious injury	10 (66.7)	20 (54.1)	
or death			
Psychopathology			
CAPS-5, $M(SD)$	37.87 (11.18)	7.57 (6.22)	-
Comorbid axis-I disorder, N (%)	11 (73.3)	6 (16.2)	-
Major depressive disorder	7 (46.7)	2 (5.4)	
Dysthymia	2 (13.3)	1 (2.7)	
Panic disorder (without agoraphobia)	5 (33.3)		
Agoraphobia	8 (32.0)	1 (2.7)	
Social anxiety disorder	3 (20.0)		
Generalized anxiety disorder	2 (13.3)		
Obsessive compulsive disorder	-	1 (2.7)	
Intake of antidepressant medication, $N(\%)$	9 (60.0)	1 (2.7)	-

*Note.* PTSD group, trauma-exposed group with full PTSD N = 15; TE-PTSS group, trauma-exposed group with subthreshold levels of posttraumatic stress symptoms N = 37; NE-CG, non-exposed healthy control group, N = 18; LMHAT, List of Mental Health Advisory Team; CAPS-5, Clinical Administered PTSD Scale for DSM-5.

			PTSD group					TE-PTSS Group				
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	never	one time	2-4 times	5-9 times	+10	
	the LMHAT, $N(\%)$					times					times	
1	Being attacked or ambushed	1 (6.7)	2 (13.3)	6 (40.0)	1 (6.7)	2 (13.3)	20 (54.1)	7 (18.9)	6 (16.2)	1 (2.7)	-	
2	Seeing destroyed homes and villages	-	-	1 (6.7)	-	12 (80.0)	4 (10.8)	2 (5.4)	5 (13.5)	4 (10.8)	-	
3	Receiving small arms fire	3 (20.0)	2 (13.3)	4 (26.7)	1 (6.7)	3 (20.0)	21 (56.8)	5 (13.5)	8 (21.6)	-	-	
4	Seeing dead bodies or human remains	1 (6.7)	-	6 (40.0)	4 (26.7)	2 (13.3)	12 (32.4)	7 (18.9)	9 (24.3)	3 (8.1)	2 (5.4)	
5	Handling of uncovering dead bodies	5 (33.3)	3 (20.0)	3 (20.0)	-	1 (6.7)	24 (64.9)	6 (16.2)	3 (8.1)	-	1 (2.7)	
6	Witnessing an accident which results serious	3 (20.0)	2 (13.3)	5 (33.3)	1 (6.7)	2 (13.3)	14 (37.8)	9 (24.3)	10 (27.0)	1 (2.7)	-	
	injury or death											
7	Witnessing violence within the local population	1 (6.7)	2 (13.3)	6 (40.0)	1 (6.7)	2 (13.3)	22 (59.5)	2 (5.4)	9 (24.3)	1 (2.7)	-	
8	Seeing dead or seriously injured fellow soldiers	3 (20.0)	3 (20.0)	4 (26.7)	2 (13.3)	1 (6.7)	16 (43.2)	4 (10.8)	10 (27.0)	2 (5.4)	2 (5.4)	
9	Knowing someone who was seriously injured or	3 (20.0)	4 (26.7)	4 (26.7)	2 (13.3)	-	16 (43.2)	11 (29.7)	6 (16.2)	1 (2.7)	-	
	dead											
10	Participating in demining operations	3 (20.0)	2 (13.3)	5 (33.3)	3 (20.0)	-	31 (83.8)	1 (2.7)	2 (5.4)	-	-	
11	IED/ Booby trap exploded near you	1 (6.7)	5 (33.3)	4 (26.7)	1 (6.7)	2 (13.3)	26 (70.3)	7 (18.9)	1 (2.7)	-	-	
12	Working in areas that are mined or had IEDs	2 (13.3)	2 (13.3)	2 (13.3)	2 (13.3)	5 (33.3)	26 (70.3)	3 (8.1)	3 (8.1)	-	2 (5.4)	

Continuation of Table C3 on the following page.

Continuation of Table C3. List of military related traumatic events of participants based on the LMHAT, N = 70.

			PTSD Group					TE-PTSS Group				
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	Never	one time	2-4 times	5-9 times	+10	
	the LMHAT, $N(\%)$					times					times	
13	Having hostile reactions from civilians	1 (6.7)	-	2 (13.3)	4 (26.7)	6 (40.0)	13 (35.1)	6 (16.2)	11 (29.7)	3 (8.1)	1 (2.7)	
14	Disarming civilians	4 (26.7)	2 (13.3)	4 (26.7)	1 (6.7)	2 (13.3)	27 (73.0)	4 (10.8)	1 (2.7)	2 (5.4)	-	
15	Being in threatening situations where you were	8 (53.3)	-	2 (13.3)	2 (13.3)	1 (6.7)	27 (73.0)	2 (5.4)	4 (10.8)	1 (2.7)	-	
	unable to respond because of the ROE											
16	Shooting or directing fire at the enemy	4 (26.7)	2 (13.3)	4 (26.7)	-	3 (20.0)	28 (75.7)	1 (2.7)	3 (8.1)	2 (5.4)	-	
17	Calling in fire on the enemy	7 (46.7)	4 (26.7)	1 (6.7)	-	1 (6.7)	32 (88.5)	2 (5.4)	-	-	-	
18	Being involved in close combat action	10 (66.7)	1 (6.7)	2 (13.3)	-	-	30 (81.1)	3 (8.1)	1 (2.7)	-	-	
19	Clearing/ searching homes or buildings	6 (40.0)	1 (6.7)	4 (26.7)	2 (13.3)	-	30 (81.1)	1 (2.7)	2 (5.4)	-	1 (2.7)	
20	Clearing/ searching caves or bunkers	7 (46.7)	3 (20.0)	2 (13.3)	1 (6.7)	-	32 (86.5)	-	2 (5.4)	-	-	
21	Witnessing brutality/ mistreatment toward non-	8 (53.3)	1 (6.7)	4 (26.7)	-	-	30 (81.1)	2 (5.4)	2 (5.4)	-	-	
	combatants											
22	Being wounded	9 (60.0)	2 (13.3)	2 (13.3)	-	-	31 (83.8)	3 (8.1)	-	-	-	
23	Seeing ill/ wounded women and children who	2 (13.3)	4 (26.7)	4 (26.7)	1 (6.7)	2 (13.3)	23 (62.2)	3 (8.1)	3 (8.1)	3 (8.1)	2 (5.4)	
	you were unable to help											

Continuation of Table C3 on the following page.

contribution of fuote con List of miniary forated dualinatie of ents of participants custa on the List in 11, 17	Continuation of Table C3.	List of military related traur	natic events of participants base	ed on the LMHAT, $N = 70$ .
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	PTSD Group				TE-PTSS Group					
Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	never	one time	2-4 times	5-9 times	+10
the LMHAT, $N(\%)$					times					times
Receiving incoming artillery, rocket, or mortar	4 (26.7)	2 (13.3)	1 (6.7)	1 (6.7)	5 (33.3)	21 (56.8)	2 (5.4)	6 (16.2)	2 (5.4)	3 (8.1)
fire										
Being directly responsible for the death of an	9 (60.0)	2 (13.3)	-	-	1 (6.7)	32 (86.5)	1 (2.7)	-	-	-
enemy combatant										
Observing violation of the Geneva Convention	12 (80.0)	1 (6.7)	-	-	-	30 (81.1)	1 (2.7)	2 (5.4)	-	-
Being responsible for the serious injury or death	13 (86.7)	-	-	-	-	32 (86.5)	1 (2.7)	-	-	-
of a comrade										
Witnessing how a comrade got seriously injured	6 (40.0)	5 (33.3)	1 (6.7)	1 (6.7)	-	28 (75.7)	3 (8.1)	3 (8.1)	-	-
Had a close call, dud landed near you	5 (33.3)	3 (20.0)	3 (20.0)	1 (6.7)	1 (6.7)	28 (75.7)	3 (8.1)	3 (8.1)	-	-
Had equipment being shot away from you	13 (86.7)	-	-	-	-	33 (89.2)	-	-	-	-
	the LMHAT, <i>N</i> (%) Receiving incoming artillery, rocket, or mortar fire Being directly responsible for the death of an enemy combatant Observing violation of the Geneva Convention Being responsible for the serious injury or death of a comrade Witnessing how a comrade got seriously injured Had a close call, dud landed near you	the LMHAT, N (%) Receiving incoming artillery, rocket, or mortar 4 (26.7) fire Being directly responsible for the death of an 9 (60.0) enemy combatant 9 (60.0) enemy combatant 12 (80.0) Being responsible for the Geneva Convention 12 (80.0) Being responsible for the serious injury or death 13 (86.7) of a comrade 13 (86.7) Witnessing how a comrade got seriously injured 6 (40.0) Had a close call, dud landed near you 5 (33.3)	Military related traumatic event, according to the LMHAT, N (%)neverone timeReceiving incoming artillery, rocket, or mortar4 (26.7)2 (13.3)fire2 (13.3)12 (13.3)Being directly responsible for the death of an enemy combatant9 (60.0)2 (13.3)Observing violation of the Geneva Convention12 (80.0)1 (6.7)Being responsible for the serious injury or death13 (86.7)-of a comrade5 (33.3)3 (20.0)	Military related traumatic event, according to the LMHAT, N (%)neverone time2-4 timesReceiving incoming artillery, rocket, or mortar4 (26.7)2 (13.3)1 (6.7)fire9 (60.0)2 (13.3)-Being directly responsible for the death of an enemy combatant9 (60.0)2 (13.3)-Observing violation of the Geneva Convention12 (80.0)1 (6.7)-Being responsible for the serious injury or death13 (86.7)of a comradeWitnessing how a comrade got seriously injured6 (40.0)5 (33.3)1 (6.7)Had a close call, dud landed near you5 (33.3)3 (20.0)3 (20.0)	Military related traumatic event, according to the LMHAT, N (%)neverone time2-4 times5-9 timesReceiving incoming artillery, rocket, or mortar4 (26.7)2 (13.3)1 (6.7)1 (6.7)fire9 (60.0)2 (13.3)Being directly responsible for the death of an enemy combatant9 (60.0)2 (13.3)Observing violation of the Geneva Convention Being responsible for the serious injury or death12 (80.0)1 (6.7)Ga comradeWitnessing how a comrade got seriously injured6 (40.0)5 (33.3)1 (6.7)1 (6.7)Had a close call, dud landed near you5 (33.3)3 (20.0)3 (20.0)1 (6.7)	Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10           the LMHAT, N (%)         times         times           Receiving incoming artillery, rocket, or mortar         4 (26.7)         2 (13.3)         1 (6.7)         1 (6.7)         5 (33.3)           fire         state         state	Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10         never           the LMHAT, N (%)         times         times         times         times         times           Receiving incoming artillery, rocket, or mortar         4 (26.7)         2 (13.3)         1 (6.7)         1 (6.7)         5 (33.3)         21 (56.8)           fire              1 (6.7)         5 (33.3)         21 (56.8)           enemy combatant         9 (60.0)         2 (13.3)         -         -         1 (6.7)         32 (86.5)           onemy combatant         9 (60.0)         1 (6.7)         -         -         30 (81.1)           Being responsible for the death of an         9 (60.0)         1 (6.7)         -         -         30 (81.1)           Being responsible for the Serious injury or death         13 (86.7)         -         -         -         32 (86.5)           of a comrade           5 (33.3)         1 (6.7)         1 (6.7)         2 (8 (75.7)           Had a close call, dud landed near you         5 (33.3)         3 (20.0)         3 (20.0)         1 (6.7)         2 (6.7)	Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10         never         one time           the LMHAT, N (%)         times         times         times         times         times         2 (5.4)           Receiving incoming artillery, rocket, or mortar         4 (26.7)         2 (13.3)         1 (6.7)         1 (6.7)         5 (33.3)         21 (56.8)         2 (5.4)           fire               1 (6.7)         5 (33.3)         21 (56.8)         2 (5.4)           enemy combatant          9 (60.0)         2 (13.3)         -          1 (6.7)         32 (86.5)         1 (2.7)           Being directly responsible for the death of an         9 (60.0)         1 (6.7)         -          30 (81.1)         1 (2.7)           enemy combatant           1 (6.7)         -           30 (81.1)         1 (2.7)           Being responsible for the serious injury or death         13 (86.7)         -           32 (86.5)         1 (2.7)           of a comrade <td>Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10         never         one time         2-4 times           the LMHAT, N (%)         times         time</td> <td>Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10         never         one time         2-4 times         5-9 times           the LMHAT, N (%)        </td>	Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10         never         one time         2-4 times           the LMHAT, N (%)         times         time	Military related traumatic event, according to         never         one time         2-4 times         5-9 times         +10         never         one time         2-4 times         5-9 times           the LMHAT, N (%)

Continuation of Table C3 on the following page.

Continuation of Table C3. List of military related traumatic events of participants based on the LMHAT, N = 70.

			PTSD Group					TE-PTSS Group				
Item	Military related traumatic event, according to	never	one time	2-4 times	5-9 times	+10	Never	one time	2-4 times	5-9 times	+10	
	the LMHAT, $N(\%)$					times					times	
31	Being shot but protective vest saved your life	13 (86.7)	-	-	-	-	33 (89.2)	1 (2.7)	-	-	-	
32	Had a comrade shot or hit who was near to you	11 (73.3)	1 (6.7)	1 (6.7)	-	-	32 (86.5)	2 (5.4)	-	-	-	
33	Told a comrade about the death of another	8 (53.3)	3 (20.0)	1 (6.7)	-	1 (6.7)	30 (81.1)	3 (8.1)	-	-	-	
	comrade											

Note. PTSD group, trauma-exposed group with full PTSD N = 15; TE-PTSS Group, trauma-exposed group with subthreshold posttraumatic stress symptoms, N = 37; LMHAT,

List of Mental Health Advisory Team; due to missing information of some participants frequencies do not sum up to 100% in all categories.

#### ad 3.3. Attentional bias

### ad 3.3.1. Measure of attentional maintenance

We found a significant three-way interaction ( $F_{(3.68, 121.36)} = 4.19$ , p = .004,  $\eta^2 = 0.11$ ) and a significant main effect of AOI ( $F_{(1, 66)} = 24.92$ , p < .001,  $\eta^2 = 0.27$ ). Successive two-way ANOVAs found a significant effect of Group x AOI on general threat stimuli ( $F_{(2, 66)} = 5.35$ , p = .007,  $\eta^2 = 0.14$ ), and on combat stimuli ( $F_{(2, 66)} = 6.17$ , p = .004,  $\eta^2 = 0.16$ ). First, successive one-way ANOVAs found a significant effect of Group on dwell time to general threat associated neutral AOIs ( $F_{(2, 67)} = 3.76$ , p = .028). Compared to both control groups the PTSD group dwelled shorter on general threat referring neutral AOIs (NE-CG:  $t_{(31)} = -2.61$ , p = .014, Cohen's d = -0.91; TE-PTSS group:  $t_{(50)} = -2.41$ , p = .020, Cohen's d = -0.74). Second, successive one-way ANOVAs found a significant effect of Group on dwell time to combat associated neutral AOIs ( $F_{(2, 67)} = 6.50$ , p = .003). Compared to both control groups the PTSD group dwelled shorter on combat referring neutral AOIs (NE-CG:  $t_{(31)} = -3.06$ , p = .004, Cohen's d = -1.07; TE-PTSS group:  $t_{(50)} = -3.28$ , p = .002, Cohen's d = -1.00). See Table C4.

	PTSD Group		TE-PT	SS Group	NE-CG		
	М	SD	М	SD	М	SD	
Combat related pictures							
Combat related	5745.52	1367.26	5379.32	1078.64	5172.89	1156.52	
Neutral	2105.60	1022.24	3039.18	891.69	3118.38	877.52	
General threat pictures							
General threat	5184.75	1432.69	4828.95	828.08	4451.89	971.69	
Neutral	2963.18	763.65	3560.63	826.88	3660.72	766.22	
Emotional facial expressions							
Negative valence	3619.25	810.42	3989.92	1077.58	3979.22	1032.46	
Neutral	3913.55	800.58	3643.66	944.99	3815.71	1133.65	

*Table C4.* Dwell time to AOI in ms, N = 70.

#### ad 3.3.2. First fixation measures

Latency: We found a significant three-way interaction effect ( $F_{(4.00, 132.00)} = 3.00$ , p = .021,  $\eta^2 = 0.08$ ) and a significant main effect of AOI ( $F_{(1,66)} = 9.58$ , p = .003). Successive twoway ANOVAs found a significant effect of Group x AOI on general threat stimuli ( $F_{(2, 66)} = 5.72$ , p = .005,  $\eta^2 = 0.15$ ). Successive one-way ANOVAs found a significant effect of Group on latency to general threat AOIs ( $F_{(2, 67)} = 4.54$ , p = .014). The TE-PTSS group entered faster to general threat related AOIs in contrast to the NE-CG ( $t_{(21.80)} = -2.33$ , p = .030, Cohen's d = -0.82). See Table C5.

	PTSD Group		TE-PI	TSS Group	NE-CG		
	М	SD	М	SD	М	SD	
Combat-related pictures							
Combat related	580.57	267.98	500.74	247.81	708.94	583.41	
Neutral	1004.26	555.06	907.15	410.06	1170.06	846.70	
General threat pictures							
General threat	563.85	304.77	553.15	248.99	827.26	468.57	
Neutral	797.16	349.99	907.15	410.06	756.91	435.91	
Emotional facial expressions							
Negative valence	812.56	469.79	662.99	403.44	736.43	357.81	
Neutral	918.69	369.41	944.54	407.58	1214.16	702.92	

Spatial orienting: We found a non-significant three-way interaction effect ( $F_{(2.74, 88.97)} =$  1.72, p = .173,  $\eta^2 = 0.05$ ) and a significant main effect of AOI ( $F_{(1, 65)} = 29.22$ , p < .001,  $\eta^2 = 0.31$ ). See Table C6.

	PT	PTSD Group		TSS Group	NE-CG	
	М	SD	М	SD	М	SD
Combat-related pictures						
Combat related	6.07	1.39	6.64	1.17	6.28	1.25
Neutral	5.93	1.39	5.36	1.17	5.72	1.27
General threat pictures						
General threat	5.20	1.27	5.19	1.37	4.83	0.92
Neutral	4.80	1.26	4.81	1.37	5.17	0.92
Emotional facial expression	ns					
Negative valence	2.53	0.65	2.82	0.52	2.74	0.54
Neutral	2.59	0.65	2.18	0.52	2.26	0.54

*Table C6.* Counts on location of initial fixation to AOI, N = 70.

Average initial fixation duration: We found a non-significant three-way interaction effect ( $F_{(4.00, 132.00)} = 0.57$ , p = .686,  $\eta^2 = 0.02$ ), and no other significant interaction or main effects. See Table C7.

	PTSD Group		TE-PT	TE-PTSS Group		E-CG
	М	SD	М	SD	М	SD
Combat related pictures						
Combat related	317.66	92.80	301.44	65.40	301.44	65.40
Neutral	269.64	60.22	299.44	66.60	275.17	60.84
General threat pictures						
General threat	297.13	119.99	294.86	68.77	278.72	59.12
Neutral	297.70	84.02	307.97	79.01	268.52	62.99
Emotional facial expressions						
Negative valence	342.00	204.20	285.33	70.61	290.29	84.93
Neutral	323.33	100.14	281.87	56.77	304.30	133.35

*Table C7.* Duration of initial fixation to AOI in ms, N = 70.

#### ad 3.3.3. Attention bias variability

We found a non-significant three-way interaction effect ( $F_{(4, 132)} = 1.36$ , p = .252,  $\eta^2 = 0.04$ ) and a significant main effect of AOI ( $F_{(1, 66)} = 10.65$ , p = .002,  $\eta^2 = 0.14$ ). The betweengroup effect reached significance ( $F_{(2, 66)} = 3.84$ , p = .026,  $\eta^2 = 0.10$ ). The PTSD group showed an increased fluctuation of attention in contrast to both control groups (TE-PTSS group: p = .031; NE-CG: p = .050). See Table C8.

	PTSD-Group		TE-P	TSS Group	1	NE-CG
	М	SD	М	SD	М	SD
Combat-related pictures						
Combat-related	0.34	0.34	0.31	0.13	0.35	0.16
Neutral	0.66	0.35	0.49	0.22	0.55	0.22
General threat pictures						
General threat	0.47	0.27	0.36	0.15	0.32	0.14
Neutral	0.61	0.21	0.48	0.23	0.42	0.19
Emotional facial expressions						
Emotional valence	0.50	0.36	0.39	0.33	0.36	0.17
Neutral	0.49	0.27	0.36	0.28	0.43	0.41

*Table C8.* Indicator of attentional bias variability to AOI, N = 70.

### ad 3.4. Reliability analysis

Internal consistency was not acceptable for latency and for average duration of initial fixation across and within groups. For average dwell time, the internal consistency was between acceptable and high for combat related stimuli and AOIs and facial expression stimuli and AOIs in the entire sample. Descriptive results are presented in Table C9.

	Full sample	PTSD group	TE-PTSS	NE-CG
			Group	
	Cronbach's α	Cronbach's a	Cronbach's a	Cronbach's a
Average dwell time				
Overall threat (overall neutral)	0.83 (0.74)	0.85 (0.70)	0.82 (0.63)	0.84 (0.84)
Combat pictures (neutral)	0.79 (0.74)	0.86 (0.83)	0.73 (0.64)	0.81 (0.65)
General related pictures (neutral)	0.60 (0.49)	0.74 (0.49)	0.41 (0.45)	0.52 (0.45)
Emotional faces (neutral)	0.79 (0.71)	0.69 (0.50)	0.81 (0.75)	0.80 (0.79)
Average duration of initial fixation				
Overall threat (overall neutral)	0.54 (0.55)	0.46 (0.53)	0.59 (0.71)	0.65 (0.42)
Combat pictures (neutral)	0.43 (0.53)	0.70 (0.60)	0.34 (0.49)	0.28 (0.58)
General related pictures (neutral)	0.45 (0.48)	0.58 (0.59)	0.40 (0.39)	0.32 (0.53)
Emotional faces (neutral)	0.31 (0.33)	0.36 (0.35)	0.07 (0.57)	0.52 (0.25)
Latency				
Overall threat (overall neutral)	0.71 (0.67)	0.51 (0.33)	0.65 (0.53)	0.81 (0.82)
Combat pictures (neutral)	0.34 (0.51)	-0.29 (0.22)	0.42 (0.26)	0.45 (0.74)
General related pictures (neutral)	0.43 (0.23)	-0.46 (-0.04)	0.32 (0.17)	0.46 (0.37)
Emotional faces (neutral)	0.67 (0.67)	0.65 (0.59)	0.70 (0.60)	0.64 (0.72)

Table C9. Internal consistency of dependent variables using Cronbach's alpha, N = 70.

#### ad Discussion

#### ad 4.1.1. Measure of attentional maintenance

Evidence is provided for the maintenance hypothesis. The PTSD group dwell shorter on neutral AOIs that were concurrently presented with combat related AOIs or with general threat related AOIs in contrast to both control groups. These findings using the alternative grouping are in overall accordance with the findings when using the original grouping [for further discussion of these results please refer to the main body of the manuscript].

#### ad 4.1.2. First fixation measures

No robust support can be provided for group differences on hypervigilant orienting to threat in PTSD in contrast to controls, neither regarding latency nor regarding spatial orienting. No group differences on initial fixation duration are evident in the current data, providing no indication of difficulties in initial attention disengagement in PTSD in contrast to control groups. The current results using the alternative grouping agree with the results when using the original grouping [for further discussion of these results please refer to the main body of the manuscript].

### ad 4.1.3. Measure of attention bias variability

Preliminary and limited support is found for patterns of ABV in PTSS. Subjects with PTSD show circumscribed patterns of increased fluctuation of attention in contrast to the healthy control groups. The findings when using the alternative grouping are in line with the findings using the original grouping [for further discussion of these results please refer to the main body of the manuscript].

#### Conclusion regarding the re-grouping

The allocation of study participants either following our a priori defined 'original grouping' or following an 'alternative re-grouping' did not impact significantly on the results

of the current investigation. Regarding first fixation measures and indicator of ABV, no discrepancies were evident in dependance of the way of group allocation, at all. About dwell time, some group differences were slightly more pronounced under the 'original grouping' variation in contrast to the 'alternative grouping' variation. However, no substantial discrepancies resulted that could be objective to interpretation. These findings may be supportive for the assumption that patterns of attentional bias would be rather associated with dimensional characteristics of PTSS than with a categorical diagnostic status of PTSD, underscoring a dimensional understanding of attentional bias and psychopathology (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007; Lazarov et al., 2019).

#### References Appendix C

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- Lazarov, A., Suarez-Jimenez, B., Tamman, A., Falzon, L., Zhu, X., Edmondson, D. E., & Neria, Y. (2019). Attention to threat in posttraumatic stress disorder as indexed by eye-tracking indices: A systematic review. *Psychological medicine*, 49(5), 705-726. doi:10.1017/S0033291718002313

### **STUDY 4 – Supplementary Material**

	P	re-treatme	ent assessment <sup>1</sup>	Pe	ost- treati	ment assessment <sup>2</sup>		Follow-u	ip assessment <sup>3</sup>
	М	SD		М	SD		М	SD	
Photographic scenes - valence									
Combat related	7.35	0.92	7 - 2.02 = 4.001	7.27	1.05	7 - 2.02 = -0.02	6.95	0.79	7 - 2.02 = -0.02
Neutral-to-combat	3.40	1.16	<i>Z</i> = -3.92, <i>p</i> < .001	3.65	1.13	Z = -2.93, p = .003	3.09	1.06	Z = -2.93 p = .003
General threat	6.81	1.03	7 2.02 001	6.54	1.19	7 2.04 - 002	6.43	1.05	7 2.04 - 002
Neutral-to-general threat	3.18	1.20	Z = -3.92, p < .001	2.95	1.24	Z = -2.94, p = .003	3.32	1.20	Z = -2.94, p = .003
Photographic scenes – arousal									
Combat related	6.52	1.68	7 2.02 001	5.64	1.99	7 2.04 - 002	5.55	1.80	7 2 04 - 002
Neutral-to-combat	2.70	1.44	Z = -3.92, p < .001	2.14	1.21	Z = -2.94, p = .003	1.89	1.03	Z = -2.94, p = .003
General threat	5.78	2.11	7 2.92 < 0.01	4.46	2.03	7 2.02 - 002	4.15	1.73	7 2 04 - 002
Neutral-to-general threat	2.85	1.40	Z = -3.83, p < .001	2.00	0.98	Z = -2.93, p = .003	2.34	1.27	Z = -2.94 p = .003
Facial expressions – correct iden	tification (%	)							
Neutral	78.88	15.92		85.83	13.42		86.81	13.38	
Fear	62.00	28.21		61.82	30.27		80.00	12.65	
Disgust	93.00	22.73		87.27	20.54		96.36	8.09	
Anger	96.00	8.21		96.36	8.09		94.55	9.34	

Table 2. Results of Wilcoxon signed-rank test on arousal and valence of picture stimuli and on perceptibility of facial expressions by time (manipulation check).

Note. <sup>1</sup>, N = 21; <sup>2</sup>, N = 11, <sup>3</sup>, N = 11; Bonferroni corrected level of statistical significance set at p < .006.

Table 3. Results of Mann-Whitney U test on	differences between	n treatment completer	s versus non-completers
regarding photographic scenes at pre-interventi	ion assessment, N =	24.	

	Treatment co	ompleters <sup>1</sup>	Non-comple	ters <sup>2</sup>			
	Mean Rank	Rank Sum	Mean Rank	Rank Sum	Comparison		
Combat related							
Mean entry time in ms	10.64	117.00	13.25	159.00	<i>Z</i> =92, <i>p</i> = .356		
Mean dwell time in %	13.82	152.00	10.33	124.00	<i>Z</i> = -1.23, <i>p</i> = .218		
Average fixation duration in ms	10.91	120.00	13.00	156.00	Z =74, p = .460		
Mean initial fixation duration in ms	12.27	135.00	11.75	141.00	<i>Z</i> =19, p = .854		
Neutral-to-combat							
Mean entry time in ms	12.18	134.00	11.83	142.00	<i>Z</i> =12, <i>p</i> = .902		
Mean dwell time in %	10.27	113.00	13.58	163.00	Z = -1.17, p = .242		
Average fixation duration in ms	9.91	109.00	13.92	167.00	Z = -1.42, p = .157		
Mean initial fixation duration in ms	12.00	132.00	12.00	144.00	Z = .00, p = .999		
General threat							
Mean entry time in ms	12.00	132.00	12.00	144.00	Z = .00, p = .999		
Mean dwell time in %	13.45	148.00	10.67	128.00	<i>Z</i> =99, <i>p</i> = .325		
Average fixation duration in ms	13.00	143.00	11.08	133.00	Z =68, p = .498		
Mean initial fixation duration in ms	14.18	156.00	10.00	120.00	Z = -1.48, p = .140		
Neutral-to-general threat							
Mean entry time in ms	14.36	158.00	9.83	118.00	Z = -1.60, p = .110		
Mean dwell time in %	12.36	136.00	11.67	140.00	<i>Z</i> =25, <i>p</i> = .806		
Average fixation duration in ms	12.36	136.00	11.67	140.00	<i>Z</i> =25, <i>p</i> = .806		
Mean initial fixation duration in ms	12.95	142.50	11.13	133.50	<i>Z</i> =65, <i>p</i> = .518		

*Note.* <sup>1</sup>, N = 11; <sup>2</sup>, N = 13; Bonferroni corrected level of statistical significance set at p < .002.

Table 4. Results of Mann-Whitney U test on differences	between treatment completers versus non-completers
regarding emotional facial expressions at pre-intervention a	assessment, $N = 24$ .

	Treatment co	ompleters <sup>1</sup>	Non-comple	ters <sup>2</sup>	
	Mean Rank	Rank Sum	Mean Rank	Rank Sum	Comparison
Fear					
Mean entry time in ms	13.00	143.00	11.08	133.00	Z = -68., p = .498
Mean dwell time in %	12.09	133.00	11.92	143.00	<i>Z</i> =06, <i>p</i> = .951
Average fixation duration in ms	10.64	117.00	13.25	159.00	<i>Z</i> =92, <i>p</i> = .356
Mean initial fixation duration in ms	11.36	125.00	12.58	151.00	<i>Z</i> =43, <i>p</i> = .667
Neutral-to-fear					
Mean entry time in ms	11.27	124.00	12.67	152.00	<i>Z</i> =49, <i>p</i> = .622
Mean dwell time in %	10.64	117.00	13.25	159.00	<i>Z</i> =92, <i>p</i> = .356
Average fixation duration in ms	12.91	142.00	11.17	134.00	<i>Z</i> =62, <i>p</i> = .538
Mean initial fixation duration in ms	11.27	124.00	12.67	152.00	<i>Z</i> =49, <i>p</i> = .622
Disgust					
Mean entry time in ms	10.91	120.00	13.00	156.00	<i>Z</i> =74, <i>p</i> = .460
Mean dwell time in %	13.18	145.00	10.92	131.00	<i>Z</i> =80, <i>p</i> = .424
Average fixation duration in ms	10.82	119.00	13.08	157.00	<i>Z</i> =80, <i>p</i> = .424
Mean initial fixation duration in ms	12.45	137.00	11.58	139.00	<i>Z</i> =31, <i>p</i> = .758
Neutral-to-disgust					
Mean entry time in ms	14.09	155.00	10.08	121.00	Z = -1.42, p = .157
Mean dwell time in %	12.45	137.00	11.58	139.00	<i>Z</i> =31, <i>p</i> = .758
Average fixation duration in ms	13.00	143.00	11.08	133.00	<i>Z</i> =68, <i>p</i> = .498
Mean initial fixation duration in ms	12.91	142.00	11.17	134.00	<i>Z</i> =62, <i>p</i> = .538

Table 4 continues following page.

Continuation of Table 4.	Treatment co	ompleters <sup>1</sup>	Non-comple	ters <sup>2</sup>	
	Mean Rank	Rank Sum	Mean Rank	Rank Sum	Comparison
Anger					
Mean entry time in ms	10.09	111.00	13.75	165.00	<i>Z</i> = -1.29, <i>p</i> = .196
Mean dwell time in %	15.45	170.00	8.83	106.00	<i>Z</i> = -2.34, <i>p</i> = .019
Average fixation duration in ms	12.82	141.00	11.25	135.00	<i>Z</i> =55, <i>p</i> = .580
Mean initial fixation duration in ms	12.82	141.00	11.25	135.00	<i>Z</i> =55, <i>p</i> = .580
Neutral-to-anger					
Mean entry time in ms	12.09	133.00	11.92	143.00	<i>Z</i> =06, <i>p</i> = .951
Mean dwell time in %	12.36	136.00	11.67	140.00	<i>Z</i> =25, <i>p</i> = .806
Average fixation duration in ms	13.91	153.00	10.25	123.00	<i>Z</i> = -1.29, <i>p</i> = .196
Mean initial fixation duration in ms	13.82	152.00	10.33	124.00	<i>Z</i> = -1.23, <i>p</i> = .218

*Note.* <sup>1</sup>, N = 11; <sup>2</sup>, N = 13; Bonferroni corrected level of statistical significance set at p < .002.

	Non-co	ompleters	Treatment completers									
Mean entry time in ms	pre-tr	eatment	pre-tre	atment	tment post-treatment		comparison pre- to pre-treatment		atment	3-mont	h follow	comparison pre- to
	asses	sment <sup>1</sup>	assess	ment <sup>2</sup>	asses	sment <sup>2</sup>	post-treatment <sup>2</sup>	assessment <sup>3</sup>		up assessm		follow up <sup>3</sup>
	М	SD	М	SD	М	SD		М	SD	М	SD	
Photographic scenes												
Combat related	712.98	607.54	568.96	546.71	726.13	770.82	Z = -1.69, p = .091	779.66	785.69	728.88	726.45	Z =09, p = .929
Neutral-to-combat	971.55	573.30	1089.22	822.77	1291.04	816.33	Z = -1.07, p = .286	1133.47	858.00	676.03	463.17	Z = -1.16, p = .248
General threat	565.98	339.70	594.57	357.13	850.68	1267.87	<i>Z</i> =27, <i>p</i> = .790	598.28	355.09	525.03	522.38	Z = -1.60, p = .110
Neutral-to-general threat	640.71	261.85	948.35	498.76	708.33	420.03	Z = -1.51 p = .131	940.84	506.79	678.98	393.29	Z = -1.42, p = .155
Facial expressions												
Disgust	630.09	240.15	611.20	413.15	747.56	316.52	<i>Z</i> =71, <i>p</i> = .477	671.25	389.42	468.74	266.29	Z =71, p = .477
Neutral-to-disgust	617.18	283.71	1052.90	774.60	1233.27	911.46	<i>Z</i> =18, <i>p</i> = .859	933.17	781.50	892.55	508.06	Z =09, p = .929
Fear	869.44	1017.75	663.35	398.35	678.75	355.47	Z =09, p = .929	664.56	397.04	801.22	527.75	Z =09, p = .929
Neutral-to-fear	939.49	648.50	686.37	342.18	926.52	384.29	Z = -1.42, p = .155	717.89	355.70	700.14	384.56	Z =00, p = .999
Anger	824.35	587.50	534.37	277.76	806.36	949.93	<i>Z</i> =36, <i>p</i> = .722	572.64	245.31	652.64	358.62	Z =45, p = .657
Neutral-to-anger	1113.97	690.44	1085.20	575.85	949.81	386.31	<i>Z</i> =53, <i>p</i> = .594	967.19	487.92	869.59	672.75	Z =27, p = .790

Table 5. Results of Wilcoxon signed-rank test on mean entry time to area of interests (AOI) by group, time, and stimulus type, N = 24.

	Non-completers pre-treatment assessment <sup>1</sup>		Treatment completers									
Mean dwell time in %			pre-treatment assessment <sup>2</sup>		post-treatment assessment <sup>2</sup>		comparison pre- to post-treatment <sup>2</sup>	pre-treatment assessment <sup>3</sup>		3-month follow up assessment <sup>3</sup>		comparison pre- to follow up <sup>3</sup>
Photographic scenes												
Combat related	54.50	15.72	63.54	17.84	56.19	18.32	Z = -2.13, p = .033	60.18	17.53	49.87	25.36	Z = -2.40, p = .016
Neutral-to-combat	23.92	11.68	18.48	11.81	24.81	12.35	Z = -1.96, p = .050	20.71	12.27	23.58	17.53	Z =62, p = .534
General threat	49.13	13.19	53.24	11.71	49.64	17.55	<i>Z</i> =98, <i>p</i> = .328	52.18	10.99	51.28	20.55	Z =27, p = .790
Neutral-to-general threat	28.73	9.25	29.83	8.66	29.79	13.39	Z =09, p = .929	30.50	8.52	28.64	16.42	Z =53, p = .594
Facial expressions												
Disgust	37.29	14.31	42.80	12.35	36.32	17.55	Z = -1.07, p = .286	38.50	16.40	34.80	21.69	Z =71, p = .477
Neutral-to-disgust	34.86	11.16	38.67	14.62	38.39	16.12	Z =62, p = .534	36.42	16.20	34.22	21.06	Z = -1.07, p = .286
Fear	37.26	13.42	41.37	15.07	38.98	16.90	Z =45, p = .657	37.09	16.61	35.91	20.41	Z =00, p = .999
Neutral-to-fear	34.24	12.03	32.50	16.59	37.48	17.66	Z =71, p = .477	30.87	18.13	34.59	19.17	Z =27, p = .790
Anger	32.77	13.04	49.47	19.38	43.33	19.71	<i>Z</i> =98, <i>p</i> = .328	45.23	18.49	42.59	25.57	Z =62, p = .534
Neutral-to-anger	32.70	14.75	33.92	16.75	34.23	16.90	Z =00, p = .999	35.78	16.25	29.61	20.91	Z = -1.33, p = .182

*Table 6.* Results of Wilcoxon signed-rank test on mean dwell time to area of interests (AOI) by group, time, and stimulus type, N = 24.

	Non-co	ompleters			Treatment completers								
Average fixation	pre-treatment assessment <sup>1</sup>		pre-treatment assessment <sup>2</sup>		post-treatment assessment <sup>2</sup>		comparison pre- to post-treatment <sup>2</sup>	pre-treatment assessment <sup>3</sup>		3-month follow up assessment <sup>3</sup>		comparison pre- to follow up <sup>3</sup>	
duration in ms													
	М	SD	М	SD	М	SD		М	SD	М	SD		
Photographic scenes													
Combat related	396.71	100.75	387.56	47.50	379.65	78.98	Z =09, p = .929	379.89	33.91	335.71	96.40	Z = -1.07, p = .286	
Neutral-to-combat	313.34	80.87	284.98	70.00	318.54	68.94	Z = -1.60, p = .110	300.60	64.77	290.10	112.69	<i>Z</i> =18, <i>p</i> = .859	
General threat	365.52	78.44	373.68	47.12	359.11	77.80	<i>Z</i> =45, <i>p</i> = .657	376.13	53.98	328.84	93.01	<i>Z</i> =98, <i>p</i> = .328	
Neutral-to-general threat	325.66	62.05	330.67	50.96	334.18	74.64	<i>Z</i> =18, <i>p</i> = .859	332.85	53.66	306.91	111.06	<i>Z</i> = -36., <i>p</i> = .722	
Facial expressions													
Disgust	487.30	548.29	348.54	83.23	466.67	286.99	Z =89, p = .374	312.17	74.59	299.58	115.81	<i>Z</i> = -36., <i>p</i> = .722	
Neutral-to-disgust	327.35	89.30	360.16	76.04	403.88	173.07	Z =89, p = .374	329.95	74.23	335.02	91.14	Z =80, p = .424	
Fear	333.00	93.42	330.72	91.81	404.15	229.79	<i>Z</i> =53, <i>p</i> = .594	292.96	93.17	323.37	118.40	Z = -1.07, p = .286	
Neutral-to-fear	389.38	296.68	352.97	60.99	373.48	92.06	<i>Z</i> =71, <i>p</i> = .477	318.73	95.44	365.21	109.29	<i>Z</i> =98, <i>p</i> = .328	
Anger	335.69	100.21	374.66	105.09	463.87	286.40	<i>Z</i> =45, <i>p</i> = .657	349.62	70.30	389.66	151.77	Z = -1.33, p = .182	
Neutral-to-anger	319.63	114.96	383.58	121.21	398.85	113.04	Z =09, p = .929	367.19	100.73	331.61	83.14	<i>Z</i> = -98., <i>p</i> = .328	

*Table 7.* Results of Wilcoxon signed-rank test on average fixation duration to area of interests (AOI) by group, time, and stimulus type, N = 24.

	Non-completers pre-treatment assessment <sup>1</sup>		Treatment completers									
Mean initial fixation			pre-treatment assessment <sup>2</sup>		post-treatment assessment <sup>2</sup>		comparison pre- to post-treatment <sup>2</sup>	pre-treatment assessment <sup>3</sup>		3-month follow up assessment <sup>3</sup>		comparison pre- to follow up <sup>3</sup>
duration in ms												
	М	SD	М	SD	М	SD		М	SD	М	SD	
Photographic scenes												
Combat related	307.85	100.49	304.17	37.86	320.13	64.63	Z =80, p = .424	302.41	36.42	276.66	73.17	Z =89, p = .374
Neutral-to-combat	259.94	68.17	260.84	61.66	260.59	50.55	Z =09, p = .929	273.73	54.41	232.08	59.88	<i>Z</i> = -1.78, <i>p</i> = .075
General threat	271.90	77.06	288.78	50.45	281.78	49.75	<i>Z</i> =18, <i>p</i> = .859	301.21	73.03	250.33	54.45	Z = -1.51, p = .131
Neutral-to-general threat	262.60	77.55	273.31	34.04	280.28	67.32	Z =89, p = .374	269.22	34.08	249.97	74.60	<i>Z</i> =80, <i>p</i> = .424
Facial expressions												
Disgust	421.06	541.02	296.79	71.24	357.42	220.52	<i>Z</i> =36, <i>p</i> = .722	280.42	84.07	232.53	102.05	<i>Z</i> = -1.25, <i>p</i> = .213
Neutral-to-disgust	270.62	66.20	299.83	62.65	353.17	209.11	Z =27, p = .790	281.34	66.48	298.35	106.44	<i>Z</i> =18, <i>p</i> = .859
Fear	277.53	105.29	280.41	85.03	434.75	348.22	Z = -1.87, p = .062	246.46	92.06	295.61	106.71	Z = -1.51, p = .131
Neutral-to-fear	335.99	280.95	297.71	124.73	315.34	101.90	Z =53, p = .594	245.87	93.35	296.18	70.69	Z = -1.16, p = .248
Anger	263.85	109.90	285.28	79.98	347.15	167.38	Z = -1.25, p = .213	285.58	80.46	301.67	118.30	Z =62, p = .534
Neutral-to-anger	280.39	99.34	338.34	106.09	371.70	139.68	Z =62, p = .534	321.97	96.61	344.08	128.97	Z =53, p = .594

*Table 8.* Results of Wilcoxon signed-rank test on initial fixation duration to area of interests (AOI) by group, time, and stimulus type, N = 24.

## **CURRICULUM VITAE**

Curriculum Vitae is not included for privacy reasons.

Therefore, pages 325 and 326 are not included in the online version of this dissertation.

### CURRICULUM VITAE AND LIST OF OWN PUBLICATIONS

## LIST OF OWN PUBLICATIONS

**Publications in peer-reviewed journals** (Publications marked with an \* represent the core studies of this dissertation thesis)

### 2022

- Schumacher, S., Engel, S., Klusmann, H., Niemeyer, H., Küster, A., Burchert, S., Skoluda, N., Rau, H., Nater, U., Willmund, G., & Knaevelsrud, C. (2022). Trauma-related but not PTSD-related increases in hair cortisol concentrations in military personnel. *Journal* of Psychiatric Research. doi:https://doi.org/10.1016/j.jpsychires.2022.02.031
- \* Kuester, A., Schumacher, S., Niemeyer, H., Engel, S., Spies, J., Weiß, D., Muschalla, B., Burchert, S., Tamm, S., Weidmann, A., Bohn, J., Willmund, G., Rau, H., & Knaevelsrud, C. (2022). Attentional bias in German Armed Forces veterans with and without posttraumatic stress symptoms – An eye-tracking investigation and group comparison. *Journal of Behavior Therapy and Experimental Psychiatry*, 76 (101726). https://doi.org/10.1016/j.jbtep.2022.101726.

### 2021

- Engel, S., Schumacher, S., Niemeyer, H., Küster, A., Burchert, S., Klusmann, H., Rau, H.,
   Willmund, G.-D., & Knaevelsrud, C. (2021). Associations between oxytocin and vasopressin concentrations, traumatic event exposure and posttraumatic stress disorder symptoms: Group comparisons, correlations, and courses during an internet-based cognitive-behavioral treatment. *European Journal of Psychotraumatology*, *12*(1). https://doi.org/10.1080/20008198.2021.1886499
- Schumacher, S., Engel, S., Niemeyer, H., Küster, A., Burchert, S., Skoluda, N., ... & Knaevelsrud, C. (2021). Salivary Cortisol and Alpha-Amylase in Posttraumatic Stress Disorder and Their Potential Role in the Evaluation of Cognitive Behavioral Treatment Outcomes. *Journal of traumatic stress*. https://doi.org/10.1002/jts.22683

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- \* Kuester, A., Niemeyer, H., Schumacher, S., Engel, S., Spies, J., Weiß, D., Muschalla, B., Burchert, S., Tamm, S., Weidmann, A., Willmund, G., Rau, H., & Knaevelsrud, C. (2020). Attentional Bias in Veterans with Deployment-related Posttraumatic stress disorder before and after Internet-based Cognitive Behavioral Therapy – An Eyetracking Investigation. *Journal of Behavioral and Cognitive Therapy*. https://doi.org/10.1016/j.jbct.2020.03.003
- Engel, S., Schumacher, S., Niemeyer, H., Küster, A., Burchert, S., Rau, H., Willmund, G.-D., & Knaevelsrud, C. (2020). Beeinflusst Oxytocin den psychotherapeutischen Prozess?
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- Niemeyer, H.\*, Knaevelsrud, C.\*, Schumacher, S., Engel, S., Kuester, A., Burchert, S., Muschalla, B., Weiss, D., Spies, J., Rau, H.\*\*, & Willmund, G.-D.\*\* (2020). Evaluation of an internet-based intervention for service members of the German armed forces with deployment-related posttraumatic stress symptoms. *BMC Psychiatry*, 20(1), 205. https://doi.org/10.1186/s12888-020-02595-z \* shared first authorship; \*\* shared last authorship
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  Associations Between Difficulties in Emotion Regulation and Post-Traumatic Stress
  Disorder in Deployed Service Members of the German Armed Forces. *Frontiers in Psychiatry*, 11, 973. https://doi.org/10.3389/fpsyt.2020.576553

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Schumacher, S., Engel, S., Niemeyer, H., Küster, A., Spies, J., Rau, H., ... & Knaevelsrud, C. (2019). Effects of psychotherapeutic treatment on cortisol and alpha-amylase concentrations: An investigation in soldiers of the German Armed Forces suffering from PTSD. *Psychoneuroendocrinology*, 100, S56.

### 2017

- \* Kuester, A., Köhler, K., Ehring, T., Knaevelsrud, C., Kober, L., Krüger-Gottschalk, A., ...
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### 2016

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### **Book chapters**

Knaevelsrud, C., **Küster, A.,** & Zagorscak, P. (2016). E-Mental-Health. In: I. Hauth, P. Falkai & A. Deister (Eds.) Psyche Mensch Gesellschaft (pp. 25-30). Berlin: Springer.

# EIGENSTÄNDIGKEITSERKLÄRUNG

Hiermit versichere ich, dass ich die vorgelegte Arbeit selbstständig verfasst und ohne unerlaubte Hilfe angefertigt habe.

Alle Hilfsmittel, die ich verwendet habe, wurden von mir angegeben.

Die Dissertation ist in keinem früheren Promotionsverfahren angenommen oder abgelehnt worden.

Berlin, im Mai 2022

Annika Küster