

OPEN

Efficacy of an Intensive Exposure Intervention for Individuals With Persistent Concussion Symptoms Following Concussion: A Concurrent Multiple Baseline Single-Case Experimental Design (SCED) Study

Skye King, MSc; Sven Z. Stapert, PhD; Ieke Winkens, PhD; Joukje van der Naalt, PhD, MD; Caroline M. van Heugten, PhD; Marleen M. Rijkeboer, PhD

Objective: After a concussion, 1 in 3 patients report persistent symptoms and experience long-term consequences interfering with daily functioning, known as persistent concussion symptoms (PCS). Evidence suggests PCS is (partly) maintained by anxious thoughts about brain functioning, recovery, and experienced symptoms, leading to avoidance behaviors, which may prevent patients from meeting life demands. We aimed to investigate the efficacy of a newly developed intensive exposure intervention for individuals with PCS after concussion aimed to tackle avoidance behavior. **Setting:** Participants took part in the intervention at the Maastricht University faculty. **Participants:** Four participants who experienced PCS after concussion partook in the exploratory study. Participants' age ranged between 20 and 32 (mean = 26.5, SD = 5.9) years, with an average length of time after the concussion of 9.8 months. **Design:** A concurrent multiple-baseline single-case design was conducted. The baseline period (A phase) length was randomly determined across participants (3, 4, 5, or 6 weeks). The exposure intervention (B phase) was conducted by psychologists over a 4-week period and consisted of 3 stages: exploration (2 sessions), active exposure (12 sessions conducted over 1 week), and 2 booster sessions. **Main Measures:** Participants answered daily questions on a visual analog scale related to symptom experience, satisfaction with daily functioning, and degree of avoidance of feared activities. Additional outcomes included symptom severity, catastrophizing, fear of mental activity, anxiety, depression, and societal participation. **Results:** Tau-U yielded significant effects ($P < .05$) for all participants on all measures when comparing baseline and intervention phases. The pooled standardized mean difference was high for all measures (symptom experience = 0.93, satisfaction of daily functioning = 1.86, and activity avoidance = -2.05). **Conclusions:** The results show efficacy of the newly developed intensive exposure treatment for PCS after concussion, which is based on the fear avoidance model. Replication in a larger heterogeneous sample is warranted and needed. **Key words:** brain injuries, concussion, exposure therapy, fear avoidance model, intensive exposure therapy, mild traumatic brain injury, persistent concussion symptoms, postconcussive symptoms, single-case experimental designs, traumatic

Author Affiliations: Departments of Neuropsychology and Psychopharmacology (Ms King and Drs Stapert, Winkens, and van Heugten) and Clinical Psychological Science (Dr Rijkeboer), Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, the Netherlands; Limburg Brain Injury Centre, Maastricht University, Maastricht, the Netherlands (Ms King and Drs Winkens and van Heugten); Department of Clinical and Medical Psychology, Zuyderland Medical Centre, Sittard-Geleen, the Netherlands (Dr Stapert); and Department of Neurology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands (Dr van der Naalt).

The authors thank all therapists and participants for their time and their willingness to partake in this study.

Funding for the study was received by the Hersenstichting NL (project number: DR-2020-00368).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.headtraumarehab.com).

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

The authors declare no conflict of interest. This study was not preregistered. Datasets generated and analyzed during the study are not available.

Corresponding Author: Ieke Winkens, PhD, Department of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht 6229 ER, the Netherlands (i.winkens@maastrichtuniversity.nl).

INDIVIDUALS who have suffered a concussion are likely to recover fully within a few weeks or months without specialized intervention.¹ However, approximately 1 in 3 people report persistent symptoms and experience long-term consequences interfering with daily functioning and quality of life.² These persistent, chronic cognitive, emotional, and somatic symptoms are referred to as persistent concussion symptoms (PCS).³ The treatment of PCS remains controversial in somatic and mental healthcare and evidence-based treatments are limited.⁴⁻⁶

The fear avoidance model (FAM) may explain how PCSs develop, are maintained, and worsen over time. It posits that if symptoms are catastrophically (mis)interpreted as threatening, then disproportionate symptom-related fear may arise leading to safety-seeking behaviors such as avoidance and hypervigilance. These avoidance behaviors can contribute to disuse, disability, and depression, paradoxically worsening secondary symptoms in later stages.^{7,8} The FAM has shown a significant association with chronic disability after traumatic brain injury (TBI) (ranging from mild to severe) and other conditions (ie, chronic pain), demonstrating a possible explanation for persistent PCS and delayed/absence of recovery after TBI.⁹ Therefore, this model provides the theoretical underpinnings of effective and common treatment options for these patients, for instance exposure therapy.¹⁰

Recently, studies demonstrated that exposure involves inhibitory learning, which modifies memory structures underlying emotions, so that new safety-based expectations inhibit the previous danger-based ones.¹¹ This has led to the development of therapeutic strategies, which cultivate nonthreat associations and enhance retrieval of these newly learnt associations.¹² In the current study, it is postulated that anxiety (related to cognitive effort termed “cogniphobia”¹³) may be reduced successfully by exposing patients to the feared/avoided activities without the feared outcomes occurring. Consequently, the patient’s conditioned fear response will fade, PCSs reduce, and the patient will regain confidence in their functioning, thereby improving participation and well-being.

Intensive exposure therapy programs provide therapy in frequent sessions over a compact period—usually several consecutive days—in different contexts,¹⁴ and sometimes include therapist rotation.¹⁵ Patients receive a similar total number of hours of therapy compared with standard exposure therapy programs, but in a shorter timeframe. These intensive therapy programs have shown success in treatment outcomes, faster recovery of patients, less patient dropouts, and higher therapist treatment fidelity in patients with strong avoidance, posttraumatic stress disorder, and panic disorder.^{14,16,17}

Given that no one evidence-based treatment has preference⁴⁻⁶ and the substantial medical and socioeconomic burdens on patients, family systems, and the healthcare system, effective treatments for PCS are vital.¹⁸ Due to the robustness of psychological predictors of PCS¹⁹ and the underlying psychological mechanisms of fear, avoidance, and catastrophizing as seen in the FAM, a newly developed intensive exposure therapy program (henceforth termed “intervention”) was piloted in this study. The goal of the treatment was to reduce PCS by confrontation, adaptation of catastrophizing thoughts of symptoms, generalization to new and future contexts with eventual restoration of quality of life, and premorbid levels of participation. Therefore, the aim of this study was to investigate the efficacy of this intervention for PCS. The following research questions were posed: RQ1) Does the intervention lead to changes in subjective perceptions of well-being (reducing symptoms, improving satisfaction, and reducing avoidance of feared activities) in participants with PCS? RQ2) Does the intervention increase social participation and life satisfaction in participants with PCS? RQ3) After treatment and follow-up, is there a reduction in catastrophizing thoughts, fear avoidance behaviors, and anxiety and depressive symptoms?

METHODS

Design

A concurrent multiple-baseline A-B follow-up single-case experimental design (SCED) with randomized baseline was conducted in 4 participants. The baseline period range was 21 to 42 days (A phase). The intervention (B phase) comprised 3 distinct subphases: exploration phase (B1, 1 week), exposure phase (B2, 1 week), and booster phase (B3, 2 weeks starting 1 week after B2). The baseline phase served as a control phase before the intervention onset, allowing participants to be their own controls.²⁰ The exploration phase (B1), in which idiosyncratic case conceptualizations were made, served as an additional control phase by providing attention for participants’ problems without active intervention, enhancing the design power. The exposure phase (B2) consisted of 12 active exposure sessions during 1 week, and the booster phase (B3) included 2 booster sessions promoting generalization to the home environment. After the intervention (B phase), there was a 6-week follow-up phase (see Fig 1). Repeated measurements were taken daily (baseline and intervention) and weekly (follow-up), and additional measurements were taken at 6 different time points throughout the study (see Fig 1). Nine psychologists (referred to as therapists) with differing levels of experience provided the treatment. All therapists were trained on the protocol. The first training session

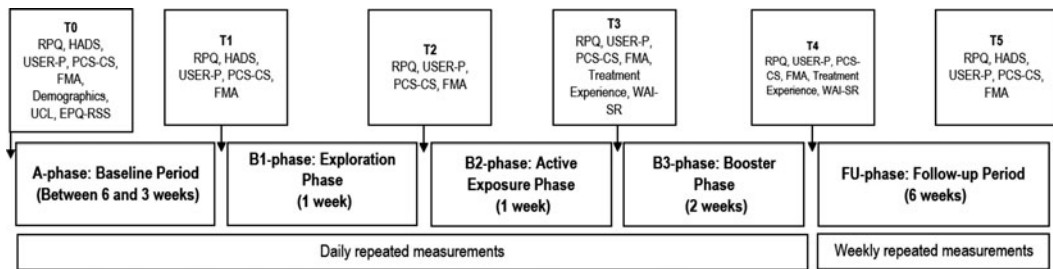


Figure 1. Study design flowchart.

discussed elements of exposure and was provided to therapists with no formal exposure training. The next 2 training sessions, where discussions on the protocol and practice with fictitious patient scenarios took place, was given to all therapists. The Ethical Review Committee of Psychology and Neuroscience of Maastricht University (ERCPN-250_44_03_2022) provided approval.

Participants

Participants were recruited via advertisements placed on social media. Inclusion criteria were: having sustained a single, noncomplicated concussion 6 to 18 months prior; aged 18 to 65 years; self-reporting at least 3 PCSs occurring after injury, which interfere with daily life and societal participation; symptoms not explained by other known pathologies or medical conditions; fluent in Dutch; available to attend therapy sessions and stay at the nearby hotel for 5 nights during the active exposure phase; and preferably no changes in medication regimen for the study duration. One participant decreased medication (amitriptyline) by half on the second day of treatment in consultation with the treating neurologist and the team neurologist, and no negative outcomes were experienced as a result. Exclusion criteria were: TBI with hospital admission in the past and/or a history of neurological disorder, comorbid psychiatric disorder(s) for which a specialized treatment was currently received, other severe comorbidities, which might affect the outcome (eg, addiction); a history of exposure treatment for the consequences of concussion; currently receiving help by other health professionals (specifically clinical psychological treatment for consequences of concussion; occupational or physio-therapy was accepted) for PCS; autonomy or dependence issues prior to the concussion (defined as the inability to independently perform tasks); currently enrolled in a personal insurance injury case/legal procedure related to the incident that developed into PCS; and currently enrolled in a PCS treatment research study.

Procedure

Interested participants contacted one of the researchers (S.K.) who preliminarily checked the inclusion/exclusion criteria. Those who met the criteria were

put forward for an online intake with a neurologist (J.v.d.N.) to check participation eligibility. Participants fulfilled inclusion criteria according to the newly formulated criteria from the American Congress of Rehabilitation Medicine (ACRM).²¹ To finalize eligibility, a clinical psychologist (M.R.) and a neuropsychologist (C.v.H.) screened participants during an online meeting. After signing the informed consent, randomization (using Microsoft Excel “RAND”) of the baseline period was determined per participant. Participants were directed via email to complete the first measures (T0) independently in their own time via the online testing environment. Participants were also directed to download a free mobile application (m-Path, <https://m-path.io/>) where the repeated measurements were recorded. Participants completed the intervention concurrently. Additional measures were conducted: prior to the start of the intervention (T1); after the exploration phase (T2); after the exposure phase (T3); after the booster phase (T4); and at the end of the follow-up phase (T5). See Supplemental Digital Content Table 1 (available at: <http://links.lww.com/JHTR/A771>) for schedule.

Intervention

Participants received a total of 22 hours of therapy, namely two 60-minute online case conceptualization sessions over 1 week (B1), twelve 90-minute active exposure sessions provided in person over 5 days (B2), and two 60-minute online booster sessions provided once a week for 2 weeks starting 1 week after B2. Therapist rotation was used (participants had sessions with various therapists) to optimize treatment effects and to prevent relapse.^{15,22} See Supplemental Digital Content Appendix 1 (available at: <http://links.lww.com/JHTR/A772>) for additional information on the intervention.

Materials

Primary outcomes

Repeated measures

During the baseline and intervention phases, participants were asked daily to rate 3 statements using a sliding

bar visual analogue scale via the mobile app. To assess symptom experience, the statement “today my symptoms were . . .” was assessed from 0 (very bad) to 10 (very good/not present). The question “how satisfied are you with your daily functioning?” was assessed from 0 (not at all) to 10 (very satisfied) assessing satisfaction with daily functioning (referred to as satisfaction). To measure the degree of avoidance of feared activities (referred to as activity avoidance), the statement “I have avoided certain activities today because of my symptoms” was measured from 0 (strongly disagree) to 10 (strongly agree). During the follow-up phase, participants answered these same questions weekly.

For all the following measures, measurements were taken in the online testing environment (see Supplemental Digital Content Table 1, available at: <http://links.lww.com/JHTR/A771>, for the measurement schedule).

Postconcussion symptoms

The Rivermead Postconcussion Questionnaire (RPQ)²³ measures the presence and severity of PCS experienced over the last 24 hours as compared with before the head injury. The 16 items are rated on a 5-point Likert scale ranging from “not experienced at all” (0) to “a severe problem” (4). Higher scores indicate more severe PCS experiences. It demonstrates good interrater and test-retest reliability for total and individual symptom scores,²⁴ good construct validity,²⁵ and is widely used in TBI patients.

Secondary outcomes

Anxiety and depression symptoms

The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-rated scale examining individuals’ anxious and depressive feelings.²⁶ Scores range from 0 to 21, with higher scores indicating higher levels of depression and anxiety. A score of 8 or more is indicative of depression or anxiety symptoms in patients with TBI.²⁷ The Dutch translation of the HADS demonstrated good test-retest reliability, internal consistency, and content validity.²⁸

Participation

The Utrecht Scale for Evaluation of Rehabilitation–Participation (USER-P) measures 3 aspects of participation: frequency of behaviors, participation restrictions experienced due to health condition, and satisfaction with participation.²⁹ Participation in different life areas is assessed (ie, work activities [paid and unpaid], general household activities, lifestyle, and social activities, etc). The questionnaire consists of 31 items and a score ranging from 0 to 100 is calculated for each scale. Higher scores indicate more participation, less restriction, and more satisfaction. The questionnaire

is a reliable and valid measure in patients with brain injury.³⁰

Catastrophizing thoughts

The Postconcussion Symptoms–Catastrophizing Scale (PCS-CS) assesses the level of catastrophizing thoughts regarding PCS and cogniphobia. The PCS-CS is an adaptation of the Pain Catastrophizing Scale³¹ (Dutch version) where the word “pain” is replaced with “these symptoms,” which refer to “cognitive complaints, headache, or fatigue.”⁸ The 13 items are rated on a 5-point Likert scale (0 = not at all, 4 = all the time), with higher scores being indicative of higher levels of catastrophizing thoughts. Concurrent validity, convergent validity, internal consistency, and test-retest reliability were sufficient.⁹

Fear of mental activity

The Fear of Mental Activity (FMA) scale assesses the level of fear avoidance regarding PCS and cogniphobia. The FMA is an adaptation of the valid and reliable Dutch version of the Tampa Scale of Kinesiophobia.³² The word “pain” was replaced with “these symptoms” referring to “cognitive complaints, headache, or fatigue.”⁸ The 17 items are rated on a 4-point Likert scale (1 = strongly disagree, 4 = strongly agree), with higher scores indicating stronger fear for mental activities. The concurrent validity, convergent validity, internal consistency, and test-retest reliability were acceptable.⁹

Other parameters

Coping

The Utrecht Coping List (UCL)³³ assesses 7 different coping styles. The UCL consists of 47 items, scored on a 4-point scale, with higher scores indicating higher use of a particular coping style. The UCL is a valid and reliable measure, frequently used in patients with TBI.³⁴

Neuroticism

The Eysenck Personality Questionnaire–Revised Short Scale (EPQ-RSS)³⁵ measures neuroticism, extraversion, and psychoticism. Forty-eight items are scored with a dichotomous (yes/no) response option. A sum score is calculated, ranging from 0 to 12, with higher scores indicating higher levels of the trait measured. The EPQ-RSS is a valid and reliable measure.³⁶

Therapeutic alliance

The Working Alliance Inventory–Short Revised (WAI-SR) is a 12-item questionnaire measuring 3 key aspects of therapeutic alliance: a) agreement on the tasks of therapy, b) agreement on the therapy goals, and c) development of an affective bond. Items are rated on a 5-point Likert scale (1 = never, 5 = always) and scores

on all 3 scales (ranging from 5 to 20) form the strength of therapeutic alliance. The WAI-SR shows good psychometric properties in different samples.³⁷

Treatment experience

A written survey with open-ended questions provided qualitative insights of therapists and participants into the treatment (eg, what participants and therapists liked/did not like, treatment expectations, overall treatment ratings, questions about materials and information provided, training materials, and therapist training).

Demographic information

At the beginning of the study, participants completed a self-reported questionnaire containing demographic questions (ie, age, gender, education, marital and living situation, and occupational information) and questions on injury-related variables.

Data analysis

The symptom experience, satisfaction, and activity avoidance were plotted graphically per participant using Prism GraphPad 9 for visual analysis of change. Visual analyses were conducted following the recommendations of Ledford and Gast.³⁸ Horizontal lines were depicted to observe changes in the average (mean) per phase. Trend was determined by the slope and di-

rection of the best fitting straight line for each phase, using simple regression lines. Trend stability was defined by a stability window of $\pm 25\%$ of the trend line. Tau-*U* was calculated, as a measure of effect, using the Single Case Research online calculator (<http://singlecaseresearch.org/calculators/tau-u>). Tau-*U* can be understood as a continuous index of improvement, and can be interpreted as 0.20 small change, 0.20 to 0.60 moderate change, 0.60 to 0.80 large change, and above 0.80 as very large change.³⁹ The pooled standardized mean difference (calculated using Shiny SCDA application v2.8, <http://34.251.13.245/scda/>⁴⁰) was used to compare the mean of the baseline phase (A) to the combined intervention phases (B1, B2, and B3) and the follow-up phase for all participants.³⁸

For the RPQ, HADS, USER-P, PCS-CS, and FMA, descriptive and visual inspection were utilized. Descriptive analysis was used to analyze the questionnaires across all time points (T1 to T5) and compare them to baseline (T0) for each participant. Demographic variables, participant profiles (coping and neuroticism), and therapeutic alliance were described.

RESULTS

Characteristics of the 4 participants can be found in Table 1. Participant background, symptom profiles, and case formulation are in Supplemental Digital Content

TABLE 1 Participant characteristics

Participant	1	2	3	4
Sex	Female	Male	Female	Female
Age	31	31	23	19
Education level	Higher professional education	Secondary vocational education	Higher general and preuniversity education	Higher general and pre-university education
Occupation pre-injury	Employed 36 h	Employed 40 h	Students and employed 16 h	Students and employed 10 h
Occupation post-injury	Employed 9 h	Employed 0 h.	Stopped studying; unemployed	Stopped studying; unemployed
Marital status and living situation (pre-/post-injury)	Cohabiting with partner	Cohabiting with partner	Single; independent (pre)/with parents (post)	Single; independent (pre)/with parents (post)
Time since injury, mo	6	16	9	7
Cause of injury	Sports accident	Car accident	Sports accident	Accident (fall)
Neuroimaging done (CT/MRI, (ab)normal)	No	Yes, normal	Yes, normal	Yes, normal
LOC	No	Yes	No	Yes
PTA	No	Yes	No	Yes
Avoidant coping ^a	17	18	23	25
Neuroticism ^b	9	6	6	2

Abbreviations: CT/MRI, computed tomography scan/magnetic resonance imaging; LOC, loss of consciousness; PTA, posttraumatic amnesia

^aAvoidance coping measured by the Utrecht Coping List (UCL).

^bNeuroticism measured by the Eysenck Personality Questionnaire–Revised Short Scale (EPQ-RSS).

(available at: <http://links.lww.com/JHTR/A771>). Participants 1, 2, 3, and 4 were randomly assigned to a baseline length of 42, 35, 28, and 21 days, respectively. For participant 1, there were too few scores in the follow-up phase for analysis of this phase to take place.

The repeated symptom experience, satisfaction, and activity avoidance scores are represented visually in Figures 2, 3, and 4. Characteristics of phase lengths, measurements, and trend stability percentages are denoted in Supplemental Digital Content Tables 2 and 3 (available at: <http://links.lww.com/JHTR/A771>). Tau-U analysis results are presented in Table 2.

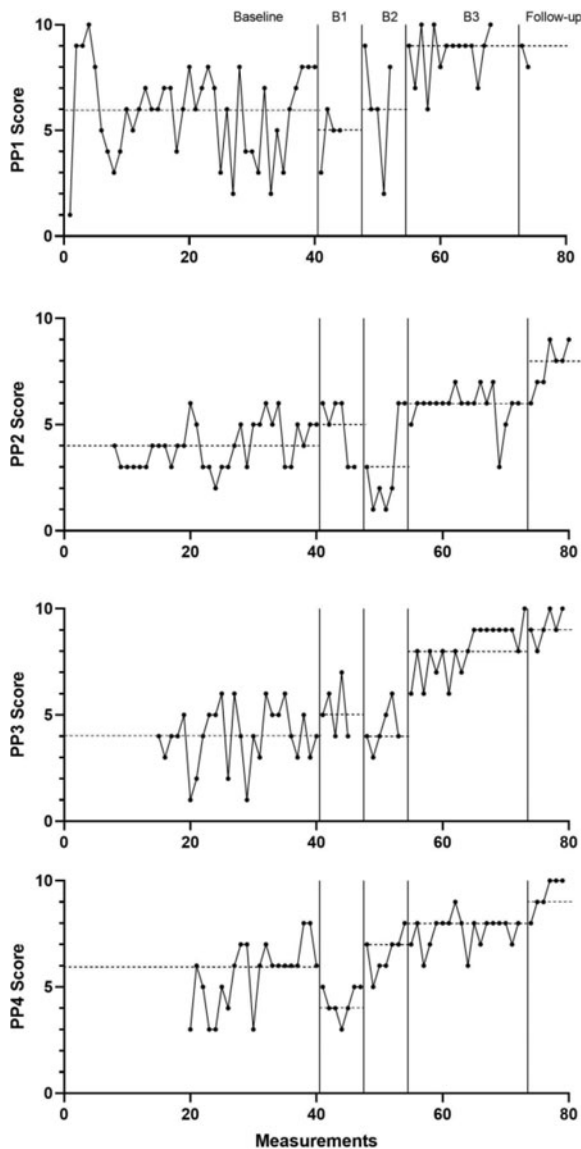


Figure 2. Graphical representation of participant *symptom experience*. Repeated-measures visual analog scale scores of symptom experience per participant measured daily over baseline and intervention (B1 = exploration phase, B2 = active exposure phase, and B3 = booster phase), and weekly over follow-up.

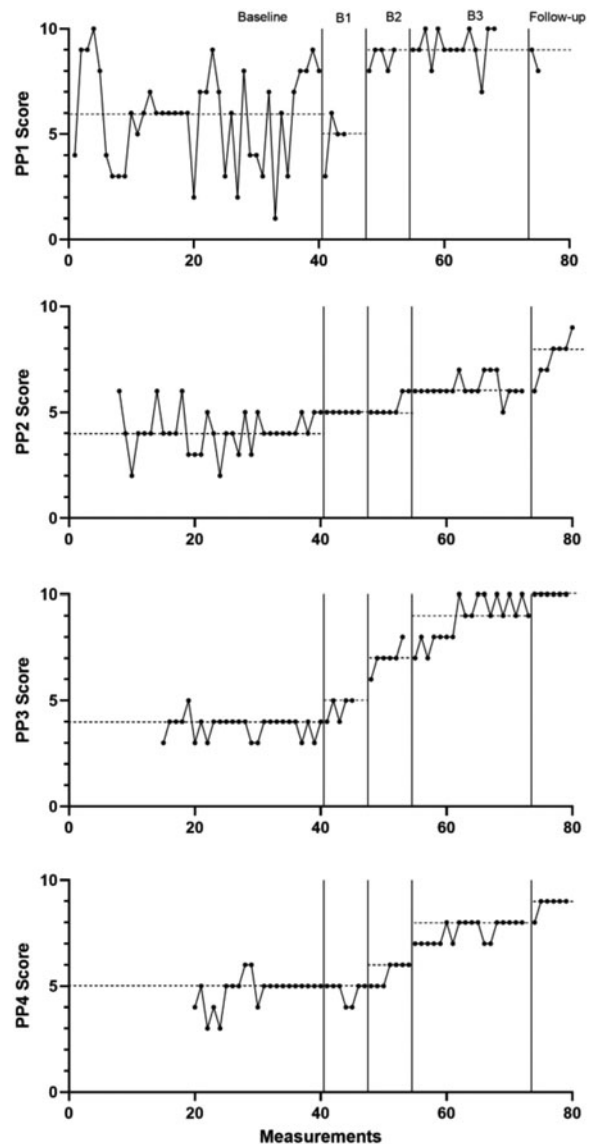


Figure 3. Graphical representation of participant *satisfaction with daily functioning*. Repeated-measures visual analog scale scores of symptom experience per participant measured daily over baseline and intervention (B1 = exploration phase, B2 = active exposure phase, and B3 = booster phase), and weekly over follow-up.

Visual analysis

Visual analysis showed that for all participants the average symptom experience and satisfaction scores increased (improvement in the desired treatment direction) between the baseline and intervention phases. For participants 2, 3, and 4, these changes were maintained during the follow-up phase. For all participants, the average activity avoidance decreased between the baseline and intervention phases in the desired treatment direction. For participant 2, this decrease was seen only after B1, with the decrease maintaining through intervention

TABLE 2 *Tau-U analysis for all participants between all phases^a*

	PP1	PP2	PP3	PP4
Symptom experience				
Baseline vs B1	-0.36 (0.24)	-0.36 (0.16)	0.43 (0.13)	-1.14 (0.00) ^b
Baseline vs B2	0.12 (0.68)	-1.01 (0.00) ^b	0.09 (0.74)	-0.21 (0.41)
Baseline vs B3	0.75 (0.00) ^b	0.56 (0.00) ^b	0.98 (0.00) ^b	0.54 (0.01) ^b
Baseline vs follow-up	...	0.36 (0.14)	1 (0.00) ^b	0.29 (0.28)
B1 vs B2	0.50 (0.22)	-5.24 (0.12)	-0.40 (0.27)	0.94 (0.00) ^b
B2 vs B3	0.66 (0.03) ^b	0.71 (0.01) ^b	0.97 (0.00) ^b	0.60 (0.02) ^b
B3 vs follow-up	...	0.81 (0.00) ^b	0.55 (0.05)	0.86 (0.00) ^b
Satisfaction with daily functioning				
Baseline vs B1	-0.35 (0.25)	0.64 (0.01) ^b	0.67 (0.02) ^b	-0.09 (0.73)
Baseline vs B2	0.76 (0.01) ^b	0.71 (0.00) ^b	1 (0.00) ^b	0.58 (0.02) ^b
Baseline vs B3	0.84 (0.00) ^b	0.91 (0.00) ^b	1 (0.00) ^b	1 (0.00) ^b
Baseline vs follow-up	...	0.99 (0.00) ^b	1 (0.00) ^b	1 (0.00) ^b
B1 vs B2	1 (0.01) ^b	0.29 (0.39)	1 (0.01) ^b	0.69 (0.03) ^b
B2 vs B3	0.44 (0.15)	0.72 (0.01) ^b	0.85 (0.00) ^b	1 (0.00) ^b
B3 vs follow-up	...	0.77 (0.00) ^b	0.68 (0.01) ^b	0.91 (0.00) ^b
Activity avoidance				
Baseline vs B1	0.53 (0.09)	-0.15 (0.95)	0.17 (0.55)	-0.14 (0.60)
Baseline vs B2	-0.79 (0.00) ^b	-1 (0.00) ^b	-0.41 (0.12)	-0.85 (0.00) ^b
Baseline vs B3	-0.79 (0.00) ^b	-1 (0.00) ^b	-0.81 (0.00) ^b	-0.89 (0.00) ^b
Baseline vs follow-up	...	-1 (0.00) ^b	-0.41 (0.12)	-0.90 (0.00) ^b
B1 vs B2	-1 (0.01) ^b	-1 (0.00) ^b	-1 (0.01) ^b	-0.67 (0.04) ^b
B2 vs B3	-1 (0.00) ^b	0.60 (0.02) ^b	0.26 (0.34)	-0.05 (0.86)
B3 vs follow-up	...	-0.59 (0.03) ^b	0.07 (0.80)	-0.11 (0.69)

Abbreviations: B1, exploration phase of intervention; B2, exposure phase of intervention; B3, booster phase of intervention.

^b $P < .05$.

^a*Italicized numbers indicate Tau-U corrected baseline was used due to significant baseline trend.*

and follow-up phases. For participants 3 and 4, activity avoidance was at floor level through B2, B3, and follow-up. All phases for all measures had high trend stability and trend changes for all participants.

For *symptom experience* immediacy of score, changes were seen between baseline and B1 (all participants), between B1 and B2 (participants 1 and 4), between B2 and B3 (all participants), and between B3 and follow-up (participant 3). For *satisfaction* immediacy of score, changes were seen between baseline and B1 (participant 1), B1 and B2 (participants 1 and 3), between B2 and B3 (participants 3 and 4), and between B3 and follow-up (participant 3). Immediacy of score changes were seen for the *activity avoidance* measure between baseline and B1 (participant 1, 3, and 4), B1 and B2 (all participants), and between B2 and B3 (participant 2).

Tau-U and pooled standardized mean difference

For *symptom experience*, Tau-U analysis revealed significant effects between baseline and B3, and between B2 and B3, for all participants. For participant 2, significant effects were also shown between baseline and B2, and between B3 and follow-up. Additionally, participant 3 showed significant effects between baseline and follow-up. Significant effects were also shown between baseline

and B1, B1 and B2, and B3 and follow-up for participant 4. For *satisfaction*, Tau-U analysis revealed significant effects between baseline and B2, and baseline and B3 for all participants. Participants 2, 3, and 4 also showed significant effects between baseline and follow-up, B2 and B3, and B3 and follow-up. Participants 2 and 3 had significant effects between baseline and B1, and participants 1, 3, and 4 showed significant effects between B1 and B2. For *activity avoidance*, Tau-U analysis revealed significant effects between baseline and B3, and between B1 and B2 for all participants. Significant effects were seen between baseline and B2 (participants 1, 2, and 4), baseline and follow-up (participants 2 and 4), B2 and B3 (participants 1 and 2), and B3 and follow-up (participant 2). The pooled standardized mean difference was 0.93 (*symptom experience*), 1.86 (*satisfaction*), and -2.05 (*activity avoidance*).

Secondary outcomes and additional parameters

In Supplemental Digital Content Table 4 (available at: <http://links.lww.com/JHTR/A771>), the raw scores of the RPQ, HADS, USER-P, PCS-CS, FMA, and WAI-SR are presented. The UCL avoidance scale and the EPQ-RSS neuroticism scale are presented in Table 1. Participant 1 showed a high level of neuroticism, and participants 3 and 4 showed high levels of avoidance

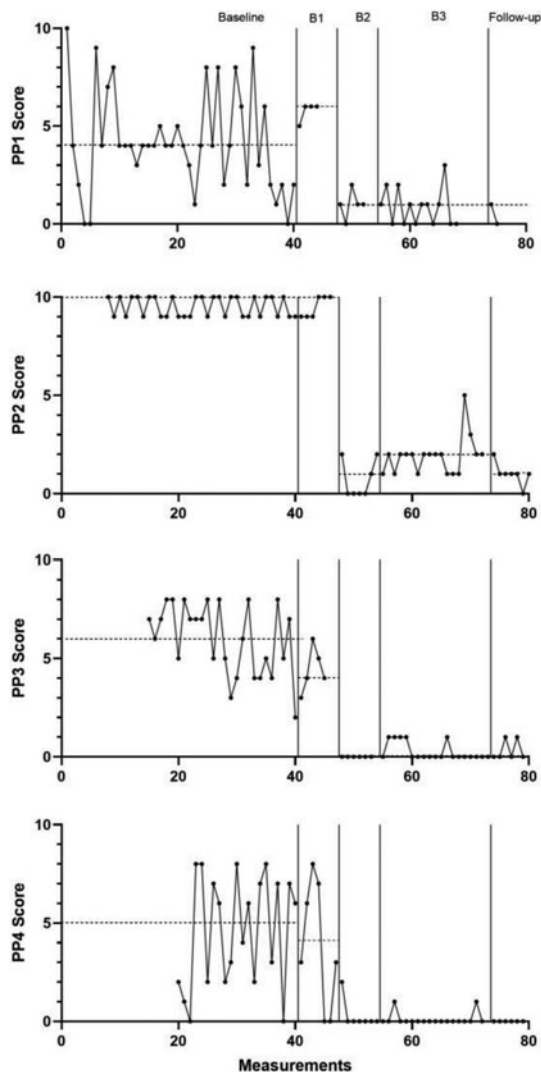


Figure 4. Graphical representation of participant *activity avoidance*. Repeated-measures visual analog scale scores of symptom experience per participant measured daily over baseline and intervention (B1 = exploration phase, B2 = active exposure phase, and B3 = booster phase), and weekly over follow-up.

coping style. Using the reference guidelines,⁴¹ all participants experienced clinically relevant scores on the RPQ at baseline (T0) as compared with after intervention (T3, T4, and T5) where scores reached nonclinically relevant levels. At baseline (T0), participants noted fatigue (3 participants), concentration problems (2 participants), and hypersensitivity to light and noise (2 participants) as “a large problem.” At the end of follow-up (T5), participants 1 and 4 indicated “not a problem anymore” for all RPQ symptoms. Participant 2 noted “a small problem” (a decrease from baseline) for headaches, fatigue, irritability, and frustration and “not a problem anymore” for all remaining RPQ symptoms. Participant 3 noted “a small problem” (a decrease from baseline) for sleep

problems, fatigue, depression, forgetfulness, and concentration problems, and “not a problem anymore” for all remaining RPQ symptoms. All participants showed little to no change in anxiety and depressive symptoms (HADS) at the end of follow-up (T5) compared with baseline (T0), with all participants scoring at a clinically relevant level (≥ 8). Participants 1, 2, and 4 showed improvements in levels of participation (USER-P frequency) from T0 to T5. Participant 3 scores started high at T0, decreased at T2, and then increased and stabilized (T3) through to T5. All participants showed improvement in subjective ratings of participation (USER-P restrictions scale) and satisfaction with participation (USER-P satisfactions scale) from T0 to T5. After the treatment (T4) and at the end of follow-up (T5), there was a reduction in catastrophizing thoughts about the PCS (PCS-CS), and in fear avoidance behaviors in both active avoidance and somatic focus (FMA), as compared with baseline (T0) for all participants. Participants experienced high therapeutic alliance (goal mean = 18.5, task mean = 18, and bond mean = 15.5). According to the treatment experience questions, participants rated the treatment highly (mean = 9.75) and positively. All participants noted that despite experiencing difficulty in the sessions, the session duration, amount, and content (real-world application, personal guidance) were good, and the therapists were also in agreement. All participants thought the treatment was beneficial for them and that they could see improvement (commenting that they had their life back), and all participants would recommend this treatment to others with PCS.

DISCUSSION

The goal of the current study was to investigate the efficacy of a newly developed intensive exposure therapy program for PCS. Findings showed that all participants experienced moderate to very large improvements in their subjective perceptions of well-being (reduction in symptom experience, improved satisfaction, and reduction of activity avoidance) between baseline and intervention phases, which were maintained during follow-up. Three out of 4 participants experienced symptom exacerbation⁴² during the treatment; however, all 4 participants demonstrated symptom improvement by the end of treatment. For all participants, symptom levels and severity decreased to clinically nonrelevant levels after the intervention and this decrease was maintained through to the end of the study. At baseline all participants' symptom profiles were highest in the somatic domain (ie, fatigue, headaches, hypersensitivity, etc)⁴³ than the emotional or cognitive domains. For 2 participants after treatment through to the end of follow-up, all symptoms were noted as no longer a problem. For the other 2 participants, the symptoms

fell across the domains (somatic and emotional, for participant 2 and additionally cognitive for participant 3) but at much lower levels of severity. No change to depression and anxiety symptoms was seen, possibly because the intervention was not focused on these symptoms but rather focuses on PCS and avoidant behaviors. All participants indicated that this 1 week of intensive exposure treatment made them have “their lives back again.” Catastrophizing thoughts were decreased, fear avoidance or safety behaviors were reduced (and extinguished in certain participants), participants’ radius of action improved, all participants went back to work or started their studies again, and improvements in participation (social activities, general household activities, lifestyle activities, etc) and general life satisfaction were also seen.

It is of note that the intervention was done from a purely psychological perspective (no physical aspects were taken into account) with only psychologists performing the intervention. The treatment is easily disseminated and good insight into the FAM of PCS is important. For all participants, the therapeutic alliance between the therapists and participants was high after the treatment. This finding is interesting and adds to the current literature, as therapist rotation was a key feature of the intervention,¹⁵ and despite common understanding, it did not lessen therapeutic alliance. The advantage of therapist rotation is generalization (ie, different contexts in which extinction takes place, reducing return of fear after treatment^{22,44}). Moreover, after treatment participants indicated that the fact that many people (not just one) showed confidence that they could safely perform various activities helped them by improving their realization that they were indeed safe and capable. Therapists and participants both qualitatively reported that while the intervention was intensive, improvements were demonstrated quickly and the intervention was feasible (ie, delivery style and frequency, etc).

A strength of the current study is the intricate design with multiple control phases, which provide more power to the study. Additionally, more in-depth information was gained from each phase of the intervention, providing greater insight into the treatment efficacy. The study adhered to the quality guidelines for SCED (eg, SCRIBE and RoBiNT),^{45,46} thus strengthening the findings that intensive exposure treatment has efficacy in treating participants with PCS after concussion. Furthermore, despite the intensity of the treatment, no adverse events occurred for any of the participants. A limitation of the study is the homogeneity of the sample in terms of gender, age, and symptom profiles (vestibular and other symptoms). The profile of the participants is likely due to the recruitment and sampling methodology. Therefore, the findings of the current study might not be generalizable to PCS patients outside of these demographic ranges, limiting the external validity of the study. Furthermore, minor deviations in the inclusion/exclusion criteria for participation occurred (ie, no loss of consciousness or posttraumatic amnesia); however, these participants fit the new definition of mTBI of the ACRM.²¹ Additionally, the participants were highly motivated to succeed and recover, and the treatment and hotel stay were paid for, which may have biased the findings. As such, future research should investigate the efficacy of this treatment in a more heterogeneous group in demographic and motivational variables.

In conclusion, this study provides first evidence for the efficacy of this intensive exposure treatment for participants with PCS after concussion experiencing severe somatic and cognitive complaints. This intervention successfully improved participants’ subjective perceptions of well-being, catastrophizing, fear avoidance behaviors, and increased societal participation. Replications with more diverse samples of participants are needed to obtain further evidence for the efficacy and eventually clinical effectiveness of this treatment.

References

1. Cassidy JD, Boyle E, Carroll LJ. Population-based, inception cohort study of the incidence, course, and prognosis of mild traumatic brain injury after motor vehicle collisions. *Arch Phys Med Rehabil*. 2014;95(3, suppl):S278–S285. doi:10.1016/j.apmr.2013.08.295
2. van der Naalt J, Timmerman ME, de Koning ME, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. *Lancet Neurol*. 2017;16(7):532–540. doi:10.1016/S1474-4422(17)30117-5
3. Permenter CM, Fernández-de Thomas RJ, Sherman Al. *Postconcussive Syndrome*. StatPearls Publishing; 2022.
4. Sullivan KA, Kaye S-A, Blaine H, et al. Psychological approaches for the management of persistent postconcussion symptoms after mild traumatic brain injury: a systematic review. *Disabil Rehabil*. 2020;42(16):2243–2251. doi:10.1080/09638288.2018.1558292
5. Teo SH, Fong KNK, Chen Z, Chung RCK. Cognitive and psychological interventions for the reduction of post-concussion symptoms in patients with mild traumatic brain injury: a systematic review. *Brain Inj*. 2020;34(10):1305–1321. doi:10.1080/02699052.2020.1802668
6. Rytter HM, Graff HJ, Henriksen HK, et al. Nonpharmacological treatment of persistent postconcussion symptoms in adults: a systematic review and meta-analysis and guideline recommendation. *JAMA Netw Open*. 2021;4(11):e2132221. doi:10.1001/jamanetworkopen.2021.32221

7. Silverberg ND, Panenka WJ, Iverson GL. Fear avoidance and clinical outcomes from mild traumatic brain injury. *J Neurotrauma*. 2018;35(16):1864–1873. doi:10.1089/neu.2018.5662
8. Wijenberg MLM, Stapert SZ, Verbunt JA, Ponsford JL, Van Heugten CM. Does the fear avoidance model explain persistent symptoms after traumatic brain injury? *Brain Inj*. 2017;31(12):1597–1604. doi:10.1080/02699052.2017.1366551
9. Wijenberg MLM, Hicks AJ, Downing MG, van Heugten CM, Stapert SZ, Ponsford JL. Relevance of the fear-avoidance model for chronic disability after traumatic brain injury. *J Neurotrauma*. 2020;37(24):2639–2646. doi:10.1089/neu.2020.7135
10. Volders S, Boddez Y, De Peuter S, Meulders A, Vlaeyen JWS. Avoidance behavior in chronic pain research: a cold case revisited. *Behav Res Ther*. 2015;64:31–37. doi:10.1016/j.brat.2014.11.003
11. Craske MG, Treanor M, Conway CC, Zbozinek T, Vervliet B. Maximizing exposure therapy: an inhibitory learning approach. *Behav Res Ther*. 2014;58:10–23. doi:10.1016/j.brat.2014.04.006
12. Weisman JS, Rodebaugh TL. Exposure therapy augmentation: a review and extension of techniques informed by an inhibitory learning approach. *Clin Psychol Rev*. 2018;59:41–51. doi:10.1016/j.cpr.2017.10.010
13. Silverberg ND, Iverson GL, Panenka W. Cogniphobia in mild traumatic brain injury. *J Neurotrauma*. 2017;34(13):2141–2146. doi:10.1089/neu.2016.4719
14. Hendriks L, Kleine RA, Broekman TG, Hendriks G-J, Minnen Av. Intensive prolonged exposure therapy for chronic PTSD patients following multiple trauma and multiple treatment attempts. *Eur J Psychotraumatol*. 2018;9(1):1425574. doi:10.1080/20008198.2018.1425574
15. Van Minnen A, Hendriks L, Kleine RD, Hendriks G-J, Verhagen M, De Jongh A. Therapist rotation: a novel approach for implementation of trauma-focused treatment in post-traumatic stress disorder. *Eur J Psychotraumatol*. 2018;9(1):1492836. doi:10.1080/20008198.2018.1492836
16. Stech EP, Grierson AB, Chen AZ, Sharrock MJ, Mahoney AEJ, Newby JM. Intensive one-week internet-delivered cognitive behavioral therapy for panic disorder and agoraphobia: a pilot study. *Internet Interventions*. 2020;20:100315. doi:10.1016/j.invent.2020.100315
17. Goetter EM, Blackburn AM, Stasko C, et al. Comparative effectiveness of prolonged exposure and cognitive processing therapy for military service members in an intensive treatment program. *Psychol Trauma*. 2021;13(6):632–640. doi:10.1037/tra0000956
18. Moussavi Z, Suleiman A, Rutherford G, et al. A pilot randomised double-blind study of the tolerability and efficacy of repetitive transcranial magnetic stimulation on persistent post-concussion syndrome. *Sci Rep*. 2019;9(1):5498. doi:10.1038/s41598-019-41923-6
19. Mikolić A, Polinder S, Steyerberg EW, et al. Prediction of global functional outcome and post-concussive symptoms after mild traumatic brain injury: external validation of prognostic models in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study. *J Neurotrauma*. 2021;38(2):196–209. doi:10.1089/neu.2020.7074
20. Kazdin AE. Single-case experimental designs. Evaluating interventions in research and clinical practice. *Behav Res Ther*. 2019;117:3–17. doi:10.1016/j.brat.2018.11.015
21. Silverberg ND, Iverson GL, Cogan A, et al. The American Congress of Rehabilitation Medicine diagnostic criteria for mild traumatic brain injury. *Arch Phys Med Rehabil*. 2023;104(8):1343–1355. doi:10.1016/j.apmr.2023.03.036
22. Craske MG, Treanor M, Zbozinek TD, Vervliet B. Optimizing exposure therapy with an inhibitory retrieval approach and the OptEx Nexus. *Behav Res Ther*. 2022;152:104069. doi:10.1016/j.brat.2022.104069
23. King N, Crawford S, Wenden F, Moss N, Wade D. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *J Neurol*. 1995;242(9):587–592. doi:10.1007/BF00868811
24. Plass AM, Van Praag D, Covic A, et al. The psychometric validation of the Dutch version of the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) after traumatic brain injury (TBI). *PLoS One*. 2019;14(10):e0210138. doi:10.1371/journal.pone.0210138
25. Eyres S, Carey A, Gilworth G, Neumann V, Tennant A. Construct validity and reliability of the Rivermead Post-Concussion Symptoms Questionnaire. *Clin Rehabil*. 2005;19(8):878–887. doi:10.1191/0269215505cr905oa
26. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*. 1983;67(6):361–170. doi:10.1111/j.1600-0447.1983.tb09716.x
27. Whelan-Goodinson R, Ponsford J, Schönberger M. Validity of the Hospital Anxiety and Depression Scale to assess depression and anxiety following traumatic brain injury as compared with the Structured Clinical Interview for DSM-IV. *J Affect Disord*. 2009;114(1-3):94–102. doi:10.1016/j.jad.2008.06.007
28. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med*. 1997;27(2):363–370. doi:10.1017/s0033291796004382
29. van der Zee CH, Priesterbach AR, van der Dussen L, et al. Reproducibility of three self-report participation measures: the ICF Measure of Participation and Activities Screener, the Participation Scale, and the Utrecht Scale for Evaluation of Rehabilitation-Participation. *J Rehabil Med*. 2010;42(8):752–757. doi:10.2340/16501977-0589
30. Post MW, van der Zee CH, Hennink J, Schafrat CG, Visser-Meily JM, van Berlekom SB. Validity of the Utrecht Scale for Evaluation of Rehabilitation-Participation. *Disabil Rehabil*. 2012;34(6):478–485. doi:10.3109/09638288.2011.608148
31. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess*. 1995;7(4):524–532. doi:10.1037/1040-3590.7.4.524
32. Goubert L, Crombez G, Vlaeyen JW, Van Damme S, Van den Broeck A, Van Houdenhove B. De Tampa schaal voor kinesiofobie: psychometrische karakteristieken en normering. *Gedrag Gezond*. 2000;28:54–62.
33. Schreurs P, Van de Willige G, Brosschot J, Tellegen B, Graus G. *De Utrechtse Copinglijst: UCL*. [The Utrecht Coping List: UCL]. Swets en Zeitlinger; 1993;
34. Wolters G, Stapert S, Brands I, Van Heugten C. Coping styles in relation to cognitive rehabilitation and quality of life after brain injury. *Neuropsychol Rehabil*. 2010;20(4):587–600. doi:10.1080/09602011003683836
35. Eysenck SBG, Eysenck HJ, Barrett P. A revised version of the psychoticism scale. *Person Indiv Differ*. 1985;6(1):21–29. doi:10.1016/0191-8869(85)90026-1
36. Sanderman R, Arrindell W, Ranchor A. *Measuring personality aspects with the Eysenck Personality Questionnaire (EPQ)*. 2nd ed. Research Institute SHARE; 2012.
37. Munder T, Wilmers F, Leonhart R, Linster HW, Barth J. Working Alliance Inventory-Short Revised (WAI-SR): psychometric properties in outpatients and inpatients. *Clin Psychol Psychother*. 2010;17(3):231–239. doi:10.1002/cpp.658
38. Ledford J, Gast D. *Single Case Research Methodology: Applications in Special Education and Behavioral Sciences*. 3rd ed. Routledge; 2018.
39. Vannest KJ, Ninci J. Evaluating intervention effects in single-case research designs. *J Counseling Dev*. 2015;93(4):403–411. doi:10.1002/jcad.12038

40. Bulté I, Onghena P. The single-case data analysis package: analysing single-case experiments with R software. *J Modern Appl Stat Methods*. 2013;12(2):450–478. doi:10.22237/jmasm/1383280020
41. Zeldovich M, Bockhop F, Covic A, et al. Reference values for the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) from general population samples in the United Kingdom, Italy, and the Netherlands. *J Clin Med*. 2022;11(16):4658. doi:10.3390/jcm11164658
42. Larsen SE, Stirman SW, Smith BN, Resick PA. Symptom exacerbations in trauma-focused treatments: associations with treatment outcome and non-completion. *Behav Res Ther*. 2016;77:68–77. doi:10.1016/j.brat.2015.12.009
43. Rivera D, Greving S, Arango-Lasprilla JC, et al. Comparability of (post-concussion) symptoms across time in individuals after traumatic brain injury: results from the CENTER-TBI Study. *J Clin Med*. 2022;11(14):4090. doi:10.3390/jcm11144090
44. Bouton ME, Winterbauer NE, Todd TP. Relapse processes after the extinction of instrumental learning: renewal, resurgence, and reacquisition. *Behavioural Processes*. 2012;90(1):130–141. doi:10.1016/j.beproc.2012.03.004
45. Tate RL, Perdices M, Rosenkoetter U, et al. Revision of a method quality rating scale for single-case experimental designs and n-of-1 trials: the 15-item Risk of Bias in N-of-1 Trials (RoBiNT) Scale. *Neuropsychol Rehabil*. 2013;23(5):619–638. doi:10.1080/09602011.2013.824383
46. Tate RL, Perdices M, Rosenkoetter U, et al. The Single-Case Reporting Guideline in Behavioural Interventions (SCRIBE) 2016: explanation and elaboration. *Arch Sci Psychol*. 2016;4(1):10–31. doi:10.1037/arc0000027