

Improvements in cardiorespiratory fitness are not significantly associated with post-traumatic stress disorder symptom reduction in intensive treatment

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ABSTRACT

Background: Physical activity has been found to have positive effects on symptoms of post-traumatic stress disorder (PTSD). However, the importance and role of cardiorespiratory fitness (CRF) in relation to PTSD treatment outcome is not yet clear.

Objective: The purpose of the present study was to test the hypothesis that CRF would increase following intensive trauma-focused treatment (TFT) of PTSD augmented with physical activity, and that improved CRF would be associated with a significant decline in PTSD symptoms.

Method: One hundred-eight individuals with severe PTSD (72% women; mean age = 40.44, *SD* = 11.55) were enrolled in an intensive TFT programme of 8 days within 2 consecutive weeks that consisted of daily prolonged exposure (PE), eye movement desensitization and reprocessing (EMDR) therapy and 6 hours of physical activity each day. CRF levels were assessed at baseline and post-treatment with a 6-Minute Walk Test (6MWT) and, in a subsample, with a submaximal ergometer test (PWC_{75%}/kg). Severity of PTSD symptoms was measured with the PTSD Symptom Scale-Self Report (PSS-SR).

Results: A significant increase in CRF from pre- to post-treatment and a significant decrease of PTSD-symptoms was found. However, CRF difference scores were not associated with treatment outcome.

Conclusions: Although individuals with PTSD may show an increase in CRF following an intensive TFT programme augmented with physical activity and a decrease of PTSD-symptoms, the current findings do not support the notion that treatment outcome is related to CRF.

Mejoras en la estado físico cardiorrespiratorio no se asocian significativamente con reducción de síntomas del trastorno de estrés postraumático en tratamiento intensivo

Antecedentes: Se ha encontrado que la actividad física tiene efectos positivos sobre los síntomas del trastorno de estrés postraumático (TEPT). Sin embargo, la importancia y el papel de la actividad física cardiorrespiratoria (cardiorespiratory fitness, CFR) en relación con el resultado del tratamiento del TEPT aún no está claro.

Objetivo: El propósito del presente estudio fue probar la hipótesis de que la CFR mejoraría después del tratamiento intensivo de TEPT centrado-en-el-trauma (TFT) potenciado con actividad física, y que la CFR optimizado se asociaría con una disminución significativa de los síntomas del TEPT.

Método: Ciento ocho individuos con TEPT severo (72% mujeres; edad media = 40.44, *DE* = 11.55) se inscribieron en un programa intensivo de TFT de 8 días dentro de 2 semanas consecutivas que consistió en exposición diaria prolongada (PE), Terapia de Desensibilización y Reprocesamiento por Movimientos Oculares (EMDR) y 6 horas de actividad física cada día. Los niveles de CRF se evaluaron al inicio y después del tratamiento con una prueba de caminata de 6 minutos (6MWT) y, en una submuestra, con una prueba de ergómetro submáxima (PWC_{75%}/kg). La gravedad de los síntomas de TEPT se midió con el Informe de Escala de Síntomas del TEPT (PSS-SR). Resultados: Se encontró un aumento significativo en la CFR desde antes y hasta después del tratamiento y una disminución significativa de los síntomas de TEPT. Sin embargo, las puntuaciones de diferencia de CRF no se asociaron con el resultado del tratamiento.

Conclusiones: Aunque las personas con TEPT pueden mostrar un aumento en el CFR después de un programa intensivo de TFT potenciado con actividad física y una disminución de los síntomas de TEPT, los hallazgos actuales no respaldan la noción de que el resultado del tratamiento está relacionado con la CFR.

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PALABRAS CLAVE

trastorno de estrés postraumático; actividad física; estado físico cardiorrespiratorio; tratamiento intensivo centrado-en-el-trauma; prueba de caminata de 6 minutos; prueba de ergómetro submáxima

关键词

创伤后应激障碍; 体育活动; 心肺适能; 强化创伤焦点治疗; 6分钟步行测试; 次极限测力计测试

HIGHLIGHTS

- PTSD patients showed markers of poor physical health at baseline.
- Besides PTSD symptoms, patients' CRF and blood pressure improved after 8 days of treatment.
- No association was found between CRF improvement and treatment outcome.

心肺适能的改善与强化治疗中创伤后应激障碍症状的减少无显著相关

背景：已经发现体育活动对创伤后应激障碍（PTSD）的症状有积极影响。然而，心肺适能（CRF）对创伤后应激障碍治疗结果的重要性和作用尚不清楚。

目的：本研究的目的是检验以下假设：CRF会随增加了体育活动的PTSD强化创伤焦点治疗（TFT）提高，且提高的CRF与PTSD症状的明显下降相关。

方法：108名重度PTSD患者（72%为女性；平均年龄为40.44，标准差为11.55）连续2周参加8天的强化TFT计划，包括每日延长暴露（PE），眼动脱敏与再加工疗法（EMDR）和每天6小时的体育活动。在基线和治疗后使用6分钟步行测试（6MWT），并在子样本中使用次极限测力计测试（PWC75%每千克）评估CRF水平。用自评式PTSD症状量表（PSS-SR）测量PTSD症状的严重程度。

结果：发现治疗前后CRF显著提高，PTSD症状显著降低。然而，CRF的分数差异与治疗结果并无相关。

结论：尽管患有PTSD的个体可能在参与增加了体育活动的强化TFT计划后CRF有所提高且PTSD症状有所下降，本研究结果并不支持治疗结果与CRF有关。

1. Introduction

Prolonged exposure (PE) therapy, and eye movement desensitization and reprocessing (EMDR) therapy are among the most effective therapies for people with post-traumatic stress disorder (PTSD) to date (e.g., Cusack et al., 2016). Nonetheless, these treatments still show high dropout rates and non-response rates which emphasizes the need for optimization of therapies used to treat PTSD (e.g., Lee et al., 2016). More recently, physical activity has been proposed as a promising stand-alone treatment (Fetzner & Asmundson, 2015) and addition to existing psychological treatments for PTSD patients. A meta-analysis by Rosenbaum, Vancampfort et al. (2015), including four controlled studies, showed that stand-alone, augmenting and supplemental physical activity was associated with a significantly stronger PTSD symptom decline after treatment than standard psychological care, or a wait-list control condition.

In accordance with these positive results, new intensive trauma-focused treatments have been developed that incorporate physical activity together with PE and EMDR therapies. These treatments have shown low dropout rates and strong reductions in PTSD symptoms within a short time frame of 5 to 8 treatment days (Van Woudenberg et al., 2018; Zepeda Méndez, Nijdam, Ter Heide, Van Der, & Olf, 2018). However, the relation between physical activity and PTSD treatment outcome is not yet clear.

Over the past years, the benefits of physical activity have been repeatedly demonstrated for people with depression and anxiety disorders (Asmundson et al., 2013; Stubbs et al., 2017). For example, a meta-analysis examining the relationship between depression and cardiorespiratory fitness (CRF), a common indicator of physical fitness, showed that physical activity resulted in an increase in CRF among people with depression (Stubbs, Rosenbaum, Vancampfort, Ward, & Schuch, 2016). Additionally, high CRF has been associated with a lower risk of depressive symptoms (Sui et al., 2009). This could imply that an increase in CRF is related to treatment outcome. Given that low CRF is also a strong

predictor of cardio-metabolic diseases (Kodama et al., 2009) and patients with PTSD display a high prevalence of comorbid cardio-metabolic health problems, such as high BMI and blood pressure (Rosenbaum, Stubbs, et al., 2015), CRF may be of special interest for its potential contribution in the physical and mental recovery of PTSD patients.

Whether CRF plays a role in the augmented effect of physical activity on PTSD treatment outcome is still unclear. This lack of knowledge about CRF is underlined by the fact that only two of the included studies in recent meta-studies took CRF into account (Rosenbaum, Vancampfort et al., 2015; Vancampfort et al., 2017). A randomized controlled trial by Rosenbaum, Sherrington, and Tiedemann (2015) investigated CRF before and after treatment. They used the 6-Minute Walk test (6MWT) in a subsample of 35 PTSD patients and found that PTSD symptoms were more strongly reduced when three resistance-training sessions per week, plus a pedometer based walking programme were added to a 12 week psychological treatment compared to only psychological treatment. Although they did find an increase in CRF in the intervention group compared to a decrease in CRF in the control group, this difference did not reach significance. A small subsample, lack of an objective heart rate based CRF measure such as a submaximal ergometer test, a focus on resistance training rather than on aerobic activities, and a low attendance rate at unsupervised sessions may explain these null findings. Another study that involved CRF found that lower baseline CRF was associated with greater reductions in hyperarousal and avoidance symptoms of PTSD after a two-week aerobic training of six stationary cycling sessions without additional psychological treatment in 32 PTSD patients (LeBouthillier, Fetzner, & Asmundson, 2016). An explanation for the greater reduction in PTSD symptoms could be that low baseline CRF levels yield room for larger increases in CRF. Thus, the magnitude of change in CRF could be related to the decrease in PTSD symptoms. Unfortunately, LeBouthillier et al. (2016) only took baseline CRF into account without measuring a possible change in CRF after training.

The purpose of the current study is to determine whether CRF increases in PTSD patients after intensive trauma-focused treatment augmented with physical activity, and whether this increase is associated with a better treatment outcome. In line with Rosenbaum, Sherrington et al. (2015), CRF will be measured with the 6-Minute Walk test. In addition, to increase validity of measuring CRF, an objective heart-rate based CRF was used in a subsample of patients. It is hypothesized that CRF will increase after intensive treatment including physical activity and that this increase in CRF will be associated with a significant decline in PTSD symptoms. Because CRF is also related to cardio-metabolic physical health issues relevant for PTSD-patients, we exploratively investigated the influence of our augmented trauma-focused treatment programme on the physical health factors BMI and blood pressure.

2. Methods

2.1. Participants

A total of 151 patients (73% women) with a mean age of 40.01 ($SD = 11.33$) participated in this study. Ten patients dropped out of treatment (see Figure 1). Reasons for dropout were: being unable to continue ($n = 4$; one patient due to a physical injury), unwilling to continue (e.g., homesickness, $n = 5$) and being sent home because of inappropriate aggressive behaviour ($n = 1$). Furthermore, 33 patients had missing data on the PSS-SR or could not complete the 6MWT measures due to practical reasons (see Figure 1). Thus, the final study group consisted of 108 patients (72% women; mean age = 40.44, $SD = 11.55$). All participants were treated between January 2nd and June 17th (2017) at the Psychotrauma Expertise Centre (PSYTREC; the Netherlands) and were referred by their general practitioner, psychologist, or psychiatrist. Inclusion criteria

were (1) a diagnosis of PTSD based on the Clinician-Administered PTSD Scale (CAPS-IV or CAPS-5) (2) being at least 18 years old (3) sufficient knowledge of the Dutch language to undergo treatment. Participants were excluded when they (1) had a history of suicide attempts in the three months prior to treatment and (2) were medically unfit to participate in the fitness measures (e.g., recent cardiovascular pathology such as acute cardiac event, unstable angina, embolus or infarction; acute infections; physical impairments that necessitate use of a wheelchair or crutches).

2.2. Measures

The Dutch version of the PTSD Symptom Scale-Self Report questionnaire (PSS-SR; Mol, Arntz, Metzmakers, Dinant, & Knottnerus, 2005) was used to measure self-reported PTSD symptom severity in the past week. The PSS-SR consists of 17 items rated on a 4-point Likert scale ranging from 0 (*not at all*) to 3 (*very much*) with a total scoring range of 0–51. The PSS-SR has a strong internal consistency ($\alpha = .91$; Foa, Riggs, Dancu, & Rothbaum, 1993) and internal consistencies of the PSS-SR are also high for the present sample at baseline and post-treatment (Cronbach's alpha's of .81 and .95, respectively).

The 6-Minute Walk Test (6MWT; Enright, 2003) was used to assess CRF in a group-format (maximum of 10 people per group). The test was measured indoors, with a walking course of 10 metre, or outside with a walking course of 20 metre. Baseline and follow-up measures were always administered in the same setting (indoor/outdoor). Outcome was the distance walked in six minutes, expressed in metres. Laps, and metres of the last lap, were counted by physical activity instructors and research assistants. Participants received the instruction to walk as far, back and forth, as possible in six minutes. They

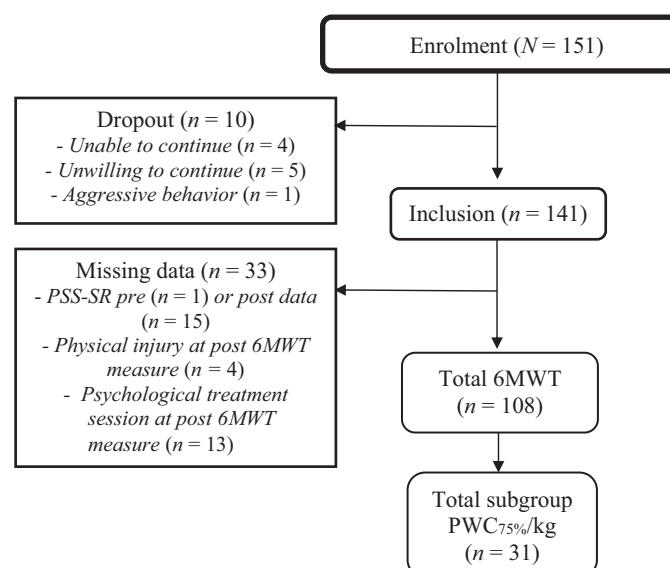


Figure 1. Participant flow chart. 6MWT = 6-Minute Walk Test; PWC_{75%}/kg = submaximal ergometer test.

were reminded to not run or jog. Standardized phrases for encouragement were given every minute during the whole test.

A submaximal, multistage cycle ergometer test, administered on a Christopeit BT-2 Ergometer was used to individually measure CRF in a subsample of 31 participants ($PWC_{75\%/kg}$; Batcho, Thonnard, & Nielsens, 2012). Physical working capacity at 75% of the predicted maximal HR per kilogram of body weight ($PWC_{75\%/kg}$), based on the protocol by Batcho et al. (2012), was used as CRF index. During the whole test, participants had to maintain a pedalling rate of 60 revolutions per minute (RPM). After a warm-up period of 2 minutes without resistance (0 watts/KP) the test started with 40 watts. Every 2 minutes the resistance was increased by 20 watts. The HR of participants was continuously monitored with a Polar A300 wrist and chest band. Every 30 seconds, participants' HR in beats per minute (BPM) was recorded. The test stopped when the HR of the participant reached, or exceeded the 75% of the maximum HR. For the calculation of the $PWC_{75\%/kg}$ scores see section '2.5. Analyses'. Higher $PWC_{75\%/kg}$ scores are associated with higher fitness levels. The $PWC_{75\%/kg}$ fitness index has a very high intraclass correlation ($ICC = .96$) with a previously validated fitness index that uses resting state HR ($WCI_{65\%HR_{reserve}/kg}$; Batcho et al., 2012), illustrating that a resting state HR is not necessary for assessing the fitness index. To check the perceived exertion of participants during the test, participants were asked to verbally report their perceived exertion on the OMNI-cycle scale to the researcher after every 2 minutes in a specific workload (Nakamura et al., 2010).

The International Physical Activity Questionnaire Short Form (IPAQ-SF; Craig et al., 2003) is a self-report measure that was used to assess the subjective health-related physical activity of the participants during the past 7 days at baseline. The IPAQ-SF consists of 7-items spread over 4 domains; (1) vigorous activity (makes breathing more difficult than normal), (2) moderate activity (makes breathing somewhat more difficult than normal), (3) walking and (4) time spent sitting. Data was scored with the IPAQ-SF scoring manual. The IPAQ has an acceptable concurrent validity ($r = 0.46$) for estimating the physical activity of patients with PTSD (Rosenbaum, Tiedemann, Sherrington, & van der Ploeg, 2014).

The Dutch versions of the Clinician-Administered PTSD Scale for DSM-IV and DSM-5 (CAPS-IV, Hovens, Luinge, & Van Minnen, 2005; CAPS-5; Boeschoten et al., 2018) were used to establish PTSD diagnosis. Both versions were administered because PSYTREC transferred from the CAPS-IV to the CAPS-5 during the data collection period of the current study. The CAPS-IV and CAPS-5 have strong internal consistency and excellent reliability (Weathers et al., 2017; Weathers, Keane, & Davidson, 2001).

A modified self-report version of the Interview for Traumatic Events in Childhood (ITEC; Lobbestael, Arntz, Harkema-Schouten, & Bernstein, 2009) was used to assess trauma characteristics. The non-modified ITEC has good reliability on all subscales (Mean $\alpha = .79$; ICC between .72 and 1.0; Lobbestael et al., 2009).

The Mini International Neuropsychiatric Interview Dutch version (MINI; Overbeek, Schruers, & Griez, 1999) was used to screen comorbid suicidal ideation, anxiety and mood disorders, based on criteria of the DSM-IV. The MINI has a good test-retest ($Kappa = 0.76-0.93$) and inter-rater reliability ($Kappa = 0.88-1.0$; Lecrubier et al., 1997).

Of the subsample that executed the $PWC_{75\%/kg}$ test, participants' weight and length was measured with a weighing machine and measuring rod. Body Mass Index (BMI) was calculated with the formula; $Weight(kg)/(Length(m)^2)$. A Contec CMS-08A was used to assess systolic and diastolic blood pressure.

2.3. Procedure

Ethical exemption was assigned by the Medical Ethical Review Committee of VU University Medical Centre (registered with the US Office for Human Research Protections (OHRP) as IRB00002991, FWA number FWA00017598). During intake sessions, a trained clinical psychologist assessed whether patients met the inclusion criteria for treatment using the CAPS and the MINI. In addition, the ITEC was administered to assess trauma characteristics. After assuring eligibility for the intensive trauma-focused treatment for PTSD, and when patients met the inclusion criteria of the study, they were informed about the study and asked to sign an informed consent form for use of their data for scientific research. After the intake session, questionnaires were given on paper to the patients to assess baseline PTSD severity (PSS-SR) and self-report physical activity (IPAQ-SF). On the first treatment day of the intensive trauma-focused treatment programme, baseline objective indices of CRF (6MWT and $PWC_{75\%/kg}$) were indexed by trained researchers and physical activity instructors. Of all participants who engaged in the 6MWT, two participants with relatively low and two with relatively high scores on the 6MWT were approached for contribution in the ergometer test to ensure enough variation in CRF ($PWC_{75\%/kg}$). The $PWC_{75\%/kg}$ test followed a standardized protocol for measuring weight, length, blood pressure and heart rate before and during the ergometer test. Directly after these baseline measures, all participants received the same intensive trauma-focused treatment in a short 8-day time frame (2 x 4 days within 2 consecutive weeks). After the first 4 treatment days, patients went home for 3 days. For detailed treatment procedures see section '2.4. Treatment'. On the last day of treatment, post-treatment measures of the 6MWT and $PWC_{75\%/kg}$

test were carried out. Furthermore, post-treatment assessment of PTSD severity was administered 9 days after the last treatment day (PSS-SR).

2.4. Treatment

Treatment consisted of 3 hours of individual trauma-focused treatment, 6 hours of group physical activity and 2 hours of psycho-education in groups per day (Van Woudenberg et al., 2018). The individual trauma-focused treatment consisted of 90 minutes PE and 90 minutes EMDR therapy. Sessions were provided by clinical therapists, who were trained in PE therapy and EMDR therapy.

2.4.1. Prolonged exposure (PE)

The PE sessions followed a modified version of the PE protocol by Foa, Hembree, and Rothbaum (2007). In accordance with Foa's protocol, during the PE session, patients were exposed to the memories of the traumatic events through imagining the memories as vividly as possible and describing these in detail, aloud, and in the present tense, for at least 60 minutes. Instead of in vivo homework material, in vivo materials that reminded the patient of the trauma (e.g., pictures, sounds) were incorporated in the PE session (for information, see Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014).

2.4.2. EMDR therapy

The EMDR sessions were delivered according to a manualized standard EMDR protocol (De Jongh & Ten Broeke, 2013; Shapiro, 2001). During the EMDR session, participants were instructed to recall a memory of the traumatic event and keep it in mind while the therapist moved his or her hand from left to right in front of the participants' eyes, or used a moving light bar. These methods result in rapid sets of eye movements. If needed, the procedure could be combined with clicking sounds from left to right (earphones), and/or buzzers taken in the hands that provided alternating-bilateral tactile stimulation in order to maximize taxation of the working memory (De Jongh, Ernst, Marques, & Hornsvelt, 2013). When anticipatory fear and avoidance behaviour were present, the 'flashforward protocol' was applied (Logie & De Jongh, 2014).

2.4.3. Physical activity

Every treatment day, in between the trauma-focused treatment sessions, participants were offered 4 timeslots of physical activity in a group format. The physical activity programme varied in intensity levels during the day and consisted of mainly aerobic activities. The activities were performed indoors and outdoors. Every treatment day started and ended with a low to moderate intensity walk. The aerobic activities in the other timeslots differed per day; e.g., badminton, mountain biking, Ultimate Frisbee and soccer. Three times a week, one

timeslot was focused on indoor resistance training. Each participant was offered the opportunity to participate at their own preferred level of intensity, but encouraged to participate as intensively as possible. Physical activity sessions were provided by trained instructors with a degree in human movement sciences.

2.4.4. Psycho-education

Every evening, patients participated in the psycho-education programme in a group format and received information about PTSD related topics, such as re-experiences and avoidance behaviour (e.g., National Institute for Health and Clinical Excellence (NICE), 2018).

2.5. Analyses

All statistical analyses were performed with IBM SPSS Statistics version 25 and a significance level of $\alpha = .05$ (two-sided) was adopted. Five outliers were detected in the 6MWT difference scores and one outlier in the $PWC_{75\%/kg}$ difference scores. Including or excluding these outliers did not have an effect on outcome. To check for significant differences on baseline characteristics between the group that was excluded from analysis and the completers sample, independent samples t-tests and chi-square tests were conducted on gender, mean age, comorbidity rate and CAPS, PSS-SR, 6MWT, $PWC_{75\%/kg}$ scores. To check for significant differences on baseline characteristics between the subsample that underwent the $PWC_{75\%/kg}$ test and the rest of the sample, current independent samples t-tests and chi-square tests were conducted on gender, mean age, comorbidity rate and baseline CAPS, PSS-SR and 6MWT scores. All statistical assumptions for the following analyses were met. To determine the $PWC_{75\%/kg}$ fitness scores per participant, a linear regression, between the data collected workload and corresponding HR, was calculated with the method of least squares (Batcho et al., 2012). Only the last recorded HR after every 2 minutes was used in the analysis as the HR that corresponds to the workload. This resulted in individual intercept (b) and slope (a) values per participant. The 75% HR maximal was calculated with the formula; $HR_{75\%_i} = .75 * (220 - age_i)$. To obtain the final $PWC_{75\%/kg}$ score, those participant specific values were inserted in the formula and divided by the body weight of the participant; $PWC_i^{HR_{75\%}}/kg = (a_i * HR_{75\%_i} + b_i)/kg_i$. Treatment outcome was investigated with a paired samples t-test on mean PSS-SR scores before and after treatment. To investigate whether 6MWT scores changed after treatment, a paired samples t-test was conducted on mean 6MWT scores before and after treatment. Additionally, the percentage of clinically meaningful increases on the 6MWT was calculated, by multiplying the standard error of measurement (SEM) by 1.96 (95% CI) and the square root of 2 (Vancampfort et al., 2011). To investigate whether $PWC_{75\%/kg}$ scores

changed after treatment, a paired samples t-test was conducted on mean $PWC_{75\%/kg}$ scores before and after treatment. A multiple linear regression was conducted to test whether mean 6MWT change scores (post minus pre 6MWT scores) predicted PSS-SR scores post-treatment, controlled for baseline PSS-SR scores. In Step 1 of the model PSS-SR baseline scores were entered, in Step 2 6MWT change scores were entered. Another multiple linear regression was conducted to test whether mean $PWC_{75\%/kg}$ change scores (post minus pre $PWC_{75\%/kg}$ scores) predicted PSS-SR scores post-treatment, controlled for baseline PSS-SR scores. In Step 1 of the model, PSS-SR baseline scores were entered, in Step 2 $PWC_{75\%/kg}$ change scores were entered. In the subsample that underwent the $PWC_{75\%/kg}$ test ($n = 31$), changes in mean Body Mass Index (BMI), systolic and diastolic blood pressure scores before and after treatment were exploratively tested with three paired samples t-tests. To control for multiple testing, Bonferroni corrections were used ($\alpha = .017$). All effect sizes were calculated using Cohens 'd.

3. Results

The final study group consisted of 108 patients (72% women; mean age = 40.44, $SD = 11.55$). Of them, 31 (29%) patients participated in the submaximal ergometer test ($PWC_{75\%/kg}$). Table 1 shows the baseline sample characteristics of the study sample. All patients suffered from severe PTSD due to cumulative trauma of prolonged interpersonal nature, including sexual and physical abuse and high comorbidity rates. Of the total sample, 91.4% had at least one comorbid mental

disorder and the majority of the patients showed an elevated suicide risk (76.9%). No differences between the excluded ($n = 43$) and completers sample ($N = 108$) on any of the baseline characteristics (all $ps > .178$) could be detected. Also, there were no significant differences between the subsample that underwent the $PWC_{75\%/kg}$ test and the rest of the sample on any of the baseline characteristics (all $ps > .148$).

3.1. PTSD treatment outcome ($N = 108$)

Results of the paired samples t-test showed a significant decrease in mean PSS-SR scores ($t(107) = 12.52$, $p < .001$) from pre- to post-treatment, with a large effect size (Cohen's $d = 1.20$; see Table 2).

3.2. CRF change – 6MWT ($N = 108$)

Results of the paired samples t-test showed a significant increase in mean 6MWT scores ($t(107) = -4.77$, $p < .001$) from pre- to post-treatment, with a medium effect size (Cohen's $d = 0.46$; see Table 2). Of the total group of patients, 10.2% showed a clinically meaningful increase on the 6MWT test at post-treatment (81.8 metres for women and 77.2 for men).

3.3. CRF change – $PWC_{75\%/kg}$ ($n = 31$)

Results of the paired samples t-test showed a significant increase in mean $PWC_{75\%/kg}$ scores ($t(30) = -3.44$, $p = .002$) from pre- to post-treatment, with a medium effect size (Cohen's $d = 0.62$; See Table 3).

Table 1. Baseline sample characteristics ($N = 108$).

	Mean (SD)
Age	40.01 (11.34)
PTSD severity scores	
CAPS-IV ($n = 40$)	95.52 (11.83)
CAPS-5 ($n = 68$)	46.49 (9.73)
PSS-SR	33.88 (7.32)
	Percentage
Gender (% women)	72.8%
Traumatic experiences	
Sexual abuse	80.6%
Physical abuse	89.8%
Work-related	22.2%
Natural disasters, accidents and victims of war	26.9%
Comorbidity ($n = 105$)	
Anxiety disorder	62.9%
Mood disorders	86.7%
Suicide risk	
No risk	23.1%
Low	33.3%
Moderate	13.0%
High	30.6%
Highest education	
No education	0.7%
Primary school	6.0%
Secondary school	13.9%
Vocational education	53.0%
High vocational education	18.5%
University	7.9%

CAPS = Clinician Administered PTSD Scale; PSS-SR = PTSD Symptom Scale Self Report.

Table 2. The 6-Minute Walk Test (6MWT) and PTSD symptom scale self report (PSS-SR) mean scores and Standard Deviations (SD) at pre- and post-treatment ($N = 108$).

	Pre		Post		Effect size Pre-Post
	Mean	SD	Mean	SD	Cohen's d
6MWT (m)	492.86	62.64	517.97	76.93	0.46
PSS-SR	33.88	7.32	18.95	12.75	1.20

Table 3. Ergometer test ($PWC_{75\%/kg}$) and PTSD symptom scale self report (PSS-SR) mean scores and Standard Deviations (SD) at pre- and post-treatment ($n = 31$).

	Pre		Post		Effect size Pre-Post
	Mean	SD	Mean	SD	Cohen's d
$PWC_{75\%/kg}$	1.36	0.66	1.58	0.56	0.62
PSS-SR	34.50	6.64	18.23	13.25	1.42

The $PWC_{75\%/kg}$ was measured in the working capacity at 75% of the predicted maximal HR per kilogram of body weight.

3.4. CRF and PTSD treatment outcome – 6MWT (N = 108)

A multiple linear regression was performed to determine whether mean 6MWT change scores predicted PSS-SR scores post-treatment, controlled for baseline PSS-SR scores. A significant regression equation was found ($F(2, 105) = 6.73, p = .002$), with an adjusted R^2 of .097. However, the 6MWT change scores did not significantly predict PSS-SR scores post-treatment ($\beta = -0.009$, 95% CI $[-0.051, 0.034]$, $p = .687$), whereas PSS-SR baseline scores significantly predicted PSS-SR scores after treatment ($\beta = 0.581$, 95% CI $[0.264, 0.899]$, $p < .001$).

3.5. CRF and PTSD treatment outcome – $PWC_{75\%/kg}$ ($n = 31$)

A multiple linear regression was conducted to determine whether mean $PWC_{75\%/kg}$ change scores predicted PSS-SR scores post-treatment, controlled for baseline PSS-SR scores. A significant regression equation was found ($F(2, 28) = 6.39, p = .005$), with an adjusted R^2 of .264. However, the $PWC_{75\%/kg}$ change scores did not significantly predict PSS-SR scores post-treatment ($\beta = -9.553$, 95% CI $[-21.468, 2.361]$, $p = .112$), whereas PSS-SR baseline scores significantly predicted PSS-SR scores after treatment ($\beta = 1.041$, 90% CI $[0.399, 1.684]$, $p = .003$).

3.6. Baseline- and change in physical health

At baseline, patients reported a mean walking time of 431.4 ($SD = 416.4$, $Mdn = 255.0$) minutes per week; moderate physical activity of 287.9 ($SD = 357.5$, $Mdn = 140.0$) minutes per week; and vigorous physical activity of 148.3 ($SD = 266.9$, $Mdn = 0.0$) minutes per week on the IPAQ-SF ($n = 92$). Furthermore, 58.6% of the patients from the ergometer subsample were overweight or obese ($BMI \geq 25$), and showed

relatively high systolic and diastolic blood pressure scores at baseline (see Table 4). Results of the paired samples t-tests showed no significant difference in mean BMI scores ($t(28) = -1.20, p = .239$) from pre- to post-treatment (see Table 4). However, a significant decrease in mean systolic ($t(27) = 3.31, p = .003$) and diastolic ($t(27) = 3.66, p = .001$) blood pressure scores were found, both with moderate effect sizes (Cohen's $d > 0.63$; See Table 4).

4. Discussion

To our knowledge, this is the first study to investigate whether cardiorespiratory fitness (CRF) can change after an intensive trauma-focused treatment that is augmented with physical activity in a relatively large sample of severe PTSD patients, and to explore the relation between CRF and treatment outcome. The results of the present study showed an increase in CRF from pre- to post-treatment, both on the 6-Minute Walk test and on the submaximal ergometer test. Also, there was a significant decrease in PTSD symptoms. However, the increase in CRF was not associated with PTSD treatment outcome.

Remarkably, albeit our subsample showed markers of poor physical health at baseline (i.e., 58.6% was overweight or obese, $BMI \geq 25$, and many patients displayed high systolic and diastolic blood pressure baseline scores), already after two weeks of intensive physical activity, CRF and blood pressure scores of these PTSD patients could be improved. These findings are in line with the results of a meta-analysis of individuals suffering from severe mental illness showing that 10 days to 6 months of physical activity resulted in significant improvements in CRF (Vancampfort et al., 2016). Noteworthy, they found that frequency of activities (at least three times per week), and not activity duration, was a strong predictor of CRF increase. This supports the notion that it is possible to increase CRF with high frequent activities, even within a short time frame of 8 days.

Although individuals with PTSD showed an increase in CRF following our treatment programme, which is in line with results from a meta-analysis in people with depression (Stubbs et al., 2016), the current findings do

Table 4. Body Mass Index (BMI), systolic and diastolic blood pressure mean scores and Standard Deviations (SD) at pre- and post-treatment.

	Pre		Post		Effect size Pre-Post
	Mean	SD	Mean	SD	Cohen's d
BMI (kg/m^2) ($n = 29$)	26.97	6.58	27.05	6.57	<i>n.a.</i>
Systolic (mm Hg) ($n = 28$)	143.36	19.73	134.93	16.39	0.63
Diastolic (mm Hg) ($n = 28$)	87.43	12.82	81.36	11.63	0.69

n.a. = not applicable.

not support the notion that CRF is related to treatment outcome. Independently of the change in CRF, the intensive treatment resulted in a strong decrease of PTSD symptoms. Yet, it may suggest that other mechanisms could be responsible for the positive effect of physical activity on PTSD symptoms found in previous studies. For example, physical activity has been found to have a positive effect on the human stress response system (HPA-axis) through stimulation of brain structures like the hippocampus and prefrontal cortex that control the HPA-axis and its cortisol secretion (e.g., Zschucke, Renneberg, Dimeo, Wüstenberg, & Ströhle, 2015). Another underlying pathway might be through the improvement of memory and learning, modified by an increase in brain-derived neurotrophic factor (BDNF), which in turn may enhance learning effects of trauma-focused treatment (Powers et al., 2015).

The lack of a significant relation between CRF and PTSD treatment outcome could raise the question as to whether adding physical activity to intensive trauma-focused treatment programmes is necessary. Therefore, randomized controlled trials are needed to investigate the unique contribution of physical activity on PTSD symptoms and possible underlying mechanisms, such as CRF, cortisol and BDNF. Comparison with a control group will also rule out the possibility that other non-specific effects, such as motivation or state differences, could have influenced the results.

Our study has some limitations. Firstly, it could be argued that both measures of CRF are at best measures-of-proxy for CRF and that it is necessary to use a VO_{2max} test to optimally assess CRF. However, the 6-Minute Walk test has been found to be positively correlated to VO_{2peak} in psychiatric samples (Gomes et al., 2016) and it has also been shown that the currently used 2 min protocol of the submaximal ergometer test was strongly related to VO_{2peak} (Bland, Pfeiffer, & Eisenmann, 2012). Secondly, the study used a self-reported PTSD questionnaire (PSS-SR) as outcome measure, instead of the 'golden standard' Clinician-Administered PTSD Scale for the diagnosis of PTSD after treatment (CAPS). Although we did use this golden standard to establish the PTSD diagnosis, because of the transfer from the CAPS-IV to the CAPS-5 during the data collection period, we could not use these scores as an outcome measure. Nevertheless, current research emphasizes the legitimate use of self-reported questionnaires by showing that there are no differences between clinician-administered and self-reported PTSD assessments (Lenz & Luo, 2019). Thirdly, although compliance of physical activity sessions was actively checked by the trained instructors, the exact engagement in and intensity of physical activity during the treatment programme was not monitored. Therefore the precise level of physical activity could not be assessed. Additionally, CRF was not explicitly tested as an underlying mechanism for treatment outcome with

a mediation analysis and data on physical activity intensity, which should be investigated in future research. Besides monitoring compliance, future studies could monitor the intensity of the activities with heart rate monitors and investigate optimal intensities as the optimal intensity to achieve mental and physical outcomes in PTSD patients is still unknown (Silverman & Deuster, 2014). Another limitation was the missing data. Nevertheless, there were no differences between the excluded and completers sample on any of the baseline characteristics. Furthermore, although the analyses had sufficient power, the sample size in the submaximal ergometer group was quite small. Finally, it is unknown whether the positive influence on CRF is sustained after treatment. Therefore, in future research it is important to investigate the long-term effects of these changes and whether these translate to long lasting life style changes.

In conclusion, the results of the present study suggest that it is possible to positively influence the mental and physical health of PTSD patients in a short time frame. No support was found for the notion that improvements of CRF significantly contributes to treatment outcome in PTSD patients. Our findings provide input to improve treatment and recovery of individuals with PTSD and may be of importance given the commonly poor physical health in PTSD patients.

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Disclosure statement

A.v.M. receives income for published book chapters on PTSD and for the training of postdoctoral professionals in prolonged exposure. A.d.J. receives income from published books on EMDR therapy and for the training of postdoctoral professionals in this method. E.V. and S.S. have no competing interests.

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