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Effectiveness of game-based meditation therapy on neurobiological stress systems in adolescents with posttraumatic symptoms: a randomized controlled trial

Angela A. T. Schuurmans[a,b], Karin S. Nijhof[a,b], Ron Scholte[b,c,d], Arne Popma[e] and Roy Otten[a,b,f]

[a]Department of Research and Development, Pluryn, Nijmegen, the Netherlands; [b]Behavioural Science Institute, Radboud University Nijmegen, Nijmegen, the Netherlands; [c]Praktikon, Nijmegen, the Netherlands; [d]Tranzo, Tilburg University, Tilburg, the Netherlands; [e]Department of Child and Adolescent Psychiatry, VUmc/De Bascule, Amsterdam, the Netherlands; [f]ASU REACH Institute, Department of Psychology, Arizona State University, Tempe, AZ, USA

ABSTRACT

Many adolescents in residential care have experienced traumatic events and suffer from posttraumatic stress. Prolonged activation of neurobiological stress systems as the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal (HPA) axis can result in long-lasting maladaptive alternations. This study investigated the effectiveness of *Muse*, a game-based meditation intervention, on the sympathetic nervous system (SNS), parasympathetic nervous system (PNS), and cortisol basal activity and reactivity to acute stress among adolescents with posttraumatic symptoms in residential care. The intervention consisted of two gameplay sessions a week, for 6 consecutive weeks. Seventy-seven adolescents with clinical levels of posttraumatic symptoms (10–18 years old) received either *Muse* as an addition to treatment as usual ($n = 40$) or treatment as usual alone ($n = 37$). We expected reduced basal activity for the SNS and cortisol and increased basal activity for the PNS. As for the response to acute stress, we expected decreased PNS and increased HPA axis reactivity. The Muse group exhibited lower basal activity for the SNS and increased HPA reactivity to acute stress. There were no differences between conditions on SNS and HPA axis activity during rest and on SNS and PNS reactivity to acute stress. Game-based meditation therapy is a promising intervention for the treatment of adolescents with posttraumatic symptoms in residential care. Implications for clinical relevance and trauma-focused treatment purposes are discussed.

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Introduction

Most adolescents in residential care have been exposed to multiple traumatic events such as domestic violence, neglect, or sexual, physical, or emotional abuse. Worldwide, rates range between 85% and 90% (Briggs et al., 2012; Collin-Vézina et al., 2011). Exposure to trauma increases the risk of psychological problems as anxiety, depression, aggression, and behavioral problems as sexual risk behavior and delinquency (Collin-Vézina et al., 2011; Smith et al., 2006). Traumatic experiences can also negatively affect youths' physical health (Afari et al., 2014) and their neurobiological stress systems (Bauer et al., 2002; Gunnar et al., 2006). These adverse effects of traumatic experiences are likely to continue over time without adequate treatment (Hiller et al., 2016). Therefore, the development of effective trauma interventions is critical.

Research on neural correlates of posttraumatic stress has shown dysregulation of neurobiological responses to stress (Bauer et al., 2002; Gunnar et al., 2006). In individuals without trauma history, stressors activate the autonomic nervous system (ANS) and hypothalamic-pituitary-adrenal (HPA) axis systems. The ANS prepares the body for immediate action through activation of the sympathetic nervous system (SNS), prompting a rapid increase of the cardiac output. When the stressor disappears, the parasympathetic nervous system (PNS) inhibits sympathetic activation and facilitates bodily recovery (Berntson et al., 2008). Whereas physiological changes due to SNS activation only take seconds, HPA activation follows a slower onset and longer duration. HPA axis activation results in the production of steroid hormones and is typically assessed by measuring its final product cortisol (Bauer et al., 2002).

Traumatic experiences such as domestic violence, neglect, and emotional, physical, or sexual abuse result in repeated and prolonged activation of these stress systems, which can lead to autonomic and neuroendocrine dysregulation that last for long after the original stressor has disappeared (Bauer et al., 2002; Gunnar et al., 2006). Youths who suffer from posttraumatic stress can be highly physiologically reactive, even to mildly stressful stimuli. This over-reactivity is referred

CONTACT Angela A. T. Schuurmans angela.anna.schuurmans@gmail.com Department of Research and Development, Pluryn, P.O. Box 53, Nijmegen 6500, the Netherlands

to as SNS-dominated hyperarousal and often leads to misinterpretation of other people's intentions and thus to persistent affective and interpersonal problems (Cook et al., 2005). The opposite of hyperarousal is PNS-dominated hypoarousal, which refers to under-reactivity and emotional numbing (Corrigan et al., 2011). Both hyper- and hypoarousal originate from dysregulation of sensory integration and self-regulatory capacities. A recent study among adolescents in residential care showed that adolescents with posttraumatic symptoms, compared to controls without posttraumatic symptoms, exhibited higher SNS, PNS, and HPA axis activity during rest. Additionally, for stress reactivity, adolescents with posttraumatic symptoms exhibited increased PNS reactivity and blunted HPA axis reactivity to acute stress (Schuurmans et al., 2021a), which are characteristic for hypoarousal (Busso et al., 2017; Corrigan et al., 2011; Ouellet-Morin et al., 2019). Thus, traumatic experiences do not only increase the risk for a range of maladaptive psychological and behavioral outcomes but can also lead to long-lasting alterations of neurobiological stress systems. Fortunately, at an early age, neurobiological systems contain a high level of plasticity (Bauer et al., 2002) and can be effectively altered by interventions (Slopen et al., 2014).

A novel approach that is assumed to address both physiological under- and over-regulation are meditation-based interventions, that are targeted at the baseline capacity to regulate one's emotions and physiological responses (Schuurmans et al., 2020a; 2021b; Spinazzola et al., 2011). A growing number of studies support the shift from mainly cognitive-oriented and verbally dependent therapies to interventions that target physiological sensations and stress regulation abilities (Gapen et al., 2016; Van Der Kolk et al., 2016; Warner et al., 2013). Specifically, interventions with a sensory-based approach that focus on bodily sensations and relaxation, such as meditation, have the potential for physiological impact. Indeed, among adolescents with posttraumatic symptoms in residential care, meditation-based therapy has been found to reduce posttraumatic stress (Schuurmans et al., 2021b), increase attachment and self-regulation (Spinazzola et al., 2011), and result in real-time improvements in SNS and PNS activity (Schuurmans et al., 2020a). These studies show the potential for meditation-based interventions to improve neurobiological alterations after trauma. It is important to conduct research with adolescents, as dysregulation of the neurobiological stress system at a young age has been identified as one of the mechanisms through which traumatic events increase the risk of psychological, behavioral, and physiological problems at a later age (Bauer et al., 2002; Gunnar et al., 2006; Miller et al., 2011).

Therefore, the current study conducted a randomized controlled trial (RCT) to evaluate whether a game-based meditation intervention (*Muse*) can improve neurobiological alterations among adolescents with posttraumatic symptoms. Game-based interventions are a novel strategy to engage adolescents in treatment by making use of their intrinsic motivation (Granic et al., 2014). Playing *Muse* as an intervention has been shown to reduce self-reported symptoms of posttraumatic symptoms, stress, anxiety, depression, and aggression (Schuurmans et al., 2020a; 2021b). We expected that playing *Muse* as an addition to treatment as usual (TAU) would result in adaptive changes in neurobiological parameters toward the profile of controls without trauma history (Schuurmans et al., 2021a). Specifically, for ANS parameters we hypothesized reduced SNS and increased PNS activity during rest and decreased PNS reactivity to acute stress, while for HPA axis parameters, we expected deceased basal activity and increased HPA axis reactivity for Muse participants.

Methods

The current study used the neurobiological data that were collected as part of the research project that included an RCT testing a game-based meditation intervention to decrease posttraumatic stress in adolescents with posttraumatic symptoms (Schuurmans et al., 2020b, 2021b). This research project was registered in the Netherlands Trial Register under ID NL6689; NTR6859 and ethical review and approval were provided by the medical-ethical committee Arnhem-Nijmegen under protocol NL58674.091.16.

Design, setting, and procedure

The current study was designed as an RCT evaluating the effectiveness of *Muse* as an addition to TAU on basal ANS and HPA axis parameters and ANS and HPA axis reactivity to social stress among a sample of adolescents with posttraumatic symptoms in residential care. Participants were recruited from three residential institutions in The Netherlands that provide open and secured residential care for adolescents with and without an intellectual disability (ID). When admitted to these institutions, adolescents filled in the Children's Revised Impact of Event Scale (CRIES-13) (Verlinden et al., 2014). For the current study, these data were used to screen for adolescents with a CRIES-13 score of $\geq$30 as eligible participants, since this score indicates clinical levels of posttraumatic symptoms. Due to the underdiagnosis of posttraumatic stress disorder in adolescents (Miele & O'Brien, 2010), we included participants based on clinically relevant posttraumatic symptoms rather than based on a PTSD diagnosis.

Inclusion criteria were: (1) CRIES-13 score $\geq$30; (2) age 10 to 18 years; (3) being able to comprehend and speak Dutch; (4) active informed participant assent; and (5) active parental or legal guardian consent for adolescents under the age of 16 years. Exclusion criteria were: (1) negative clinician advice, for example, when the participant already received other forms of treatment and the clinician feared that treatment burden would become too heavy (at this stage, participants were not randomized yet, so this exclusion criterium equally affected both conditions); (2) simultaneous participation in another clinical intervention study; (3) acute psychotic symptoms; and (4) a current or recent (within the last 3 months) trauma treatment, such as eye movement desensitization and reprocessing (EMDR) and trauma-focused cognitive-behavioral therapy (TF-CBT). There were no restrictions for concomitant interventions not targeting posttraumatic symptoms

(e.g., medication, individual or group therapy). We kept track of the concomitant interventions and used these as covariates in the analyses. Participants received a €15 check at the pretest, a €10 check and a small present (stress ball) at post-test, and a €15 check at the 2-month follow-up for hair cortisol (hC).

Sample

The present study used data from an RCT evaluating the effectiveness of playing *Muse* on posttraumatic symptoms. Adolescents with clinical levels of posttraumatic symptoms were assessed for eligibility ($n = 135$). Reasons for exclusion were current or recent trauma treatment ($n = 19$), adolescent or parent declined study participation ($n = 11$), the adolescent would leave the institution soon ($n = 13$), or negative clinician advice ($n = 10$). A clinical sample of 77 adolescents with clinical levels of posttraumatic symptoms in residential care was recruited. The sample was 59.7% male ($n = 46$) with a mean age of 15.25 (SD = 1.79). The mean IQ score (retrieved from file analysis) was 86.42 (SD = 1.72). Adolescents were exposed to the following types of traumatic events: non-intentional traumatic events (e.g., an accident, severe illness, or a friend/family member who died; 100%), neglect (98.70%), domestic violence (98.60%), emotional abuse (90.90%), interpersonal traumatic events (85.10%), lost contact with a parent for at least 1 year (66.20%), a parent with psychiatric problems (44.10%), sexual abuse (27.30%), physical abuse (17.70%), death of a parent (8.60%). There were no baseline differences between the two conditions regarding age, gender, IQ score, disorder diagnoses, type of traumatic experiences, or concomitant therapy. Detailed demographic and clinical characteristics per condition are described in Schuurmans et al. (2020b).

Intervention

Muse

The *Muse* condition consisted of playing *Muse* in addition to TAU. *Muse* is a game-based meditation application with a brain-sensing headband that utilizes neurofeedback. In the current study, Muse was played on an iPad. The intervention consisted of two individual 15–20 min gameplay sessions a week for 6 consecutive weeks. Individual intervention schedules were dependent of participants' schedules for work, school, and hobby activities, but the bi-weekly session days were scheduled with at least 1 day between (e.g., Monday and Wednesday or Tuesday and Thursday). *Muse* includes ten relaxation tutorials (e.g., deep-breathing techniques; Weisz & Kazdin, 2010), that are followed by 3-min meditation sessions. The gameplay sessions were supervised by research assistants who were trained to explain the tutorials according to the protocol. The participants completed at least two tutorials and two meditation sessions per intervention session. The brain-sensing headband provided real-time neurofeedback that was reflected by the intensity of the activity in the in-game environment that participants had selected previously (e.g., beach or rainforest). When the participant's mind was calm, the environment showed calm and settled winds, but these winds picked up and blew when the participant's mind became more active. After each meditation session, *Muse* provided participants with feedback on their performance in the form of points and awards that reflect participants' capacity to regulate their arousal. For a more detailed description of the *Muse* intervention, see Schuurmans et al. (2020a; 2020b).

Control condition

The control condition consisted of TAU: treatment as recommended by their clinicians, regardless of this study. The most common types of TAU were medication ($n = 41$), animal-assisted therapy ($n = 13$), psychomotor therapy ($n = 11$).

Measures

Basal neurobiological parameters

Basal ANS activity. ANS measures were performed using electrocardiogram (ECG) and impedance cardiography (ICG) registration by the VU University Monitoring System (VU-AMS) (De Geus et al., 1995; Willemsen et al., 1996). Five electrodes were placed on the participants' chest and two on the back. Recordings were manually inspected and analyzed with the Data Analysis and Management Software (VU-DAMS) program version 4.0 (VU University, Amsterdam, the Netherlands). SNS activity was measured with a pre-ejection period (PEP). PEP expressed in ms was derived from combined ICG and ECG recordings (Van Lien et al., 2013). PNS activity was measured with respiratory sinus arrhythmia (RSA). RSA can be influenced by respiration rate (RR) independently from PNS activity (Grossman & Taylor, 2007), so respiration rate (RR) (derived from the thorax impedance) was included as a covariate for RSA. To obtain basal ANS measures during rest, we conducted VU-AMS recordings during a 5-min aquatic video (Piferi et al., 2000) that participants watched before the start of the stress task.

Basal HPA axis activity. hC levels pg/mg hair were derived to obtain a measure of basal HPA activity. Hair samples were cut as close to the scalp as possible from a posterior vertex position. Samples were taped on paper and stored in closed envelopes until sent collectively to the laboratory of endocrinology of the Erasmus Medical Center, Rotterdam, the Netherlands. Hair samples were washed in LC-MS grade isopropanol and after solid-phase extraction, hair cortisol was quantified by liquid chromatography-tandem mass spectrometry (LCMS) (Noppe et al., 2015). At least 5 mg of the most proximal 2 cm of each hair sample was used for analysis – representing basal hC over the 8 weeks before the hair sample was taken. Thus, the pretest hair sample was cut in week 8 and the post-test hC sample in week 16.

Neurobiological reactivity to acute stress during a social stress task

The stress task was an adapted version: the Trier Social Stress Task for Children (TRIER-C) (Buske-Kirschbaum et al., 1997)

was combined with the Sing-a-Song Stress Test (SSST) (Brouwer & Hogervorst, 2014). We combined the speaking task with a song task rather than the traditional math assignment (Buske-Kirschbaum et al., 1997), to ensure comprehension. Participants received the introduction of a story and were told that they had 5 min to compose the end of the story before they would present their story for 4 min in front of a camera (Popma et al., 2006). Participants were recorded, allegedly for later assessment by a group of peers who would judge their performance. Then, participants were given a booklet with song texts and were told that they had to sing a song, also in front of the camera. Participants had thirty seconds to choose a song and had to sing the song aloud for thirty seconds. For detailed information on the measurement procedures, see the study protocol (Schuurmans et al., 2020b).

Participants received specific instructions for the measurement session: light breakfast, no caffeine, no intense exercise or smoking immediately before the session and no alcohol or drugs use 24 h before the measurement. To control for these potential confounding variables, participants were asked about their food/drinks, cigarette, alcohol, and drug use, and sleeping/sporting behavior in general in the 24 h before the measurement. Participants were assured that their answers would only be used for research purposes and would not be communicated to their group care workers or parents.

ANS reactivity. ANS parameters were measured with VU-AMS recordings during the following segments of the social stress task: (1) anticipation, (2) performing speech task, (3) anticipation song task, (4) performing song task, and (5) recovery.

HPA axis reactivity. sC samples (nmol/l) were collected before and after the stress task. Samples were collected between 13.00pm and 17.00pm using Cortisol Salivette collection tubes (Sarstedt, Nümbrecht, Germany). Six sC samples were collected: [1] 20 min before the stress task started (−20), [2] immediately before (pre), [3] immediately after (post), and [4] ten (+10), [5] twenty (+20), and [6] forty (+40) min after the stress task had ended. To establish a pre-task resting baseline, the first saliva sample (-20) was collected at least 20 min after participants entered the measurement room. Samples were stored at −20 degrees Celsius until sent collectively to the laboratory of endocrinology of the Erasmus Medical Center, Rotterdam, the Netherlands. Cortisol levels were measured using the LC-MS/MS method with the CHS MSMS Steriods Kit (Perkin Elmer, Turku, Finland) containing $^{2}H_{3}$-cortisol as an internal standard. Chromatographic separation was performed on a Waters (Milford, MA, USA) Acquity UPLC HSS T3 1.8 μm column and quantified by tandem mass spectrometry using a Xevo TQ-S system (Waters, Milford, MA).

Randomization, masking, and sample size

The participants were randomly allocated (1:1 ratio) into two conditions. The Python script randomization was executed by the first author and stratified by gender and ID (ID versus no ID) to ensure equal ratios in both conditions. The allocation of the conditions was not masked. It was not feasible to blind participants or mentors, but they were not informed about the specific hypotheses and were only told that *Muse* was designed to help participants cope with general stress. As the current study used data that were available from another RCT, an a priori power analysis was not available. Therefore, we conducted a posthoc power analysis.

Statistical analyses

To compare both conditions on neurobiological basal activity during rest, multivariate analysis of variance (MANOVA) was used to compare post-test parameters between the two conditions with pretest parameters as covariates. To evaluate intervention effects on neurobiological reactivity to acute stress, we followed Lindauer et al. (2006) and calculated three reactivity variables for each physiological parameter: (1) *baseline*, (2) *response*, and (3) *recovery*. The *baseline* score for ANS parameters was calculated as the mean basal score during rest while watching the aquatic video. For sC, sample 2 (pre: taken immediately before the stress task started) was used for *baseline*, since stressors cause an increase in cortisol levels that peaks after approximately 15 min (Bauer et al., 2002). The *response* for ANS parameters was calculated as the mean score on recordings during the following phases of the stress task: anticipation speech task, speech task, anticipation song task, and song task. The *response* for sC was calculated as the mean score on sample 3 (post: taken immediately after the stress task ended) and sample 4 (+10: taken 10 min after the stress task ended). The *recovery* for ANS parameters was calculated as the mean score during the recovery phase of the stress task. For sC, *recovery* was calculated as the mean score of sample 5 (+20: taken 20 min after the stress task ended) and 6 (+40: taken 40 min after the stress task has ended). MANOVAs were used to compare the post-test *baseline*, *response*, and *recovery* scores for the two conditions, using the pretest measures as covariates.

In the RCT, evaluating the effectiveness of *Muse* on psychopathology outcomes (Schuurmans et al., 2021b), it was found that participants who played *Muse* reported reduced posttraumatic symptoms. To explore whether potential improvements on neurobiological parameters are associated with improvements in posttraumatic symptoms (primary outcome), we conducted chi-square tests for significant neurobiological outcomes. Outcome change on posttraumatic symptoms (declined/no change/improved) was calculated with the Reliable Change Index (RCI) method (Tröster et al., 2007).

Covariates

Variables that were considered as potential covariates were smoking (number of cigarettes), alcohol (number of consumptions) and caffeine use (number of consumptions) in the 24 h before testing, lifestyle smoking (average number of cigarettes a day), alcohol use (average number of

Table 1. Neurobiological parameters at pretest and post-test.

	Descriptives				Statistical outcomes		
	Muse ($n = 37$)		Controls ($n = 40$)				
	Mean	SD	Mean	SD	*F* (df)	*p*	η2p
Pretest (T1)							
Basal ANS activity							
PEP baseline	92.02	18.36	88.17	19.61	0.82 (1, 67)	.369	0.01
RSA baseline	63.41	31.39	76.97	49.63	0.89 (1, 67)	.350	0.01
Basal HPA activity							
hC	3.20	1.72	4.10	2.26	2.33 (1, 71)	.131	0.03
ANS reactivity							
PEP response	86.95	20.84	83.44	20.50	0.10 (1, 67)	.750	0.00
PEP recovery	86.16	20.23	82.21	20.59	0.44 (1, 67)	.511	0.01
RSA response	65.44	31.39	69.70	33.21	0.78 (1, 67)	.381	0.01
RSA recovery	69.96	33.59	78.64	44.78	0.60 (1, 67)	.442	0.01
HPA reactivity							
sC baseline	1.83	.87	1.83	1.25	0.63 (1, 71)	.431	0.01
sC response	1.60	1.03	1.60	0.96	0.74 (1, 71)	.394	0.01
sC recovery	1.27	.52	1.29	0.57	0.09 (1, 71)	.763	0.00
Post-test (T2)							
Basal ANS activity							
PEP baseline	105.02	12.57	84.66	19.53	31.00 (1, 61)	<. 001	0.32
RSA baseline	69.12	37.06	75.32	39.97	0.03 (1, 61)	.862	0.00
Basal HPA activity							
hC	2.78	1.29	3.80	1.92	3.51 (1, 67)	.065	0.05
ANS reactivity							
PEP response	104.37	11.85	87.18	18.02	1.32 (1, 61)	.255	0.02
PEP recovery	104.86	11.68	86.72	18.52	0.38 (1, 61)	.542	0.01
RSA response	67.76	29.23	72.67	33.40	0.71 (1, 61)	.401	0.01
RSA recovery	69.65	29.84	70.91	33.40	0.86 (1, 61)	.359	0.01
HPA reactivity							
sC baseline	1.69	1.18	1.99	1.32	1.68 (1, 67)	.144	0.03
sC response	1.66	.81	1.62	0.78	5.96 (1, 67)	.017	0.08
sC recovery	1.41	.72	1.42	0.61	1.67 (1, 67)	.202	0.02

Note. ANS: autonomic nervous system; PEP: pre-ejection period; RSA: respiratory sinus arrhythmia; HPA: hypothalamic-pituitary-adrenal; hC: hair cortisol; sC: salivary cortisol. hC is measured as pg/mg. sC is measured as nmol/l.

consumptions a week), sporting behavior (average hours a week), eating behavior (average daily meals and snacks), medication use, comorbid psychological and physiological disorders. Additional covariates considered for salivary cortisol were hormonal contraception, menstrual cycle phase, hours of sleep the night before testing, season (as cortisol peaks in spring), time of testing (as cortisol concentrations decrease during the day), storage time, and participants' age. For hair cortisol, additional covariates were hair treatment (i.e., dying/bleaching; yes/no) and hair washing (times a week).

Results

Data inspection revealed missing data due to participant dropout at T2 (5.19%; $n = 4$) or to technical issues related to the physiological outcome measurements such as movement during recording, not enough saliva (sC) or hair (hC) in the sample, or laboratory processing problems (sC and hC). Outcome data were missing for HR (T1: 5.62%; T2:16.95%), PEP (T1:8.23%; T2: 18.55%), RSA (T1: 6.06%; T2: 17.16%) sC (T1: 9.52%; T2: 10.82%), and hC (T1: 19.48%; T2: 48.05%). Logistic regression analysis indicated that data were missing at random. Missing data were imputed using full information maximum likelihood estimation for Markov Chains. The PEP, RSA, sC, and hC data were positively skewed and $\log^{10}$ transformed (Houtveen et al., 2002). For reasons of physiological meaningfulness, means and SDs for hC and basal PEP, and RSA in Table 1 shows absolute values instead of transformed values. Analysis outcomes with imputed, transformed data are reported. All analyses were conducted with completers-only data too. These results showed minimal differences and led to the same statistical outcomes. At pretest, there were no significant differences between the two conditions (see Table 1). Significant variables that were included as covariates were: age, gender, medication use, season, smoking (number of cigarettes), alcohol, and caffeine use (number of consumptions) in the 24 h before testing.

Main outcomes

Table 1 shows the means and standard deviations for all outcome variables per condition, and the statistics of all outcome analyses. At the pretest, there were no significant differences between the conditions (all $p < .10$). At post-test, participants in the *Muse* condition showed increased levels of basal PEP parameters ($p < .001$) and increased sC response to acute stress ($p = .017$). Post-hoc power analysis for MANOVA: repeated measures, within-between interaction with an effect size of η2p 0.08 showed that this study was powered with 70.96% power. To achieve 80% power to detect a difference between conditions, the sample should have been 95 participants.

Discussion

The present study is among the first to examine the impact of treatment on neurobiological parameters among adolescents with posttraumatic symptoms in residential care. The current study utilized an RCT to test whether game-based meditation therapy would restore neurobiological alterations after trauma. We hypothesized that participants who played *Muse* as an addition to TAU would show reduced SNS and increased PNS activity during rest and decreased PNS reactivity to stress. For the HPA axis, we expected decreased HPA axis activity during rest and increased HPA axis reactivity to acute stress. These hypotheses were partly supported. As predicted, the results indicated that participants in the *Muse* condition exhibited lower SNS activity during rest and increased HPA reactivity to acute stress. Contrary to our expectations, results showed no differences between conditions on PNS and HPA axis activity during rest.

The observed improvements on SNS and cortisol outcomes are consistent with research among adults, in that both trauma-focused treatment (Pascoe et al., 2017) and meditation (Boyd et al., 2018) can affect neurobiological parameters. We were unable to detect effects on basal PNS and basal HPA axis activity, but basal HPA activity was marginally significant. Therefore, the lack of a significant effect for HPA activity may likely be due to the lack of power in the current study. Future studies with adequate power are needed.

Among possible reasons for the lack of an effect on basal PNS activity are the small sample size of the current study and the complex nature of neurobiological parameters. It is theorized that PNS activity is a marker of emotional

regulation, whereas SNS activity is a marker of behavioral activation and inhibition (Beauchaine, 2001). As there are indications that inhibition precedes emotional regulation (Campos et al., 2004), it might be that changes in SNS activity would take longer. Also, according to the neurovisceral integration model (Thayer & Lane, 2000) dysregulations in baseline sympathetic arousal are the result of parasympathetic disinhibition. Thus, the reduced levels of sympathetic activity that were found in this study, may be mediated by increased parasympathetic activity during meditation that did not generalize to situations further than the meditation sessions. However, this remains speculative and requires future research, since we did not measure SNS or PNS parameters during meditation in the current study.

Although a feasibility study showed that participants exhibited increased real-time PNS parameters while playing *Muse* (Schuurmans et al., 2020a), which is in line with other studies reporting on increased parasympathetic activation during therapy sessions (Sack et al., 2008), we were not able to find an effect of playing *Muse* on SNS or PNS reactivity during the stress task. Other than the lack of power in the current study, this may be due to the short reaction time of ANS parameters to stress (Berntson et al., 2008). We might not have been able to detect changes in ANS reactivity because our sample size did not allow for more dynamic analyses other than time frames. HPA reactivity, on the other hand, has a slower onset and longer duration (Bauer et al., 2002), and therefore changes in HPA reactivity could be detected.

In the current study, it was found that decreases in sympathetic activity (i.e., higher PEP) during rest were associated with decreases in self-reported posttraumatic symptoms, which is in line with research stating that low levels of sympathetic activity are associated with decreased feelings of fear (Raine, 2002) and threat (Blascovich, 2008). An interesting avenue to pursue for future research would be to examine the causality of this relation. Although decreases in physiological arousal are theorized to precede cognitive changes (Nishith et al., 2002), the relation between physiological and psychological parameters is complex. More research should be conducted on this topic.

Strengths and limitations

Our study has several strengths, which lie mainly in the broad coverage of neurobiological stress systems (i.e., the SNS, the PNS, and the HPA axis) as well as the utilization of an RCT design to test both resting activity and acute reactivity to social stress. In addition, this study was conducted in a high-risk sample of adolescents in residential care with clinical levels of posttraumatic symptoms. We did not exclude potential participants based on minimal IQ scores, comorbid disorders, medication use, or concomitant forms of treatment (other than trauma-focused treatment), which is common practice and impedes the external generalizability of study results. Our study sample reflects the real-world population of adolescents in residential care and results require minimal translation to be implemented into clinical care.

In spite of the strengths, there are also several methodological limitations that should be considered. First and foremost, a post hoc power analysis showed that the study was underpowered. Therefore, we may have not been able to detect some effects that would have been significant if an adequately powered study would have been conducted. Also, except for the baseline measurement at the start of the stress test, we performed no control test that compared the stress task measures to a non-stressful condition. The study utilized a repeated measure testing design that may have allowed for a practice effect. Participants might have had expectations at the second measurement. Some participants may have been extra anxious about the repeated testing, while others may have habituated to the measurement procedures. Yet, the used laboratory stress task has been shown highly effective in inducing stress (Dickerson & Kemeny, 2004; Kudielka et al., 2004). Furthermore, although participants were assured that their answers about cigarette, drug, and alcohol use were confidential and only for research purposes, socially desirable responses cannot be ruled out. As these potentially confounding variables were not biochemically verified, it might be that these have affected the outcomes of neurobiological variables.

Conclusions

In summary, our data show that playing *Muse* not only affects psychopathological outcomes as measured with questionnaires (Schuurmans et al., 2021b) but that its effects can be observed in physiological parameters too. These physiological changes are not restricted to acute effects during therapy sessions alone (Schuurmans et al., 2020a), but effects can also be observed in neurobiological resting activity and acute reactivity to stress after playing *Muse* has ended. To our knowledge, this is the first study to examine neurobiological changes after treatment in adolescents with posttraumatic symptoms. Our results indicate the potential of game-based meditation therapy to restore alterations of neurobiological stress systems.

Disclosure statement

The authors declare that they have no competing interests.

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Notes on contributors

Angela Schuurmans is a PhD student at Radboud University Nijmegen, the Netherlands, and a psychologist at Praktijk Calm Kids, the Netherlands.

Karin Nijhof is a senior researcher at Pluryn, the Netherlands, and Radboud University Nijmegen, the Netherlands.

Ron Scholte is a professor in developmental psychopathology at Radboud University Nijmegen, the Netherlands.

Arne Popma is a professor in pediatrics at Amsterdam UMC and a psychiatrist at De Bascule, The Netherlands.

Roy Otten is a professor in developmental psychopathology at Radboud University Nijmegen.

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