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Cardiorespiratory fitness as protection against the development of memory intrusions: A prospective trauma analogue study

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ABSTRACT

Intrusive and distressing memories are at the core of post-traumatic stress disorder (PTSD). Since cardiorespiratory fitness (CRF) has been linked with improved mental health, emotion regulation, and memory function, CRF may, by promoting these capabilities, protect against the development of intrusions after trauma. We investigated the CRF-intrusion relationship and its potential mediators in 115 healthy individuals, using a trauma film to induce intrusions. As potential mediators, we assessed indices of pre-trauma mental health such as heart rate variability, subjective and psychobiological peri-traumatic responses, and memory. Critically, results showed that higher CRF was related to fewer intrusions, but no mediators emerged for the CRF-intrusion relationship. These results indicate that individuals displaying higher CRF are less prone to develop traumatic memory intrusions. Future studies may want to investigate whether promoting fitness prior to possible trauma exposure can boost resilience against the development of debilitating re-experiencing symptoms of PTSD.

1. Introduction

A central characteristic of people with post-traumatic stress disorder (PTSD) is that they often suffer from highly distressing intrusions, described as recurrent involuntary and spontaneous memories of a traumatic event (American Psychiatric Association, 2013). Although intrusions are highly prevalent in trauma survivors and constitute a normal response to aversive experiences, their early frequency and severity predicts the later development and maintenance of PTSD (Brewin, Gregory, Lipton, & Burgess, 2010), possibly by driving the development of other PTSD symptoms (Sullivan, Smith, Lewis, & Jones, 2016). Therefore, understanding and targeting these early intrusions is critical for treatment and prevention strategies aiming to reduce the risk of full-blown PTSD. While research has mainly focused on interventions or secondary post-trauma prevention, more recently there has been increased interest in early prevention (Forneris et al., 2013). That is, insight into pre-trauma resilience and vulnerability factors has enormous practical implications. For instance, if malleable factors can be non-invasively targeted to prevent PTSD development in the general community this could considerably

reduce healthcare costs (Kalisch et al., 2017). In addition, similar pre-deployment strategies may prepare personnel at risk to effectively cope with deployment or combat-related stressors and trauma.

Regular physical activity may be a particularly effective way to promote resilience, as it has often been linked with improved psychological wellbeing (e.g., Penedo & Dahn, 2005) and a reduced incidence of mood and anxiety disorders (Ten Have, Graaf, & Monshouwer, 2011). For instance, a recent meta-analysis of prospective studies showed that a higher level of self-reported physical activity was related to a lower chance of developing PTSD (Schuch, Ward, Stubbs, Meyer, & Hiles, 2019). Even though promising, such effects may not necessarily be driven by actual increases in physical fitness but rather by beneficial effects of behavioural activation itself (Etherton & Farley, 2020). Therefore, objective indices of physical fitness are needed. Regular physical activity leads to higher oxygen supply to working muscles during exercise due to more efficient circulatory and respiratory systems – which has been coined cardiorespiratory fitness (CRF; Vancampfort et al., 2017) – and can for instance be assessed by a submaximal ergometer (e.g., a stationary bicycle) test. In line with a beneficial effect

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of physical activity for mental health it has been shown that individuals with higher CRF have a better capacity to cope with perceived stress and have a lower chance of experiencing occupational burnout (Gerber, Lindwall, Lindegård, Börjesson, & Jonsdottir, 2013). However, it remains unknown whether high CRF functions as a resilience factor against the development of core symptoms of PTSD such as traumatic intrusions (Sullivan et al., 2016). Interestingly, earlier studies provide evidence of mechanisms that link with CRF on the one hand and with intrusions on the other hand, substantiating evidence for a relationship between CRF and intrusions, specifically (Baym et al., 2014; Broman-fulks, Berman, Rabian, & Webster, 2004; Chen et al., 2019; Clark, Mackay, & Holmes, 2015; Mackenzie et al., 2016; Meyer, Krans, van Ast, & Smeets, 2017; Ripley, Clapp, & Beck, 2017; Schilling et al., 2020). The current study investigated the association between CRF and the development of traumatic intrusions, while also addressing a number of potential mediators that may account for the hypothesised negative relationship between CRF and intrusions. In the search for potential mediators, we focussed on general and trauma-specific mediators for which earlier studies have revealed relationships not only with intrusions but also with CRF.

One potential pathway by which CRF may influence the development of intrusive memories is the intimate relationship between physical and general mental health. Since depression and anxiety are among the leading contributors to the global burden of disease (Rehm & Shield, 2019), we chose to focus on these and related variables as important indicators of general mental health. Indeed, some studies have linked pre-existing psychopathology, such as higher trait anxiety and level of depressive symptoms, to intrusion-development (Clark et al., 2015). Although the existing evidence on pre-existing factors is still mixed, it is most evident that pre-trauma high levels of anxiety and depression could predict more intrusive memories (Marks, Franklin, & Zoellner et al., 2018). Notably, trait anxiety and depression levels can be ameliorated by regular exercise (Broman-fulks et al., 2004). Similarly, there may be pre-trauma biological markers of emotion regulation predictive of intrusions, such as resting Heart Rate Variability (HRV; Appelhans & Luecken, 2006; Čukić & Bates, 2015). For instance, low HRV has been associated with more intrusive memories in a trauma film study (Rombold-Bruehl et al., 2017). Likewise, physical exercise has been shown to improve HRV indices (Castello et al., 2011; Chen et al., 2019; Dietrich et al., 2008). Thus, such psychological and biological markers of general mental health are likely to already exist pre-trauma, and may be a first set of possible mediators of the CRF-intrusion relationship.

In addition to these general pre-trauma factors, the CRF-intrusion relationship might be mediated by acute emotional and psychophysiological reactions to specific traumatic experiences. Importantly, such peri-traumatic factors are among the most reliable known predictors of PTSD (Marks et al., 2018). For instance, high subjective emotional responses have been repeatedly associated with more frequent intrusions following trauma film viewing (e.g., Clark et al., 2015). Similar evidence has been found for heightened sympathetic activation, as indexed by increases in skin conductance levels (Rattel et al., 2019; Ripley et al., 2017). Corroborating these observations, some evidence suggests that acute increases in heart rate predict intrusive memories (e.g., Weidmann, Conradi, Gröger, Fehm, & Fydrich, 2009). Moreover, police officers with higher levels of CRF show lower physiological stress reactivity after experiencing work-related stress (Schilling et al., 2020), in line with a role for exaggerated physiological arousal in the development of PTSD. However, not all studies have replicated positive relationships between physiological arousal and intrusions, and some even found a heart rate deceleration while watching a trauma film, which tended to predict intrusions (e.g., Chou, Marca, Steptoe, & Brewin, 2014; Holmes, Brewin, & Hennessy, 2004). As a possible explanation, acute heart rate decelerations could reflect orienting, defensive freezing, and/or dissociative reactions (e.g., Hagens, Roelofs, & Stins, 2014), and may depend on the type of aversive film (Arnaudova & Hagens, 2017). Thus, trauma-induced changes in heart rate and other indices of

physiological arousal in the development of intrusions warrant further replication. Yet, by generally promoting emotion regulation abilities (Bernstein & McNally, 2017) and cardiovascular health, CRF can be expected to mediate acute emotional and psychophysiological peri-traumatic responses to trauma, thereby enhancing resilience against the development of PTSD.

Finally, information-processing models have conceptualised PTSD as a disorder of memory, in which traumatic events are not sufficiently integrated in their original encoding context. Accordingly, a consequence of insufficient context learning is that innocuous cues that vaguely overlap with elements of the traumatic experience can readily elicit intrusions, defensive fear responses, or avoidant behaviours (Brewin, Gregory, Lipton, & Burgess, 2010; Ehlers and Clark, 2000). Indeed, experimental studies indicate that individuals with a stronger context-dependent memory are less prone to develop intrusions after analogue trauma (e.g. Meyer et al., 2017). The hippocampus has been suggested to mediate context effects on memory by binding together multiple elements of an experience into a single conjunctive representation (Eichenbaum, 2004). Critically, exercise-induced increases in CRF are associated with improved hippocampal-dependent memory (e.g., Baym et al., 2014; Erickson et al., 2011). Thus, CRF could also protect against the development of intrusions by generally enhancing context-dependent memory.

Another potential memory-based mediator that could constitute a general resilience factor for the development of intrusions is working memory (e.g. Elzinga & Bremner, 2002). That is, some studies suggest that individuals with higher working memory capacities are better capable of suppressing intrusive thoughts (e.g., Brewin & Beaton, 2002; Brewin & Smart, 2005). Since increasing CRF can improve working memory performance (Kamijo et al., 2012; Mackenzie et al., 2016), CRF might protect against the development of intrusions by improving working memory.

To summarise, different lines of research provide evidence for a link between the development of intrusions and pre-trauma mental health, peri-traumatic responses, and memory function on the one hand. Further evidence reveals that these mechanisms tune to differences in CRF on the other hand. Thus, CRF may protect against intrusion development through greater pre-trauma mental health, reduced peri-traumatic responses, and/or improved memory functioning. The present study aimed to investigate the CRF-intrusion relationship and its potential mediators by using an analogue trauma paradigm, in which participants watched a 'trauma film' and kept an intrusion-diary in the subsequent week. We hypothesised that individual differences in CRF, as assessed with a submaximal ergometer test, would be negatively associated with the development of intrusive memories. Using regression and mediation models, we then tested whether the potential CRF-intrusion relationship was partially or fully mediated by pre-trauma mental health characteristics (i.e., trait anxiety, depression, resting HRV), peri-traumatic responses to the traumatic footage (subjective emotional and psychophysiological), and/or individual differences in memory performance (i.e., context-dependent memory, working memory). As secondary analyses, we tested the same models to predict intrusion distress and the development of other PTSD analogue symptoms.

2. Methods

2.1. Participants

A total sample of 115 participants (97 women) with mean age 20.77 years ($SD = 2.81$, $range = 18-33$) completed this study. Thirteen additional participants enrolled but were excluded from all analyses because they dropped out prematurely ($n = 9$), or had unusable CRF measurements ($n = 4$). Participants were recruited through a digital platform of the University of Amsterdam. Interested candidates were informed about the aversive nature of the study materials. Exclusion criteria were (1) psychiatric problems in the past year, (2) experiences of traumatic events (e.g., physical abuse, car accident), (3) neurological or physical disorders

(e.g. cardiovascular disorder), (4) pregnancy, (5) age below 18 years, (6) medication use, (7) drinking on average more than 15 alcohol units per week, and (8) using drugs more than once a week. The ethical committee of the University of Amsterdam approved the study and participants received partial course credits or a small monetary reward for their participation. All participants provided written informed consent. The sample characteristics are displayed in Table 1. It represents a healthy sample, with 92.2% having BMI scores reflecting normal weight (BMI < 25.0 kg/m²; Korhonen, Seppälä, Järvenpää, & Kautiainen, 2014).

Table 1
Sample characteristics (n = 115).

	Percentage
Sex (% female)	84.3%
	Mean (SD)
Age	20.8 (2.8)
BMI	22.1 (3.1)
BDI	5.4 (4.1)
PCL-5	5.0 (6.8)
IES	10.2 (9.0)
IES-intrusion	6.1 (5.0)
STAI-T	35.9 (8.8)
IAMI	1.9 (0.8)
IPAQ-LF MET min per week*	
Total	2529.2 (1389.6)
Walking	419.0 (396.5)
Moderate	1166.2 (694.8)
Vigorous	944.0 (825.1)
Cycle	595.4 (410.3)

Note. BMI = Body Mass Index, BDI = Beck depression inventory, PCL-5 = PTSD Checklist for DSM-5, IES = The Impact of Event Scale, STAI-T = State-Trait Anxiety Inventory-Trait, IAMI = The Involuntary Autobiographical Memory Inventory, IPAQ-LF = The International Physical Activity Questionnaire Long Form, *Correlations among CRF and the IPAQ-LF are presented in the supplement.

2.2. Trauma film and intrusion diary

Participants watched a 14 min trauma film that consisted of a compilation of aversive film fragments: graphic scenes of a knee surgery, a person drowning, scenes of the genocide in Rwanda in 1994, an eye surgery, and a fatal car accident (Holmes, James, Coode-Bate, & Deeprose, 2009; Meyer et al., 2013, 2017). Afterwards, participants were given a paper and pencil diary to record intrusions about the trauma film for seven consecutive days. Intrusions were defined as spontaneous, involuntary memories (Brewin, Gregory, Lipton, & Burgess, 2010; Holmes, James, Coode-Bate, & Deeprose, 2009). When intrusions occurred, participants were instructed to record them as soon as possible. Otherwise, participants were asked to record the absence of intrusions at least two times a day. The diary discriminates verbal and visual intrusions about the film fragments, and participants were asked to indicate the content and trigger of each intrusion (allowing the experimenters to verify their validity according to the definition). Furthermore, participants were asked to report a distress score per intrusion on a scale from 0 (*not at all distressing*) to 10 (*extremely distressing*).

The distribution of number of intrusions was skewed to the right, with high numbers of intrusions being less frequent than low numbers. Therefore, a log-transformation was performed prior to analysis; \ln (number of intrusions + 1). An average distress score was calculated across intrusions, whereby zero was entered if participants did not report any intrusions.

2.3. PTSD analogue symptoms

The Impact of Event Scale (IES; Horowitz, Wilner, & Alvarez, 1979) measure was administered because especially the intrusions subscale is frequently used in studies using the trauma film paradigm (James et al., 2016). The IES served as a retrospective measure of intrusion-related

distress (IES-intrusion subscale) and overall PTSD-analogue symptoms and was adapted to specifically measure symptoms related to the trauma film in the past 7 days (total 15 items; $\alpha = 0.84$, intrusion subscale 7 items; $\alpha = 0.78$). In parallel, the PTSD Checklist for DSM-5 (PCL-5; Blevins, Weathers, Davis, Witte, & Domino, 2015) was administered, assessing the overall PTSD-analogue symptoms of participants with regard to the trauma film fragments over the past 7 days. It is indicated that the PCL-5 has a strong internal consistency ($\alpha = 0.90$). We added the PCL-5 since it is frequently used in clinical samples and is based on the formal PTSD criteria of the DSM-5 (American Psychiatric Association, 2013).

2.4. Cardiorespiratory fitness (CRF)

CRF was estimated with a submaximal, multistage cycle ergometer test, administered on a Monark cycle ergometer (Model 828E, Monark AB, Varberg, Sweden). Before starting the test, the cycle seat was adjusted to the participant's height. During the whole test, participants had to maintain a pedalling rate of 60 rpm. After a warm-up period of 2 min without resistance (0 watts) the test started with 30 watts. Every 2 min the resistance was increased by 30 watts. The heart rate (HR) of participants was constantly monitored with electrocardiography (ECG, see for more details the section on resting heart rate variability assessment). The test stopped when the HR of the participant reached, or exceeded the 75% of the maximum HR (whereby $HR_{max} = 220 - \text{age}$ in years; Batcho, Thonnard, & Nielsen, 2012).

As an estimate of CRF, the physical working capacity was calculated by extrapolating the HR and power output of the different stages to a HR of 170 beats per minute (PWC_{170} ; Bland, Pfeiffer, & Eisenmann, 2012).

2.5. Pre-trauma mental health characteristics

2.5.1. Depression and anxiety symptoms

The Beck Depression Inventory (BDI) was used as a self-report measure to assess depressive symptom severity. It consists of 21 items that require respondents to select one out of four statements describing different degrees of a depressive symptom. Item scores (0–3) are summed up to yield a total score ($\alpha = 0.71$; Beck, Steer, & Carbin, 1988). In addition, we used the State-Trait Anxiety Inventory-Trait (STAI-T) for the assessment of general ('trait') levels of anxiety (Spielberger, 1989). The scale consists of 20 statements describing an anxiety-related symptom, requiring respondents to indicate its frequency on 4-point Likert scales (1 = *almost never*, 4 = *almost always*; $\alpha = 0.91$).

2.5.2. Resting heart rate variability

Resting heart rate variability (HRV) was assessed with an electrocardiogram (ECG) during 5 min at rest. We assessed HRV during rest rather than during trauma-exposure itself since resting HRV specifically is considered to be an objective measure of individual differences in the ability to regulate emotional responding (e.g., Appelhans & Luecken, 2006; Porges, 2001; Thayer & Lane, 2000). The reason behind this is that it is especially the parasympathetic component that is thought to serve as an index of the ease by which an individual can transition between high and low arousal states, and this parasympathetic input to the heart is mostly present during rest (Appelhans & Luecken, 2006). Two disposable ECG electrodes (Red Dot with Micropore tape 2239, 3 M, Delft, the Netherlands) were placed left and right on the chest of the participant, and one reference electrode on the abdomen. The electrodes were attached to a custom-made portable amplifier (University of Amsterdam, Amsterdam, the Netherlands) with a 1G Ω input resistance and a bandwidth of 0.1 Hz (6 dB/oct) to 250 Hz (24 dB/oct) containing a National Instruments NI-USB6210 A/D converter (Austin, Texas, USA) to digitise the analogue data. Raw ECG signals were sampled using the software programme VSRP98 (Version 7.0, developed by the Technical Support Group Psychology at the University of Amsterdam, Amsterdam, the Netherlands) at 1000 samples per second.

ECG data were analysed using an in-house analysis programme

written in MATLAB (MathWorks, Natick, Massachusetts, USA), as implemented in VSRRP98. The ECG signal was first filtered with a Butterworth bandpass filter with 0.5 and 50 Hz as cut-offs, and then r-peaks were automatically detected. Using visual inspection missing r-peaks were manually corrected, or if too noisy, the data segment was removed. The successive r-r intervals were then extracted and imported in the Kubios HRV Package (Version 3.0.0, 2017, University of Eastern Finland, Kuopio, Finland) (Tarvainen, Lipponen, Niskanen, & Ranta-aho, 2018) to calculate HRV, whereby HRV was defined as the root mean square of successive difference (RMSSD) (Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012). The data were again corrected for artifacts, using the artifact correction sensitivity setting “very low” among the default options of the Kubios software. Two participants had a missing resting HRV measure because of a technical failure during data collection.

2.6. Peri-traumatic responses

2.6.1. Emotional responses to trauma film

To assess mood changes in response to viewing the trauma film, the state negative affect of the Positive and Negative Affect Schedule was used (PANAS-NA; Watson, Clark, & Tellegen, 1988). It consists of 10 items measuring negative affect (NA pre and post; $\alpha > 0.64$). In addition, we included four 100 mm visual analogue scales (VAS) to assess the specific negative feelings of fear, shock, sadness, and anger. NA and VAS data from two participants were lost and could not be included in the analyses.

2.6.2. Psychophysiological responses to trauma film

Heart rate (HR) was assessed with an electrocardiogram (ECG) during 5 min at rest (baseline), as well as during trauma film viewing. The same materials and methods as for resting HRV were used to collect and analyse the HR data. Two participants had a missing HR measure because of a technical failure during data collection. In parallel, electrodermal activity (EDA) was recorded to measure skin conductance levels (SCL) of participants during trauma film viewing, using VSRRP98. The 5 min rest phase served as the baseline. An input device with a sine shaped excitation voltage (0.5 V) of 50 Hz, derived from the mains frequency, was used. The signal from the input device was led through the custom-made signal-conditioning amplifier and the analogue output was digitised at 100 Hz by a 16-bit AD-converter (National Instruments, NI-USB6210, Austin, Texas, U.S.A.). The input device was connected to two Ag/AgCl electrodes of 20 by 16 mm. The electrodes were attached to the medial phalanges of the index and ring finger of the left hand. Due to defective electrodes, SCL data were not recorded for 24 participants.

SCL during baseline and trauma film viewing was defined by calculating the mean of the entire segment (i.e., baseline and trauma film).

2.7. Memory performance

2.7.1. Context-dependent memory

Context-dependent memory was assessed with a computer task (Fig. 1B), presenting a series of face-background pairs during the encoding phase. Recognition was tested in a subsequent phase, whereby

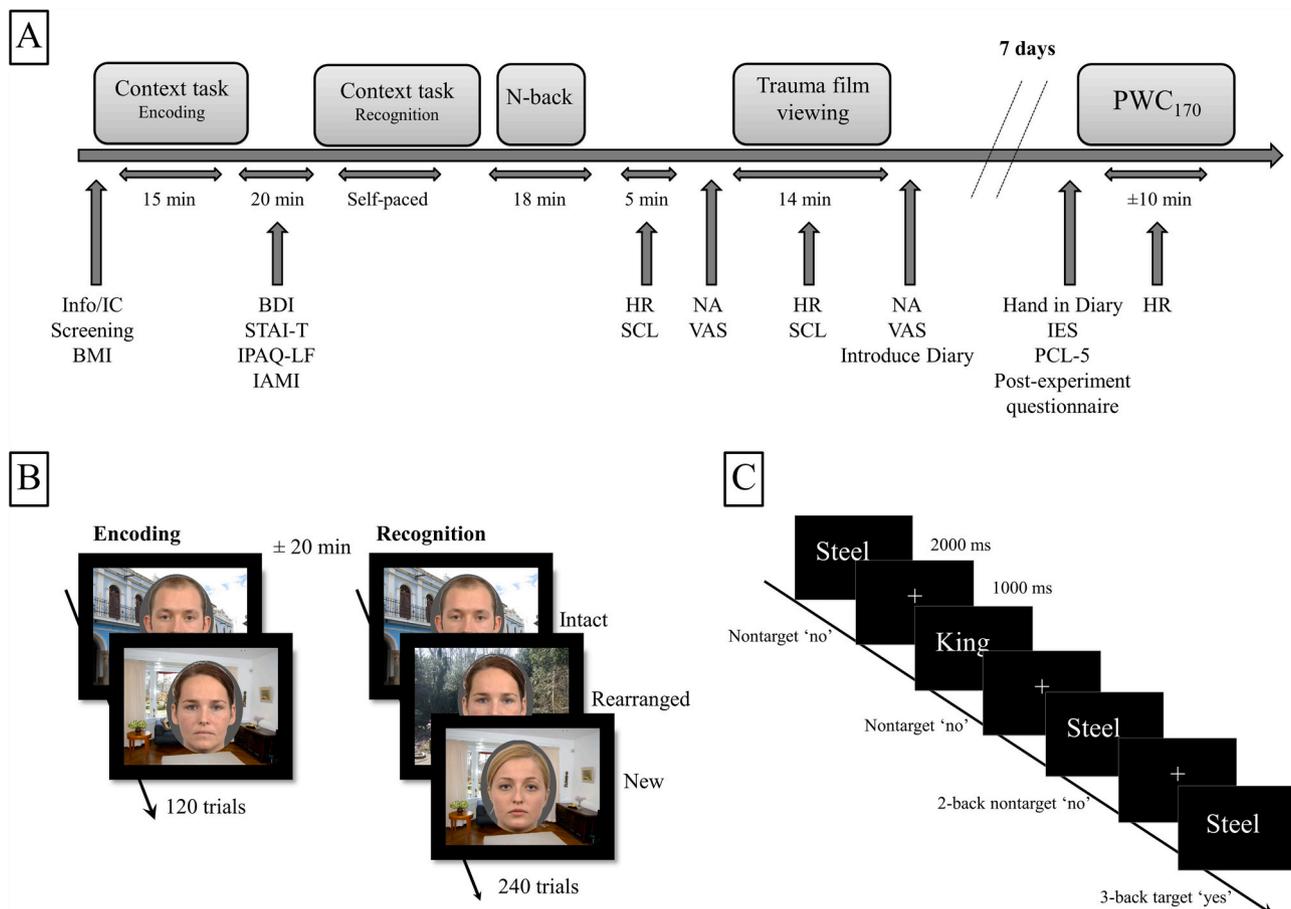


Fig. 1. (A) Timeline of the study. (B) Trial types of the context task. Recognition trials (right) either comprised old faces presented against their original encoding context (intact) or against a different context (rearranged), or new faces. The advantage of intact over rearranged contexts in discrimination performance quantifies context-dependent memory. (C) Procedure of the N-back task. IC = Informed Consent, BMI = Body Mass Index, BDI = Beck depression inventory, STAI-T = State-Trait Anxiety Inventory-Trait, IPAQ-LF = The International Physical Activity Questionnaire Long Form, IAMI = The Involuntary Autobiographical Memory Inventory, HR = Heart Rate, SCL = Skin Conductance Level, NA = Negative Affect Scale, VAS = Visual Analogue Scales, IES = The Impact of Event Scale, PCL-5 = PTSD Checklist for DSM-5, PWC₁₇₀ = physical working capacity.

the face-background pairs were intact or rearranged. Compared to rearranged pairs, intact ones typically lead to more accurate and faster recognition, and this difference serves as an index of context-dependent memory (Meyer et al., 2017; Sep, Van Ast, Gorter, Joëls, & Geuze, 2019; Van Ast, Cornelisse, Meeter, Joëls, & Kindt, 2013; Van Ast, Cornelisse, Meeter, & Kindt, 2014; Zhang, Van Ast, Klumpers, Roelofs, & Hermans, 2018). During encoding, 120 face images were presented against background images, resulting in 120 unique face-context pairs. Half of the faces were individuals with an angry expression, the other half were individuals with a neutral expression (Sep et al., 2019). Recognition of the 120 face images was assessed 20 min later. This surprise recognition test consisted of 240 trials in total; 120 'old' faces, and 120 'new' faces that functioned as 'lures'. Half of the 120 face-context pairs from encoding were presented as *intact pairs*, whereas the other half was rearranged randomly with different backgrounds (*rearranged pairs*). Participants were asked to indicate whether the presented face was 'old' or 'new' on a 6-point confidence rating scale (1 = absolutely sure it was new, 2 = somewhat sure it was new, 3 = guessing it was new, 4 = guessing it was old, 5 = somewhat sure it was old, 6 = absolutely sure it was old; Zhang et al., 2018). Accuracy was recorded for each trial.

Three participants performed below or at chance, and were therefore set at missing (see Zhang et al., 2018). Data from another participant were lost due to a technical error. Hit and false alarm rates were calculated for all conditions and then converted to *d*-prime scores (Zhang et al., 2018). Context-dependence relative to overall memory performance was then calculated as: $[(\text{Intact} - \text{Rearranged}) / ((\text{Intact} + \text{Rearranged}) / 2)]$. Hence, a greater positive difference score referred to a greater context-dependent memory (Meyer et al., 2017).

2.7.2. Working memory

Working memory performance was measured with a verbal N-back computer task (Van Ast et al., 2014), administered with E-Prime software (Version 3.0, Psychology Software Tools, Inc., Sharpsburg, USA; Fig. 1C). Participants received the overall instruction to respond as quickly and accurately to each word by pressing the button indicating a target response ('yes, this word matches the word presented 3 trials ago') or nontarget response ('no, this word does not match the word presented 3 trials ago'). The task consisted of two practice blocks of 17 trials each, and then 16 critical blocks again of 17 trials each. Half of the blocks contained neutral words, and the other half contained negative words.

D-prime scores were calculated for the neutral and negative conditions (Van Ast et al., 2014). Data from 14 participants performing below or at chance were set to missing. Data was lost for four other participants due to experimenter error. A higher *d*-prime score indicates higher working-memory performance.

2.8. Other questionnaires

The International Physical Activity Questionnaire Long Form (IPAQ-LF; Craig et al., 2003) was used as self-report measure to assess the health-related physical activity of the participants during the past 7 days. Associations among CRF and the IPAQ-LF are presented in the supplement. The Involuntary Autobiographical Memory Inventory (IAMI; Berntsen, Rubin, & Salgado, 2015) was used to assess individual differences in the tendency for involuntary autobiographical memories and involuntary future thoughts. Sample means are displayed in Table 1. These data were not further considered in the following analyses.

2.9. Procedure

The study consisted of two laboratory sessions with one week in between (see Fig. 1A). Participants were asked to refrain from smoking, caffeine and alcohol in the period from awakening till the start of both

sessions. In addition, 2 h prior to both sessions, participants were instructed not to engage in heavy exercise, and prior to the second session also to abstain from food intake. In session 1, the encoding phase of the context task was administered on a computer, followed by digital questionnaires (BDI, STAI-T, IPAQ-LF and IAMI). This was followed by the recognition part of the context task and the N-back task. Then, baseline physiology was measured for 5 min (HR and SCL) while participants watched a neutral underwater film fragment. Next, participants were asked to place their head on a chin rest 60 cm from the screen and watched the 14 min trauma film. During film viewing, participants were asked to move as little as possible for physiological data collection and to watch the film attentively without looking away. Before and after the film, subjective affective states (NA and VAS) were measured. Afterwards, the intrusion diary was extensively explained and participants kept the diary for one week in between the two sessions. In the second session, participants handed in and clarified their intrusion diary. They also filled out the IES and PCL-5. At last, the CRF test was conducted (PWC₁₇₀), followed by a full debriefing of all procedures. The CRF test was assessed at the very end of the study to ensure that it would not affect the other measures through increased cortisol levels that modulate working memory, episodic memory encoding and consolidation (Budde, Voelcker-rehage, Pietrassyk-kendziorra, Machado, & Ribeiro, 2010; Loprinzi, 2018; O'Connor & Corrigan, 1987; Van Ast, Spicer, et al., 2014; Van Ast, Cornelisse, Meeter, Joëls, & Kindt, 2013; Van Ast, Cornelisse, Meeter, & Kindt, 2014). Likewise, implementing CRF at the end of session 1 would have induced a similar issue because exercise can retroactively affect consolidation processes (Van Dongen et al., 2016). The CRF assessment is therefore implemented at the very end of the study, taking into consideration that CRF levels are relatively stable over time and have a low month-to-month variability within individuals, especially when CRF is already high (Lang et al., 2018).

2.10. Data analysis

All statistical analyses were performed using the SPSS statistical software package version 25 (SPSS, Inc., Chicago, Illinois).

2.10.1. Manipulation checks

Paired samples *t*-test were performed to assess changes in NA, VAS, HR and SCL in response to film viewing. Because the assumption of normality for NA, VAS emotions (fear, sad, angry), HR and SCL were violated, bias-corrected and accelerated bootstrap intervals (BCa) were calculated. One outlier in the HR data and one (different) outlier in the SCL data was detected. We included these outliers in our analyses since including or excluding them did not have an effect on outcome. *D*-prime scores of the context task were analysed using a 2×2 repeated measures analysis of variance (ANOVA), whereby Context (intact / rearranged face-context pairs) and Valence (neutral / angry faces) served as within factors. For the N-back task, a paired samples *t*-test was used to compare *d*-prime scores for trials with neutral and negative words. To exploratively assess initial zero-order associations between CRF, the potential mediators (pre-trauma mental health, peri-traumatic responses, and memory performance), and intrusions, we conducted Pearson correlations with SIDAK corrections for multiple comparisons (see Supplementary Table S1).

2.10.2. Primary analyses

We conducted hierarchical multiple linear regression analyses in order to investigate the relation between CRF and intrusions, as well as to point out possible mediating variables of this relation. For this analysis, missing data of predictors was imputed with a regression based multiple imputation technique (Enders, 2017), and pooled results were used. SCL was included in the explorative correlation analyses (Supplementary Table S1) but not as a predictor in regression analyses due to

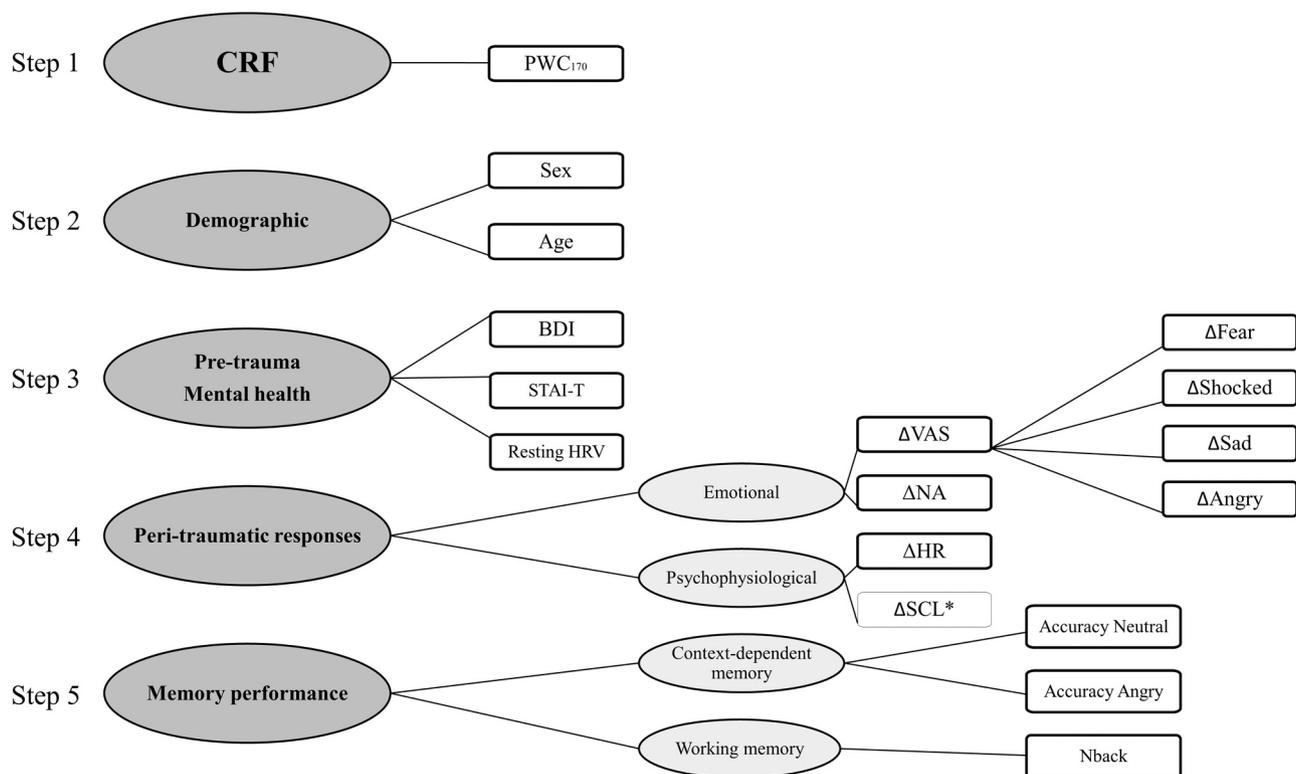


Fig. 2. Overview of the five theoretical steps, each with individual predictors of intrusions and their indices. Possible predictors were sequentially added over these five steps. PWC₁₇₀ = physical working capacity, BDI = Beck depression inventory, STAI-T = State-Trait Anxiety Inventory-Trait, HR(V) = Heart Rate (Variability), NA = Negative Affect Scale, VAS = Visual Analogue Scales, SCL = Skin Conductance Level. Δ = difference between assessment during or after film viewing minus the score during baseline. *SCL was not included in the final model due to missing data SCL.

a relatively large amount of missing data ($n = 24$). In step 1 of the model, CRF (PWC₁₇₀) was entered after which additional possible predictors were sequentially added over four steps (Fig. 2). In step 2 (demographic characteristics), we controlled the CRF measure for sex and age (Kodama et al., 2009; Vancampfort et al., 2016). Then, we entered predictors according to a sequence based on the theoretical chronology of proceedings (Ripley et al., 2017); First, *pre-trauma mental health characteristics* were entered (step 3; BDI, STAI-T, resting HRV), after that the *peri-traumatic responses* (step 4; Δ NA, Δ VAS, Δ HR) and at last *memory performance* (step 5; context task, N-back). Though memory performance can be conceptualised as a pre-trauma characteristic, it theoretically influences the formation of intrusions *after* initial responses to the trauma (i.e., the factors addressed in step 4; Brewin, Gregory, Lipton, & Burgess, 2010). No multicollinearity occurred (all VIFs < 3). To meaningfully interpret the influence of the final predictors on the log transformed number of intrusions, the exponential function of the coefficient was used (e^{cb} ; Benoit, 2011). The meaningful effect of a c -unit increase in the predictor variable multiplies the expected value of the number of intrusions by e^b .

For the mediation analyses bootstrap method tests from Hayes's PROCESS tool in SPSS were used (Field, 2013; Hayes, 2018). Since no more than 10 mediators could be investigated simultaneously (Hayes, 2018), the following procedure was performed. If a variable in the previous regression is revealed to be related to intrusion development – while controlling for the effect of CRF –, according to standard mediation logic (Baron & Kenny, 1986), this is a strong clue it would hold as “path b” in a formal mediation test. Indeed, path b tests for the relationship of the mediator and an outcome variable, while controlling for the predictor (CRF in this case). Therefore, any significant predictor to emerge from this model was further analysed as a possible mediating variable in the relation between CRF and intrusions. With a mediation test, the

following effects were examined according to standard mediation logic (Hayes, 2018): (1) the association of the mediator with individual differences in CRF (*path a*), (2) the relationship of the mediator with intrusion development, controlling for the effect of CRF (*path b*), and (3) the mediation effect, indicative of variables mediating the relationship between CRF and intrusions (*path a*b*).

2.10.3. Secondary analyses

We tested whether CRF could be a protective factor against intrusions-related distress and the development of overall PTSD analogue symptoms (IES total score, IES intrusions, and PCL-5). The same model and steps as performed on the number of intrusions were used in three additional hierarchical multiple regression analyses, while focusing on CRF and the final model (step 5).

2.10.4. Power analysis

Based on prior trauma analogue studies investigating pre-trauma mental health characteristics (Clark et al., 2015), peri-traumatic responses (e.g. Ripley et al., 2017) and memory performance (Meyer et al., 2017) reporting small to medium effect sizes, we determined that for a linear multiple regression model with 15 predictors, an initial sample size of $n = 108$ was adequate to detect an overall significant final model with a medium-effect size ($f^2 = 0.20$) and 80% power at $\alpha = 0.05$ (using G*power). Additional recruitment was planned to allow for attrition. Importantly, as we did not necessarily thrive after an overall significant model but rather were interested in individual predictors, sensitivity analyses revealed that with 15 predictors in the model the final sample of $n = 115$ (i.e., after data-cleaning) was adequately powered to detect small effects of single regression coefficients of individual predictors ($f^2 = 0.07$) for two-tailed tests at $\alpha = 0.05$ with 80% power.

3. Results

3.1. Manipulation checks

3.1.1. Intrusion development and peri-traumatic responses

Trauma film viewing successfully resulted in the development of intrusions and intrusion-related distress (Table 2). Trauma film watching resulted in a strong increase in mean NA score from pre- to post-film,

Table 2
Reported intrusions after trauma film viewing (n = 115).

		Mean (SD)	Range
Frequency	Any type	3.98 (3.38)	0–20
	Images	3.15 (3.12)	0–18
	Thoughts	2.15 (2.44)	0–11
Distress	Any type	3.55 (2.02)	0–7.67

with a large effect size ($t(112) = 10.71, p = .001$, BCa 95% CI $[-6.70, -4.68]$, Cohen's $d = 1.01$; Fig. 3A). The VAS for the emotions fear, shocked, sad and angry showed similar significant increases from pre- to post-film (all $t_s > 16.74, p_s \leq 0.001$, Cohen's $d_s > 0.78$; Fig. 3B). Furthermore, there was a significant increase in mean HR ($t(112) = 2.90, p = .021$, BCa 95% CI $[-3.17, -0.73]$, Cohen's $d = 0.27$; Fig. 3C) and SCL ($t(90) = 9.99, p = .001$, BCa 95% CI $[-3.62, -2.41]$, Cohen's $d = 1.05$; Fig. 3D) from baseline to trauma film viewing, with a large and small effect size, respectively. In conclusion, the trauma film was effective in inducing negative emotional and psychophysiological responses.

3.1.2. Context-dependent memory and working memory

Results revealed an interaction effect between Context and Valence on D-prime scores of the context task, $F(1, 110) = 10.68, p = .001, \eta_p^2 = 0.088$ (Fig. 4A). Follow-up analyses showed that intact context aided

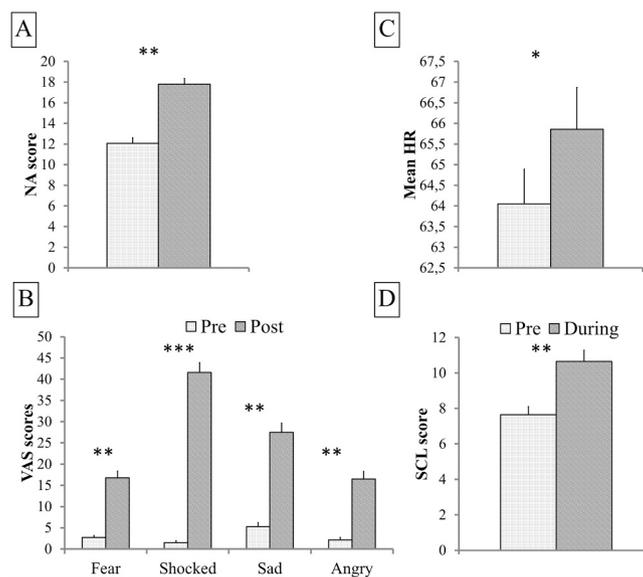


Fig. 3. Peri-traumatic responses to trauma film viewing on (A) NA, (B) VAS, (C) HR (in BPM) and (D) SCL (in μV). Error bars represent standard error of the mean (s.e.m.). NA = Negative Affect, VAS = Visual Analogue Scale, HR = Heart Rate, SCL = Skin Conductance Level. Significant differences during or after the film viewing compared to the preceding baseline are depicted with $*p < .05, **p < .01, ***p < .001$.

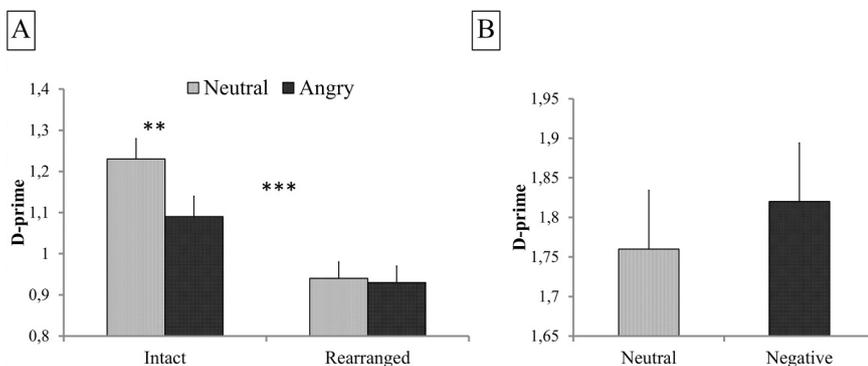


Fig. 4. (A) Context task recognition performance. Context-dependent memory performance (D-prime) as a function of context (intact or rearranged) and Valence (neutral and angry). (B) N-back task recognition performance. Working memory performance (D-prime) as a function of Valence (neutral or negative). Error bars represent standard error of the mean (s.e.m.). Significant differences between intact and rearranged and between neutral and angry are depicted with $**p < .01, ***p < .001$.

Table 3
Hierarchical multiple linear regression for assessing predictors of traumatic memory intrusions (n = 115).

	Step 1: Cardiorespiratory fitness				Step 2: Demographic characteristics				Step 3: Pre-trauma mental health characteristics				Step 4: Peri-traumatic responses				Step 5: Memory performance			
	b	SE	β	p	b	SE	β	p	b	SE	β	p	b	SE	β	p	b	SE	β	p
LogIntrusion																				
CRF*	-0.003	.002	-0.188	.044	-0.004	.002	-0.225	.035	-0.004	.002	-0.217	.050	-0.005	.002	-0.264	.017	-0.004	.002	-0.256	.024
Sex					.114	.189	.064	.546	.100	.193	.056	.607	.217	.187	.122	.249	.193	.193	.108	.321
Age					.017	.022	.073	.438	.013	.022	.057	.555	.031	.022	.133	.163	.034	.022	.146	.135
BDI									.014	.020	.090	.474	.019	.019	.120	.316	.019	.019	.120	.321
STAI-T									-0.005	.009	-0.075	.553	-0.012	.009	-0.163	.189	-0.011	.009	-0.149	.237
HRV baseline									.000	.002	-0.013	.894	.000	.002	-0.012	.905	.000	.002	-0.009	.925
ΔHR									-0.003	.010	.026	.800	-0.003	.010	.026	.800	-0.001	.010	-0.013	.903
ΔNA									-0.007	.016	-0.060	.659	-0.007	.016	-0.060	.659	-0.008	.016	-0.070	.612
ΔFear									-0.002	.005	-0.053	.680	-0.002	.005	-0.053	.680	-0.002	.005	-0.055	.683
ΔShocked**									.013	.004	.515	.001	.013	.004	.515	.001	.013	.004	.493	.001
ΔSad									.000	.003	-0.011	.926	.000	.003	-0.011	.926	.000	.003	.007	.952
ΔAngry									.000	.004	-0.012	.915	.000	.004	-0.012	.915	-0.001	.004	-0.022	.844
ContextNeut																	-0.078	.130	-0.055	.549
ContextAngry																	.156	.191	.076	.415
Nback																	.062	.108	.057	.569
R ²	R ² = .035				ΔR ² = .009				ΔR ² = .005				ΔR ² = .169				ΔR ² = .009			
Model	F(1, 113) = 4.15 *				F(2, 111) = 0.54				F(3, 108) = 0.19				F(6, 102) = 3.69 **				F(3, 99) = 0.40			
Model	F(1, 113) = 4.15 *				F(3, 111) = 1.73				F(6, 108) = 0.94				F(12, 102) = 2.39**				F(15, 99) = 1.96 *			

Note. *p < .05, **p < .01, ***p < .001. Sex; 0 = women, 1 = men, BDI = Beck depression inventory, STAI-T = State-Trait Anxiety Inventory-Trait, HRV = Heart Rate Variability, NA = Negative Affect Scale.

memory of neutral faces ($M = 1.23, SD = 0.50$) more so than angry faces ($M = 1.09, SD = 0.49; t(110) = 3.54, p = .001$), while no such difference was found between neutral faces ($M = 0.94, SD = 0.47$) and angry faces ($M = 0.93, SD = 0.45$) when the context was rearranged ($t(110) = 0.37, p = .712$). Furthermore, there was a significant main effect of Context, $F(1, 110) = 76.90, p < .001, \eta_p^2 = 0.411$, with higher d-prime scores in the intact context compared to the rearranged context. There was also a main effect of Valence, $F(1, 110) = 5.83, p = .017, \eta_p^2 = 0.050$, with higher mean d-primes in the neutral condition compared to the angry condition. Based on these findings, we used two separate d-prime difference scores for neutral and angry faces in further analyses, as indices of context-dependent memory. For working memory assessed by the N-back task, we found no significant difference on d-prime scores in the neutral and negative condition, $t(110) = -1.47, p = .144$ (Fig. 4B). Therefore, one d-prime score, collapsed over Valence, was used as index of working memory in further analyses.

3.1.3. Correlation analyses

Zero-order correlations among the predictor variables and the outcome measures are presented in [Supplementary Table S1](#).

3.2. Primary analyses

Assessing predictors of memory intrusions. CRF entered at step 1 produced a significant model (Table 3). CRF was a significant negative predictor of intrusions ($\beta = -0.188, p = .044$). The demographic characteristics entered at step 2 and pre-trauma mental health at step 3 failed to increase the explained variance. However, peri-traumatic responses at step 4 significantly increased R^2 . Specifically, subjective increases in feeling shocked after watching the trauma film was a significant positive predictor of intrusions ($\beta = 0.515, p = .001$). Finally, adding memory performance at step 5 did not significantly increase R^2 . Subjective increases in feeling shocked remained a significant positive predictor of intrusions in the final model ($\beta = 0.493, p = .001$). Each 10 unit increase (equivalent of a 1 cm increase on the 100 mm VAS scale) on the feeling shocked after trauma film viewing results in a 10% increase in the number of intrusions reported after trauma film viewing. Critically, CRF remained a significant negative predictor of intrusions in the final model ($\beta = -0.256, p = .024$; Fig. 5). Accordingly, an increase in fitness in terms of 30 Watts (equivalent of a 1-step increase on the ergometer bicycle) at a constant heart rate of 170 bpm, corresponded to an 11%

decrease in the number of intrusions reported after trauma film viewing.

Assessing mediators of the CRF-intrusion relationship. Following up on the hierarchical regression results, we tested whether decreases in subjective shock would mediate the CRF-intrusion relationship. There was no evidence that CRF would dampen subjective responses in shock (path a, $b = -0.025, p = .691$). As in the previous analysis, larger subjective increases in feeling shocked were associated with more subsequent intrusion development, when controlling for the effect of CRF (path b, $b = 0.009, p < .001$). In corroboration and in line with the absence of evidence for a relationship between CRF and level of shock, there was no significant indirect mediation effect (path a*b, $b = -0.000, BCa CI [-0.002, .001]$).²

3.3. Secondary analyses

3.3.1. Intrusions distress

There was no evidence that CRF was a predictor of intrusion distress in step 1 ($\beta = -0.048, p = .610$), nor in the final model ($\beta = -0.039, p = .706$). However, in the final model, subjective increases in feeling shocked after the trauma film was a significant positive predictor of intrusion distress ($\beta = 0.362, p = .010$), while context-dependent memory in the neutral condition was a negative predictor of intrusion distress ($\beta = -0.219, p = .011$).

3.3.2. IES scores

There was no evidence that CRF was related to IES scores in step 1 ($\beta = -0.061, p = .519$), nor in the final model ($\beta = 0.015, p = .893$). However, in the final model, higher BDI scores ($\beta = 0.262, p = .030$) and subjective increases in feeling shocked ($\beta = 0.395, p = .007$) were significantly related to higher PTSD symptoms measured with the IES. With regard to the IES intrusion subscale, CRF was also not a significant predictor in step 1 ($\beta = -0.047, p = .623$), nor in the final model ($\beta = 0.038, p = .729$). In the final model, only higher subjective increases of feeling shocked remained positively related to IES intrusion scores ($\beta = 0.465, p = .002$).

² When controlling for all predictors from the final model, there was also no significant indirect mediation effect of subjective shock (path a*b, $b = 0.001, BCa CI [-0.001, .003]$).

3.3.3. PCL-5 scores

There was no evidence that CRF was related to PCL-5 scores in step 1 ($\beta = -0.032$, $p = .736$), nor in the final model ($\beta = 0.057$, $p = .599$). Furthermore, there were no significant predictors identified in the final model (all $t < 0.1.91$, all $ps > 0.059$).

4. Discussion

The primary objective of the current study was to investigate the relation between cardiorespiratory fitness (CRF) and the development of intrusions after trauma. Furthermore, we investigated pre-trauma mental health, peri-traumatic responses, and memory performance as potential mediators of this relationship. We found that high CRF indeed predicted fewer intrusions after trauma film viewing, even after correcting for many other relevant variables. In contrast with expectations, we did not identify any significant mediators of the CRF-intrusion relationship. These findings suggest that prior studies that have linked self-reported physical activity with a lower incidence of mood and anxiety disorders (Ten Have et al., 2011), as well as PTSD (Schuch et al., 2019) were likely attributable to actual increased levels of physical fitness, rather than mere behavioural activation (Eherton & Farley, 2020). In the context of the correlational design, the current findings should function as inspiration for future research investigating interventions designed to improve CRF as preventive strategies for intrusion development after trauma.

Our results did not support pre-trauma mental health factors such as depression or trait anxiety as mediators of the relation between intrusive memories and CRF. In fact, none of these pre-trauma factors were predictive of the number of intrusions, adding to the mixed evidence reported in the literature concerning pre-trauma risk and protective factors (Marks et al., 2018). Importantly, previous studies that did find relationships used indices of more specific anxious or depressive symptomatology such as maladaptive coping strategies, negative beliefs and appraisals, trauma film-related rumination, or peri-traumatic cognitive processing (Kubota, Nixon, & Chen, 2015; Laposa & Alden, 2008; Logan & O'Kearney, 2012; Regambal & Alden, 2009). The absence of evidence for trait anxiety and depression to be pre-trauma risk factors in our study might therefore be explained by the notion that these measures could be too crude or too general to be related to the

particular and highly specific symptom of intrusions. With regard to peri-traumatic responses, a notable finding was that the subjective level of shock remained a significant negative predictor of intrusion frequency after partialling out all other factors, initially suggesting this measure as a potential mediator. This result underscores that peri-traumatic *subjective* experiences are among the most robust predictors of intrusions, when compared to the more inconsistent previous results on psychophysiological responses (Clark et al., 2015; Marks et al., 2018; Rattel et al., 2019; Ripley et al., 2017). However, on a critical note, this stronger association might be caused by the fact that the subjective level of shock and the number of intrusions are both self-report measures resulting in higher correlations than for instance between self-report and behavioural measures (Dang, King, & Inzlicht, 2020). Regardless, in the end no mediatory role existed for this peri-traumatic variable. Thus, to what degree peri-traumatic affective responsivity and psychophysiological arousal might mediate protective associations between CRF and intrusions remains to be established in future research. Finally, our data seem to contravene a mediatory role of context-dependent memory or working memory capacity in the relationship between CRF and intrusion development. In future research it might be fruitful to more directly index relational memory function whilst incorporating dentate gyrus size (a sub-region of the hippocampus), since this has been connected to CRF (e.g., Chaddock et al., 2010) and has been shown to underly vulnerability to develop traumatic intrusions upon a traumatic experience (Koch et al., 2021). Taken together, despite the inclusion of a range of variables that are theoretically plausible mediators, our data did not yield convincing evidence for a mediatory role for any of these variables. Importantly, this absence of evidence does not imply evidence of absence (Keyesers, Gazzola, & Wagenmaker, 2020). Thus, our study should be regarded as a first step in investigating pre-trauma mental health, peri-traumatic responses, and/or memory functions in relation to physical fitness and the development of intrusions.

Our secondary analyses, addressing intrusion-related *distress* and PTSD symptomatology (i.e., IES, PCL-5 scores), revealed no associations with CRF. This suggests that CRF may be specifically related to the development of traumatic memories per se, rather than being generally linked to PTSD-related symptomatology. Nevertheless, by reducing the chance of developing intrusions, the chance of the development of other PTSD symptoms may be lowered as well (Sullivan et al., 2016). Another

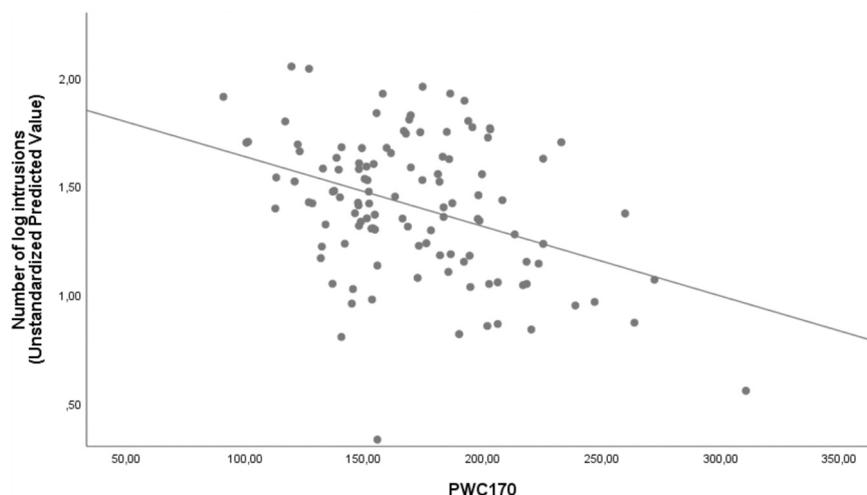


Fig. 5. Relationship of CRF (PWC₁₇₀) and number of intrusions (predicted values from the final model – log transformed). In the scatterplot it can be observed that higher physical fitness as assessed by PWC₁₇₀ predicted a smaller number of developed intrusions upon having seen the trauma analogue.

noteworthy finding from these secondary analyses was that participants who displayed stronger context-dependent memory reported lower intrusion distress. This result partially aligns with previous findings showing that stronger context-dependence predicted lower intrusion-related distress and these observations together suggest that better context-dependent memory function might pose a resilience factor against developing intrusion-related distress after potential traumatic events (Meyer et al., 2017). The overall relation between context-dependent memory and specific alterations in quality or quantity of memory intrusions remains unclear, but it suggests that there might be a significant role for contextualisation performance on intrusion-related distress. Importantly, also these secondary analyses did not identify any specific mediator for the CRF-intrusion relationship, leaving the question by what underlying mechanism CRF is associated with the development of intrusions unanswered.

Strengths of the current study are the large sample size, the combination of subjective, psychophysical and cognitive markers, and the mediation analysis. Nevertheless, some limitations of the current study should be mentioned. First of all, the correlational design precludes conclusions about causal relations. That is, our study should serve as inspiration for follow-up studies that may address causality by means of controlled experimental manipulations (e.g. prolonged trainings that enhance CRF). Such studies could also include additional biological correlates of CRF such as dentate gyrus size (Koch et al., 2021), or brain-derived neurotrophic factor (BDNF; Pitts et al., 2019), that were beyond the scope of the current study, but that each has been associated with PTSD intrusion development, and that are highly sensitive to exercise interventions (Chaddock et al., 2010; Koch et al., 2021; Pitts et al., 2019; Powers et al., 2015). Further, our initial sensitivity analyses revealed that the current sample size was adequately powered to detect small effects for each individual predictor, even given the relatively large amount of predictors. Nevertheless, in case of smaller effect sizes, our analytical approach consisting of a high number of predictors could possibly make the results of the regression analysis unstable. Furthermore, we used traumatic films in a laboratory setting and relied on a mentally and physically healthy sample of participants. This is also reflected in our sample mean CRF ($PWC_{170} = 170.1$, $SD = 38.1$), which is relatively high in comparison to other healthy samples (Bland et al., 2012), and compared to PTSD patients (Voorendonk, Sanches, De Jongh, & Van Minnen, 2019). This implies that our findings may not generalise to traumatised samples and individuals with impaired physical health, warranting complementary and more naturalistic studies, e.g., among patients with PTSD in clinical settings. In addition, our sample was predominantly female, constraining generalisation of the findings. However, no significant differences were found between females and males on intrusion frequency and distress. Previous studies also included mostly females, resulting in comparable mean numbers of reported intrusions ($M = 4.0$) and distress ($M = 3.6$) in our sample (e.g., Meyer et al., 2017; $M = 4.1$ and $M = 3.7$ respectively). However, potential mechanisms explaining why women are more vulnerable to developing PTSD-symptoms upon traumatic experiences (Breslau, 2009; Garcia, Walker & Zoellner, 2018; Rattel et al., 2019), such as menstrual phase (Garcia et al., 2018), can affect the development of intrusions and could be incorporated in future research. At last, we did not measure the number of performed physical activities during the 7 days after trauma film viewing. It has been suggested that physical activities could have a distraction effect as it helps to focus on 'the here and now' and to tune out intrusive memories, similar to a flow-state (Ley, Kramme, Lippert, & Barrio, 2017; Ley, Barrio & Koch, 2018). High CRF individuals might have performed more physical activities during these 7 days after trauma film viewing, which should be assessed in future research.

In conclusion, high CRF may aid in developing fewer intrusions after trauma, but the underlying mechanism is still unknown. A deeper understanding of the mechanisms by which CRF promotes such resilience could provide additional targets to increase resilience prior to trauma. It remains critical to conduct trauma analogue and prospective trauma

exposure studies enabling differentiation of predisposing factors from consequences of PTSD. Our findings further emphasise the importance of physical activity in the general population, since CRF can be improved with physical activity interventions and might prevent the development of distressing intrusions after trauma. This may be of critical importance, especially for personnel at risk, to effectively cope with deployment or combat-related trauma.

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Declaration of Interest

None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.biopsycho.2021.108189.

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