American Psychological Association

Journal of Consulting and Clinical Psychology

0022-006X/18/$12.00

2018, Vol. 86, No. 12, 1076–1090
http://dx.doi.org/10.1037/ccp0000340

Reducing Intrusive Memories of Trauma Using a Visuospatial Interference Intervention With Inpatients With Posttraumatic Stress Disorder (PTSD)

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Objective: The core clinical feature of posttraumatic stress disorder (PTSD) is recurrent intrusive memories of trauma. This study aimed to test a novel and simple intervention, inspired by the concepts of concurrent task interference and memory reconsolidation, to reduce the occurrence of intrusive memories among inpatients with complex PTSD. ***Method:*** In this open-label single case series 20 patients with longstanding complex PTSD in inpatient treatment monitored the occurrence of intrusive trauma memories (intrusions) over the course of their admission (5 to 10 weeks). Patients received study-specific intervention sessions (including a *memory reminder* for a specific intrusion then 25 min *Tetris* gameplay) on a weekly basis. A within-subjects multiple baseline AB design was used, in that the length of baseline ("A," preintervention, monitoring only) and postintervention ("B") phases varied within-subjects across individual intrusions. Further, some intrusions were never targeted by the intervention. The study was registered prior to analysis, ISRCTN34320836. ***Results:*** Frequency of targeted intrusions reduced by on average 64% from baseline to the postintervention phase. Conversely, never-targeted intrusions reduced in frequency by on average 11% over a comparable time-period. Of the 20 patients, 16 met our criteria for showing "response" to the intervention. ***Conclusions:*** Results provide initial evidence that this brief behavioral procedure might reduce the occurrence of intrusive traumatic memories in longstanding and complex PTSD, here delivered in an inpatient setting. The potential of this simple, focused intervention opens up new possibilities for tackling a core clinical symptom of PTSD, warranting further research.

What is the public health significance of this article?
This study provides first evidence that the frequency of intrusive memories of trauma for patients with longstanding and complex posttraumatic stress disorder might be reduced by a simple behavioral intervention. The intervention consists of a *memory reminder* procedure followed by playing the computer game *Tetris.*

Keywords: intrusive memory, posttraumatic stress disorder, computerized intervention, concurrent task interference, reconsolidation

Supplemental materials: http://dx.doi.org/10.1037/ccp0000340.supp

The experience of distressing intrusive memories of trauma that occur involuntarily in the form of sensory (mostly visual) mental images of the traumatic event(s) in posttraumatic stress disorder (PTSD) and acute stress disorder (American Psychiatric Association, 2013) forms their "core clinical feature" (a term forwarded by Kupfer & Regier, 2011).

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Existing treatments such as trauma-focused cognitive–behavioral therapy for PTSD are effective (NICE, 2005), but need highly trained therapists and require patients to describe and reexperience the memories of the traumatic event in detail, for example during imaginal exposure or enhanced reliving. Because there is a limited number of qualified therapists available and some patients are reluctant to discuss the traumatic event in detail (especially for complex PTSD; Courtois & Ford, 2015), the majority of patients do not receive adequate treatment, leading to high levels of suffering and societal costs (Kessler, 2000). One way to approach such complexity and clinical need is to follow the concept of "precision medicine" and target one key symptom—here intrusive memories—in a mechanistically driven behavioral intervention that could be provided by nonspecialists (Holmes, Craske, & Graybiel, 2014; Kazdin & Blase, 2011). Indeed a recent call in the context of PTSD has been to focus on evolving new approaches, such as those using memory reconsolidation (Hoge & Chard, 2018).

Cognitive science suggests that the perceptual-sensory (mostly visual) memories that form the basis of intrusions of trauma (Ehlers, Hackmann, & Michael, 2004; Speckens, Ehlers, Hackmann, Ruths, & Clark, 2007) can be disrupted via cognitive tasks that tax working memory, by competing for limited cognitive resources during the time window for memory consolidation (interference; Andrade, Kavanagh, & Baddeley, 1997; Baddeley & Andrade, 2000; Engelhard, van Uijen, & van den Hout, 2010; van den Hout, Muris, Salemink, & Kindt, 2001). Visuospatial tasks that have been examined in this context include concealed complex pattern tapping (Holmes, Brewin, & Hennessy, 2004) or more readily available tasks in daily life such as the computer game *Tetris* (Lau-Zhu, Holmes, Butterfield, & Holmes, 2017). Studies using the "trauma film" paradigm (James et al., 2016) with healthy participants have shown that, compared with control tasks, complex visuospatial tasks (administered during or soon after the film) can lead to reduced numbers of intrusions of experimental trauma (visual scenes from the film) during the subsequent week (Holmes, James, Coode-Bate, & Deeprose, 2009; Holmes, James, Kilford, & Deeprose, 2010).

The first studies applying the same principals to real-world trauma found that a behavioral intervention including *Tetris* gameplay in the first few hours after a traumatic event (the time window in which memory consolidation is thought to occur) reduced the occurrence of intrusive traumatic memories in the subsequent week, for both after a road traffic accident (Iyadurai et al., 2017) and after traumatic childbirth (Horsch et al., 2017). However, it remains to be demonstrated whether such an intervention could be beneficial for older memories of traumatic events in the context of longstanding and complex PTSD. This term covers patients with repetitive and long-lasting traumatic experiences, typically occurring in childhood, with the defining symptoms of PTSD but suffering from additional prolonged deficits in emotion regulation, self-perception, and relations with others (Herman, 1992).

The possibility of targeting older memories of trauma via a competing visuospatial task is suggested by the idea that there is other time windows in which memory can be altered (Visser, Lau-Zhu, Henson, & Holmes, 2018), inspired by work on memory *reconsolidation*. According to this theory, a previously consolidated memory can be rendered malleable via reactivation using a retrieval cue (Misanin, Miller, & Lewis, 1968; Nader, Schafe, & LeDoux, 2000). In order for the memory to persist it has to be restabilized—a process that can be disrupted or enhanced via an intervention. Drawing on the idea of so called "reconsolidation-update" mechanisms, it has been shown among healthy participants that a *memory reminder* procedure followed by *Tetris* gameplay could reduce the occurrence of intrusions even if administered 24 hr (James et al., 2015) after watching a trauma film. Note the term "reconsolidation-update" comes from the seminal articles translating earlier rodent findings to a human context (Schiller et al., 2010), but it is not to be confused with the term "update" used for example in cognitive behavior therapy techniques. Reconsolidation continues to be commonly defined as "the process by which memories can become destabilised at retrieval, and be updated or modified" (e.g., Vousden & Milton, 2017). Thus, the current approach seeks to target intrusive memories of older trauma by combining the ideas from visuospatial cognitive task interference with a potential reconsolidation-update mechanism.

It is worth considering some definition and debate with regards to the notion of cognitive task interference and the memory trace. In the field of experimental psychology, *"dual task methodology"* can be described as when two things are done simultaneously to be able to compare performance with each done alone. So that, if the results of doing two things concurrently is different to when they are done alone (typically deteriorate outcomes on at least one or the other process), these two tasks are thought to "*interfere*" or "*compete*" with each other, that is, compete for similar information processing resources. This interpretation of results from this approach assumes that information processing resources are limited and shareable. In terms of the effect, the "dual task" may, or may not, interfere or compete, say with a trauma memory trace which is active in working memory "at the same time as" the period the task is being performed. Thus, the term "*dual*" or "*concurrent*" alone can also refer to theory/process behind the method, that is, that two things happened at the same time. The term "dual task" is often used to refer to the task itself for example, eye movements, counting, and so forth. In this article, we use the term "concurrent task" here to mean a task performed at the same time of a memory supposedly being in mind. We next describe examples in the literature.

In the field of experimental psychopathology, elegant work by Engelhard, van den Hout, and colleagues has increasingly illuminated that the *general* ability to tax the central executive of working memory is important for reducing vividness and emotionality of that memory (e.g., Engelhard, van den Hout, & Smeets, 2011; Tadmor, McNally, & Engelhard, 2016; van den Hout & Engelhard, 2012; see also seminal work by Gunter & Bodner, 2008). Note a key outcome in this line of work has been the vividness of the memory. This work has been pivotal for the field of Eye Movement Desensitization and Reprocessing (e.g., van den Hout et al., 2011, 2012). Results provide an important insight not only theoretically, but clinically as it suggests we could increase the range of cognitive tasks that could be used. However, it is not yet known whether results on vividness extend to the reduction in number of *intrusive* memories. This line of work uses the term "dual task" interventions to mean performing two tasks simultaneously, typically instructions to engage in continuous memory recall and a secondary distracting task (e.g., making eye movements, counting). This may be contrasted to the term "single task" intervention for example, performing eye movements alone.

Other work in the field of experimental psychopathology, has also used the general notion of dual task methodology (e.g., Holmes et al., 2004; Holmes et al., 2009). In this line of work, the primary outcome measure has been the number of intrusive memories of the traumatic event. The idea visuospatial tasks might be particularly useful tasks to compete for resources with visual intrusive imagery, stems back to foundational experimental work in the lab by Andrade and colleagues (Andrade et al., 1997; Baddeley & Andrade, 2000), alongside early translational work with patients after trauma (Lilley, Andrade, Turpin, Sabin-Farrell, & Holmes, 2009), see also related work using eye movements (van den Hout et al., 2001). It has also been inspired by Brewin (e.g., Brewin, 2014).This line of work has a led to a notion that it will be useful to have at least some modality specificity between the task (e.g., eye movements) performed concurrently with the trauma memory, because most intrusive memories have a visual component (e.g., visual episodic recall to a hotspot scene within the traumatic event; Grey & Holmes, 2008; or to visual scenes in films). It seems that some visuospatial tasks (e.g., complex pattern tapping, playing *Tetris*) during or soon after the event fairly consistently lead to a reduction in the number of subsequent intrusive memories (Deeprose, Zhang, Dejong, Dalgleish, & Holmes, 2012; Holmes et al., 2004, 2009, 2010; Stuart, Holmes, & Brewin, 2006), whereas verbal tasks to date show more mixed effects (e.g., backward counting; the verbal computer game Pub Quiz; a word game); that is, some verbal tasks do reduce intrusions in some studies (e.g., Hagenaars, Holmes, Klaassen, & Elzinga, 2017), but sometimes have no effect, and in a limited number of studies can even *increase* intrusions indicating possible negative effects (Bourne, Frasquilho, Roth, & Holmes, 2010; Holmes et al., 2004, 2010). To err on the side of caution clinically, our first trial with a clinical sample used a visuospatial task (*Tetris*, Iyadurai et al., 2017). However, further research is needed to tease out the general versus modality specific aspects of those tasks most useful in translational interventions and for intrusive memories in particular. From a pragmatic point of view, the wider the range of tasks that could be used the better.

Henceforth in this article we use the term "concurrent task" or "cognitive interference task" for our use of *Tetris* in the intervention, as we provide a memory cue (hypothesized to reactivate a memory) prior to the *Tetris* game play, thus gameplay is thought to be concurrent to the memory being in mind. It is assumed that the memory trace is active concurrently, but even without method instructions for continuous memory recall during the task performance (see Visser et al., 2018). If a *memory reminder* cue had not been provided, we would not use the terms concurrent/cognitive interference task, as it could not be assumed there was a memory trace for the *Tetris* game play to interfere with (see e.g., the control conditions used in James et al., 2015).

In sum, our initial line of enquiry started out assuming the necessity of at least some modality specific taxation (visuospatial vs. verbal/conceptual). However, inspired by later research and theoretical articles by Engelhard and colleagues which shift more toward general working taxation or taxing attentional resources, and shifting away from the modality specific focus we believe it is also important to keep questioning our assumptions and test which range of tasks are optimal in future empirical studies on reducing intrusive memories.

The main question of the current study was whether, among inpatients with longstanding complex PTSD, a brief behavioral intervention including (a) briefly writing down the part of a traumatic memory corresponding to the content of a specific intrusion (intended as a memory reactivation procedure to start reconsolidation processes) then (b) 25 min of visuospatially demanding computer gameplay (*Tetris,* cognitive interference task) could reduce the frequency with which that specific intrusion of trauma was reexperienced by the patient in the following weeks.

We conducted an open-label single case series (Barlow, Nock, & Hersen, 2008) comprising 20 patients with longstanding complex PTSD who were in an inpatient setting for treatment purposes (for details see Procedure section). This sample (inpatients with PTSD) provided a number of advantages for testing the intervention procedure. First, an inpatient setting is a particularly safe and well-monitored environment for introducing a novel clinical intervention. Second, the setting is standardized across patients, reducing potential noise from variability in patients' home environments. Third, the outcome of interest (frequency of intrusive memories), requires monitoring and recording on an ongoing basis by patients, and the inpatient setting and ease of providing reminders to complete a diary facilitates this.

Patients recorded the occurrence of intrusive memories of trauma and their content (in the form of a very brief identifying label) in a paper-based diary for the duration of their inpatient admission (typically several weeks). In addition to the standard care received in the inpatient clinic (which was the same for each patient; see Procedure section), each week patients received one intervention session in which the content of an intrusive memory was targeted via the behavioral intervention summarized above (*memory reminder* plus computer gameplay). Therefore, for each patient, the targeting of specific intrusions was staggered weekly over the duration of their admission. This allowed us to examine whether targeting a specific intrusion was associated with a reduction in its frequency, via a within-subjects multiple baseline AB design (cf. Barlow et al., 2008; Nock, 2002). Further, as for most patients there were fewer intervention sessions available than number of specific intrusions (i.e., intrusions with different content), some intrusions were never targeted via the intervention (henceforth termed "nontargeted intrusions"), providing an additional within-subjects control comparison.

We hypothesized that the frequency of occurrence of a targeted intrusion would decrease following an intervention session in which it was targeted (via a *memory reminder* for that specific intrusion's content). The frequency of targeted intrusions postintervention could be compared prior to the intervention, and to intrusions that were never the focus of the intervention, all measured via a daily diary. We expected further that the reduction in intrusion frequency for targeted intrusions would be maintained for the remainder of the study. Conversely, we did not expect the frequency of nontargeted intrusions to decrease over the same time-frame. In addition, self-rated arousal levels before and after the *memory reminder* procedure, and after playing *Tetris,* alongside *Tetris* score were recorded. Finally, we collected secondary outcome measures including PTSD symptoms, depression, and anxiety each week to provide information on the broader change in symptoms over the course of the treatment.

Method

Participants

Participants were 20 adult inpatients (mean age 33.20 years [*SD* = 11.34], 19 female, all Caucasian) treated at the Department of Psychosomatic Medicine and Psychotherapy, LWL-University Hospital, Ruhr-Universität Bochum. Patients all had complex PTSD in the sense of Herman (1992). This term covers patients whose traumatic experiences were repetitive and long-lasting (typically months to years, often occurring in childhood), that suffer from the defining symptoms of PTSD (intrusions, hyperarousal, avoidance) as described in the *DSM-5* (American Psychiatric Association, 2013) and that also show prolonged deficits in—among other areas—emotion regulation, self-perception, and relations with others. On admission each new patient was screened regarding the inclusion and exclusion criteria and, if applicable, asked whether she/he was interested in participating. Inclusion criteria were as follows: (a) age 18–65; (b) diagnosis of PTSD (F43.1; International Classification of Diseases, 10th revision, World Health Organization, 1993; diagnosed prior to inpatient admission via structured clinical interviews in the outpatient department of the hospital; (c) reporting the occurrence of at least five intrusive memories of trauma during the week preceding admission (participant self-report); (d) able and willing to complete an intrusion diary over the duration of the study (corresponding to the inpatient admission period); (e) able and willing to play *Tetris* on a tablet computer; (f) fluent in written and spoken German. Exclusion criteria were (a) recent substance abuse (within past 6 months) according to participant self-report; and (b) suicidal plans or persistent ideation according to participant self-report. There were no exclusion criteria regarding other comorbid diagnoses or use of medication (see Supplementary Table 1 for details).

The study received ethical approval from the ethics committee of the Faculty of Psychology of Ruhr-Universität Bochum (No. 157/2014). All participants provided their written and informed consent. This study is registered with the ISRCTN registry, number ISRCTN34320836, with registration prior to data analysis. Supplementary Table 1 provides information about patients' demographic and clinical characteristics.

Design

The design was a single case series in accordance with guidelines as described in Kratochwill et al. (2010), with number of intrusions (intrusive memories of trauma) as the main outcome of interest. Occurrence of intrusions was measured by patients continuously during the course of their inpatient stay (~5 to 10 weeks) in a diary (see Measures section), in which they noted the number of intrusions occurring in each of three time-windows per day (morning, afternoon, evening/night). Each week of monitoring therefore comprised 21 observation points.

A within-subjects multiple baseline AB design (cf. Barlow et al., 2008; Nock, 2002) was used to provide evidence of specificity of the intervention (i.e., that the decrease in frequency of a specific intrusion was associated with the targeting of that specific intrusion in an intervention session). Following a monitoring-only period of 1 to 2 weeks (initial part of the baseline phase), patients received weekly intervention sessions in which a specific intrusion was targeted (see Intervention section below). For each specific intrusion, the period prior to that intrusion being targeted in an intervention session was designated the baseline phase ("A;" i.e., monitoring-only plus the additional weeks in which it remained untargeted by the intervention). The period after the intrusion was targeted was designated the postintervention phase ("B"). Thus, there are multiple baselines as different intrusions were targeted in different weeks. The independent variable (intervention session) was actively manipulated in that an intrusion was targeted in given intervention session. The intrusion to be targeted was selected collaboratively by patient and therapist, and was generally that that had been the most distressing over the previous week(s).

For each patient there were therefore between two and seven AB replications, depending on the number of intrusions targeted, with baseline phases for each intrusion ranging from 2 to 7 weeks. Across patients and specific intrusions, the intervention effect was investigated a total of 75 times, across seven different time-points. Multiple replications of a specific pattern of decrease in intrusion frequency following targeting in an intervention session (across both intrusions and participants) would provide compelling evidence for a specific effect of the intervention, as opposed to nonspecific effects such as passage of time or the general inpatient treatment program. As some intrusions were never targeted in an intervention session, the course of these nontargeted intrusions over time provided an additional control against which to compare the change in frequency of targeted intrusions.

Measures

Intrusion diary. The intrusion diary was adapted from that used in previous experimental and clinical studies (e.g., Iyadurai et al., 2017; Holmes et al., 2004; James et al., 2015). Instructions in how to use the diary included a definition of intrusive memories of traumatic events as being "mental images" ("in the form of pictures or a film in your mind's eye") that were distressing/disturbing and occurred involuntarily ("pop into your mind"). Participants were requested not to report verbal thoughts without sensory content.

Before using the diary, patients identified and labeled individual sections of their trauma memories that they tended to reexperience in the form of intrusions (e.g., the moment where the knife was pointed at them, i.e., "hotspots;" Grey & Holmes, 2008; Holmes, Grey, & Young, 2005). This was done with the help of a therapist and they labeled them with a keyword and a letter (e.g., Hotspot A: knife, Hotspot B: bedroom, Hotspot C: neighbor). When completing the diary, patients noted what the content of the intrusion had been by indicating the corresponding hotspot (e.g., "A"). Though it was not assessed systematically, patients commonly reported hotspots from different traumatic events, but occasionally named more than one hotspot per traumatic event.

Patients then recorded the occurrence of each specific intrusion (i.e., corresponding to each individual hotspot) continuously over the weeks of inpatient treatment (main outcome variable for each individual patient). This yielded information on the number of different specific intrusions per week corresponding to each hotspot, and the total number of intrusions per week. For example, in 1 week a patient may record 12 intrusions in total: seven corresponding to Hotspot A, four to Hotspot B, and one to Hotspot C (see Figure 1, hotspots differentiated by symbols).

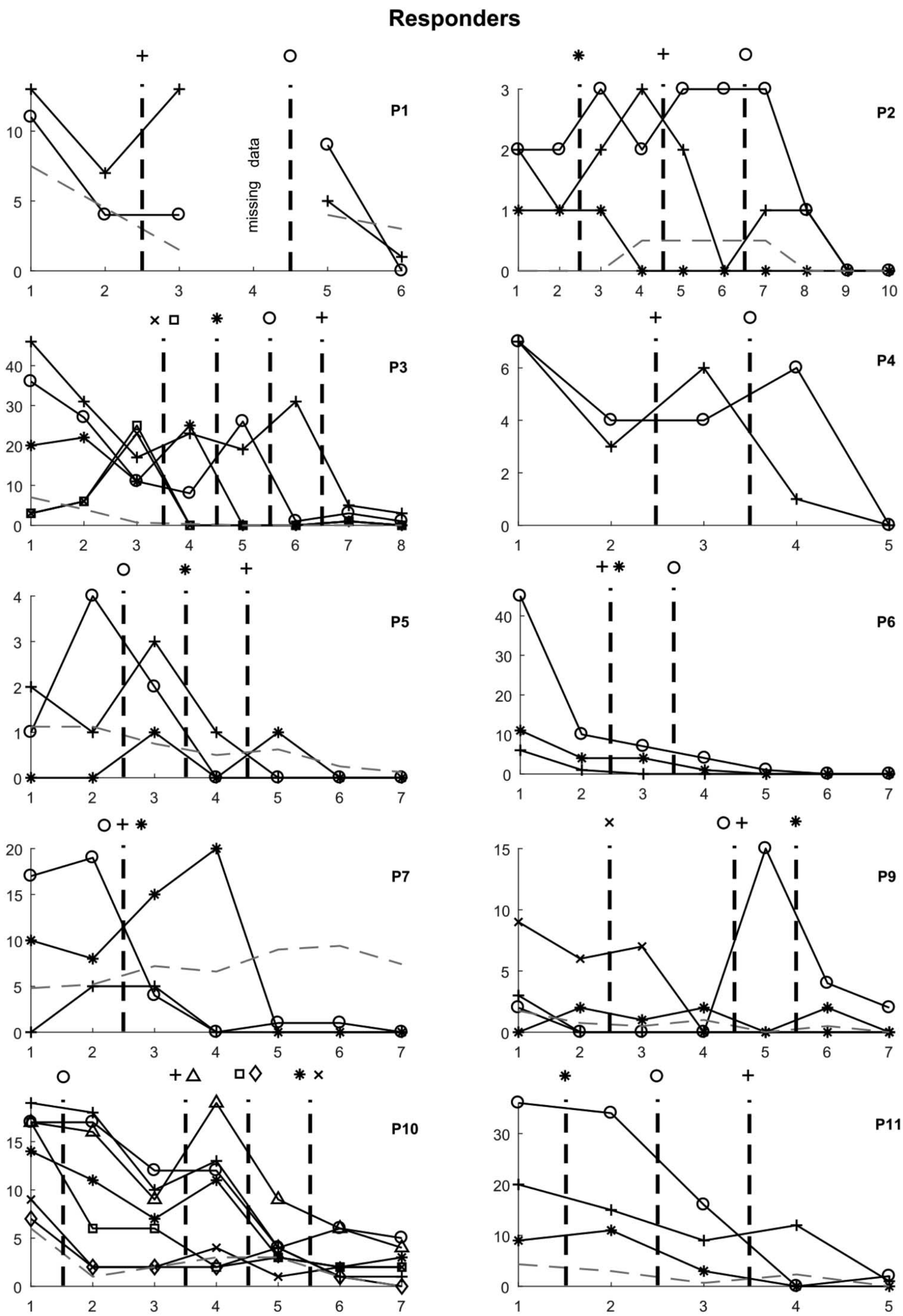

Figure 1. Individual patient time courses for each of their targeted intrusive memories of trauma (intrusions) indicating time points of intervention. Depicted is the number of intrusions per week (y-axis) for each targeted intrusion separately (solid black lines, differentiated by symbol, range 2–7 per patient) for each week of inpatient treatment stay (x-axis). All nontargeted intrusions for each patient are summarized (means per week) in one dashed gray line for comparison. Vertical dashed lines indicate time points of intervention delivery (i.e., when the intrusion is targeted) with symbol above indicating which of the targeted intrusion(s) are the focus of the intervention (represented by corresponding symbol to their lines). Multiple symbols over one vertical dashed line indicate that multiple intrusions were targeted that week (P3, Week 4; P7, Week 3 [two intrusions in one session, another intrusion in a separate session = 3 intrusions in this week]; P14, Week 3 and Week 7; P17, Week 4; P18, Week 2; P20, Week 4). Patients are classified as responders if >50% of targeted intrusions decrease by >50% after the intervention. P1–P20: Patient codes (assigned by the order of admission).

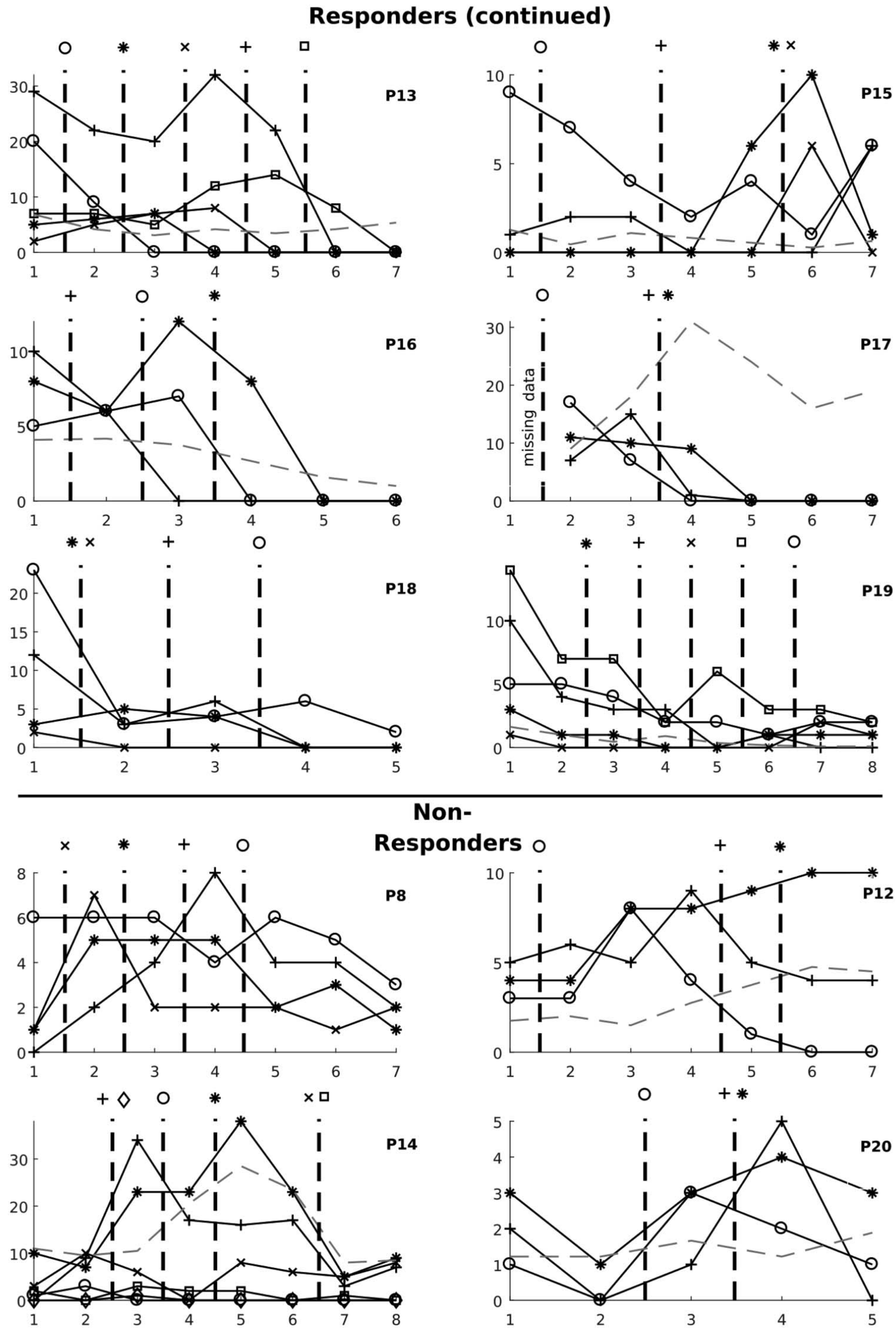

Figure 1. (*continued*)

Impact of Events Scale—Revised (IES-R). The IES-R (Weiss & Marmar, 1996) is a widely used measure assessing the severity of reexperiencing, avoidance, and hyperarousal in relation to a traumatic event. It consists of 22 items, each with a 4-point scale anchored from 0 (*not at all*) to 3 (*often*). A German version was used (Maercker & Schützwohl, 1998). The IES-R consists of three subscales (intrusions, hyperarousal, and avoidance). For the German version, Cronbach's alpha is 0.90 for the intrusion subscale, 0.90 for the hyperarousal subscale, and 0.79 for the avoidance subscale. Test–retest reliability is 0.80 for the intrusion subscale, 0.79 for the hyperarousal subscale, and 0.66 for the avoidance subscale. Convergent validity is 0.59 for the intrusion subscale, 0.72 for the hyperarousal subscale, and 0.53 for the avoidance subscale (correlated with German diagnostic Interview DIPS, "Diagnostisches Interview bei psychischen Störungen;" Schneider & Margraf, 2011). Discriminant validity has been assessed in comparison to BDI (Beck Depression Inventory), BAI (Beck Anxiety Inventory), and SCL-GSI (Symptom Check List, Global Severity Index) scores. Correlations are: intrusion subscale: 0.44 (BDI), 0.58 (BAI), 0.59 (SCL-GSI); hyperarousal subscale: 0.63 (BDI), 0.73 (BAI), 0.72 (SCL-GSI); avoidance subscale: 0.35 (BDI), 0.50 (BAI), 0.45 (SCL-GSI; Maercker & Schützwohl, 1998). Due to an error with data collection, for the final three participants there is no IES-R available.

Beck Depression Inventory-II (BDI-II). The BDI-II (Beck, Steer, & Brown, 1996) was used to assess depressed mood and has 21 self-report items each with a scale of 0–3. Scores range from 0 to 63. A German version was used (Hautzinger, Keller, & Kühner, 2006). For the German version, Cronbach's alpha is >0.84. Test–retest reliability is 0.78 for nonclinical samples, and 0.47 for clinical samples. Convergent validity is between 0.68 and 0.89 (compared with MADRS and PHQ-9), discriminant validity (compared with BAI) is between 0.60 and 0.65 (Kühner, Bürger, Keller, & Hautzinger, 2007).

Beck Anxiety Inventory (BAI). The BAI (Beck & Steer, 1993) is a measure assessing experience of symptoms of anxiety. It consists of 21 items, each with a 4-point scale anchored from 0 (*not at all*) to 3 (*strongly*). A German version was used (Margraf & Ehlers, 2002). Cronbach's alpha was found to be >0.90 in several samples, test–retest reliability was between 0.62 and 0.92 across clinical and nonclinical samples. Convergent validity was between 0.50 and 0.60 for different measures of anxiety. Discriminant validity was between 0.48 and 0.55 for correlations with measures of depression (Margraf & Ehlers, 2002).

Within-intervention session measures. Subjective levels of arousal were assessed before and after the *memory reminder* procedure, and after playing *Tetris,* on an 11-point scale from 0 (*calm*) to 10 (*maximum arousal*), anchored at extremes. This was done in order to check that patients were adequately engaged in the *memory reminder* (increase in arousal), to look for potential immediate effects of the intervention (drop in arousal possibly reflecting relief of distress) and to compare arousal changes with other clinical variables. In our work with patients we were also careful to check in on their experience throughout the session. Additionally, the highest *Tetris* score reached for each individual intervention session was recorded. *Tetris* high score was chosen for pragmatic reasons because the version of *Tetris* used in this study did not allow for calculation of a cumulative score across several games (which had been used in previous studies, cf. James et al., 2015), and we did not want patients to interrupt game play in order to write down scores of individual games.

Intervention

In each intervention session, one of the intrusive memories (hotspots) the patient reported in the diary (with some exceptions, described below) was selected for targeting based on clinical discussion. The intervention session comprised two phases, a *memory reminder procedure* (hypothesized to reactive the memory and render it labile) followed by *Tetris* gameplay, with the therapist present in the room but not actively involved.

During the first phase participants wrote down the content ("script") of the intrusion corresponding to the specific hotspot in a third person narrative (intended to create some distance from the event). Participants were instructed to provide only as much detail as necessary to remember the traumatic event but without it being emotionally overwhelming (in order to start a memory "reactivation" process but not designed as an exposure/reliving procedure per se). Patients were provided with one blank sheet of paper and a pen with no constraints concerning minimum or maximum length of the narrative. The sheet of paper containing the script was then shredded by the patient, and the content was not discussed with the therapist. Therefore, there is no exact data on how long the narratives were, but no patient had more than one hand-written page of A4 paper, most had less.

In the second phase, which followed on immediately after the first, participants played *Tetris* for 25 min on a tablet computer (restarting the game if "game over" was reached). After playing, participants continued with their daily program on the ward. Participants rated their subjective levels of arousal before and after the *memory reminder* procedure, and after playing *Tetris.* A record was also kept of their highest *Tetris* score (possible range: 0 to infinite points) reached for each session.

For six patients, there were instances where two distinct intrusive memories were targeted in one session (see Figure 1 for details), via the patients writing one script which included the content of two intrusions. This occurred when two intrusions were linked temporally or with regards to content in such a way that it was judged to make more clinical sense to write one script including the content of both intrusions rather than to separate the content out into two distinct scripts and intervention sessions.

After providing the instructions and writing materials, the person administering the intervention session remained in the room, but without actively engaging (i.e., they generally sat at a separate table and read/carried out administrative tasks). They never read the memory script nor discussed any aspect of the memory content. For the first 18 patients the intervention was administered by the patient's individual therapist, and for the final two by a research assistant. Having the intervention therapist-administered initially was chosen due to the novel nature of the procedure in this clinical population, in case intervention by a trained therapist was urgently required (e.g., if the procedure had elicited extreme distress). However, no such intervention was ever required, and because the role of the therapist was limited to providing the instructions and materials then waiting for the patient to finish (and no discussion of the content), it was judged appropriate for this to be carried out by someone without specialist therapy training.

We used the mobile version of *Tetris* created by Electronic Arts (EA Mobile Montreal Team, 2014), Version 1.0.3, set to "Marathon" on a 10.1-in. Samsung Galaxy Tab 2. In *Tetris*, seven differently shaped geometric blocks fall from the top to the bottom of the screen in a random sequence one at a time. The blocks can be moved (left, right, rotated 90° clockwise or accelerated) as they fall to the bottom of the screen by touching the tablet screen accordingly. The aim is to create complete horizontal lines across the playing area with the blocks. Each time a full horizontal line is created it disappears, and points are awarded. In the current study patients were reminded to focus on the three blocks due to fall after the one that they were currently manipulating (these blocks were displayed in a preview to the right of the screen). Patients were asked to work out in their “mind’s eye” where best to place these blocks in order to create the horizontal lines to be awarded points, as in James et al. (2015). The theoretical rationale for this was to enhance the visuospatial demands of the game by encouraging mental rotation. We note that the game is also adaptive, that is, the gameplay difficulty changes in relation to how well the player is playing.

Before the start of the intervention phase, participants had two “practice” game sessions as a “run in.” The first lasted only 5 min, aiming to check whether the participant knows how to play and addressing any queries after gameplay. The second lasted until the participant reached “game over.”

Note the person administering the intervention session was given appropriate training and monitoring by the study team. The team also had extensive experience in using the intervention procedure in an experimental lab setting before moving to a clinical setting. We note that any test of replication should involve adequate training and monitoring.

Procedure

After inclusion in the study, participants received an explanation as to how to use the diary and were asked to fill out the first set of outcome questionnaires (IES-R, BDI-II, BAI). They were given instructions on how to play *Tetris* to prepare them for the upcoming intervention sessions, as well as instructions as to completing the diary and a diary for the first week. Patients were provided with a new diary and set of questionnaires each week by a research assistant, who also collected the previous week’s diary.

During the complete period of the study (i.e., the inpatient stay) all participants received standard inpatient PTSD treatment, which each week involved one session of individual cognitive–behavioral therapy provided by experienced therapists, three sessions of trauma group therapy, two sessions of trauma stabilization group therapy, two sessions of kinesitherapy, two sessions of art therapy, physiotherapy, clinical rounds, and daily short sessions with a nurse.

During the first 1 or 2 weeks of the study participants only monitored their intrusions in the diary and had the regular inpatient treatment, but did not receive the specific intervention described above (baseline phase “A”). Three patients (P4, P8, and P17) were recruited not in their first week of inpatient treatment, but in their second or third week. P4 and P8 were asked to estimate the number of intrusions experienced before starting the intrusion diary, while no estimate could be obtained from P17 due to her high level of distress at the beginning of her admission.

The intervention period started in Week 2 or 3 (or as indicated above) and lasted until hospital discharge. From then on, participants received the study-specific intervention sessions supervised by their therapist, and were intended to take place on a weekly basis (albeit with some minor variations for practical reasons; see Results section).

The discharge date from the hospital was decided clinically in relation to the broader inpatient treatment (i.e., independent of the study procedures). Once the discharge date had been set, the last intervention was provided during the week before discharge and the last meeting with the research assistant before discharge was used to collect the last diary and to provide and collect the last questionnaire set.

Data Analysis

Intrusion data were analyzed at the level of specific intrusions. The mean number of intrusions per week (as recorded in the intrusion diary) was calculated for the baseline period (prior to which the intervention occurred) and the postintervention period (after the intervention and ending with the last meeting with the research assistant before patients’ discharge) for each individual targeted intrusion. Percentage reduction in intrusion frequency (i.e., [1 − (mean number per week postintervention/mean number per week during baseline)] ∗ 100) was calculated to provide an index corresponding to the magnitude of decrease. Similarly, mean number of intrusions per week was calculated for the first and second half of inpatient treatment for nontargeted intrusions as an equivalent time-frame for comparison, and percentage reduction scores also calculated.

To provide a metric of whether a specific intrusion had “responded” to the intervention, we classified “response” as a percentage reduction of greater than 50%. We classified a patient as a “responder” (i.e., showing a response in terms of intrusion reduction to the intervention) if more than 50% of their intrusions showed a “response.”

To test whether reduction in intrusion frequency after intervention was maintained, we examined for all targeted intrusions whether all postintervention values were below (Criterion 1) mean or (Criterion 2) minimal values of the baseline period of that intrusion.

To test whether, on average, frequency of intrusive memories was lower for targeted compared to nontargeted in the postintervention compared to baseline phase (or comparison timeframe for nontargeted intrusions), we conducted a repeated-measures ANCOVA with mean number of intrusions per week in the postintervention period (aggregated across all specific intrusions) as dependent variable, targeted versus nontargeted as within-subjects factor, and mean difference between number of intrusions per week during the baseline phase for targeted versus nontargeted intrusions as covariate. This is a common approach that has been used in other studies as well (Zhang et al., 2014).

In addition to the repeated-measures ANCOVA, we conducted another analysis, in which reduction of intraindividual means of intrusion frequency of targeted hotspots from baseline to postintervention period was compared with intraindividual means of reduction within the baseline period of later targeted hotspots (second half of baseline period vs. first half), using a paired-sample *t* test.

To find further support for the specificity of the intervention’s effect, sets of three-week intervals were constructed for each individual intrusion. Slopes of (linear) regression lines were then compared between intervals in which an intervention session had taken place in the middle of the interval (i.e., the second week of the three-week-interval, “intervals of interest”) and all other intervals. Intrusions that were targeted by our intervention were typically the most disturbing and most frequently occurring ones, while other (nontargeted) intrusions tended to occur less frequently from the beginning. In order to minimize possible floor effects due to low frequency of nontargeted intrusions, intervals of interest were also compared to other intervals only for targeted intrusions. Slopes were compared using two-tailed Mann–Whitney *U* tests.

To assess if a patient showed clinically meaningful reductions on overall symptom measures, we compared the initial and final questionnaires scores. For depression and anxiety, we used established cut-off criteria of moderate depression (BDI-II >18), and moderate levels of anxiety (BAI >15). Because no cut-off exists for the German version of the IES-R, response was defined as a 50% reduction of the total or intrusion subscale score.

In addition, we examined the correlations between the extent of reduction in intrusions with amount of overall clinical improvement (as measured by the BDI, BAI, and IES-R). To correlate reduction in intrusion frequency with overall clinical improvement, Pearson correlations were performed between change in intrusion frequency (from pre- to postintervention) and change in questionnaire scores (from first week to last week).

Changes in arousal (pre- to postmemory recall, and pre- to post-*Tetris* gameplay) were calculated. Mean change in arousal during *Tetris* gameplay and mean *Tetris* scores were compared between responding and nonresponding intrusions. Spearman correlations were conducted between relative reduction of intrusion frequency from baseline to postintervention, *Tetris* scores, and arousal change, across all targeted intrusions.

All data were analyzed using IBM SPSS statistics (versions 24 + 25), and MATLAB (the MathWorks, Inc., version R2017a).

Results

Overall Number of Intrusions and Course of Treatment

The 20 patients that comprised our sample reported a total of 159 specific intrusions (i.e., corresponding to different hotspots; individual range: 2–16). Of these, 75 were targeted by the intervention (range per patient: 2–7), while 84 remained nontargeted (range per patient: 0–11). Median duration of inpatient treatment was 7 weeks (range: 5–10 weeks).

It was planned that participants would receive one intervention session per week. However, due to practical reasons (e.g., overlap with regular inpatient treatments, stability/instability of the patient, availability of individual therapist), actual frequency of intervention sessions varied (range 0–3 sessions per week), with $M = 0.89$ ($SD = 0.34$) across all 20 patients.

Reduction in Targeted and Nontargeted Intrusions

Figure 1 displays the time courses for each of the 20 patients individually for each of their targeted intrusions (two to seven lines separately) and all nontargeted intrusions together (one line). Table 1 provides mean intrusion frequency per week separately for each targeted intrusive memory (hotspot) in the baseline (“A”) and postintervention (“B”) phases, and the intrusion frequency of nontargeted intrusive memories (hotspots) for the first and second half of treatment, aggregated over all nontargeted intrusive memories. Visual inspection suggests that targeting a specific intrusion (dashed vertical lines) is frequently followed by a sudden drop in frequency of that specific intrusion, often to zero, either in the week directly following the intervention or 1 week later on.

On average, targeted intrusions showed a reduction of 64% ($SD = 68\%$) in frequency from baseline to postintervention. Applying the criteria for an intrusion response, defined as a reduction of more than 50% from baseline to postintervention period, 77% (58 out of 75) of targeted intrusions responded to the intervention. Of the 20 patients, 16 showed responses for the majority (>50%) of their targeted intrusions, and were thus considered “responders.” Eleven patients showed response for *every* intrusion. Only one patient (P12) did not show response for any intrusions: Two of three targeted intrusions decreased only slightly, while all other intrusions showed an increase in frequency.

Concerning the question whether the reduction in intrusion frequency was maintained after the intervention, we found that across all participants, in 80.0% (60 out of 75) of targeted intrusions, all postintervention values were below the mean of the baseline period for that intrusion (Criterion 1). In 45.3% of intrusions (34 out of 75), all postintervention values were even below the minimal value within the baseline period (Criterion 2). On the patient level, for 80.0% of patients (16 out of 20), Criterion 1 was fulfilled in >50% of their targeted intrusions, and for 40.0% (eight out of 20 patients), Criterion 2 was fulfilled in >50% of targeted intrusions.

Time courses of nontargeted intrusions appeared more ambiguous on visual inspection. Because the focus of the intervention sessions had been on those intrusions that were chosen as most distressing to patients based on clinical discussion (and thus typically most frequently experienced), intrusion frequencies of those nontargeted intrusions were usually lower from the beginning of the baseline period, but also throughout the treatment. On average, nontargeted intrusions decreased by 11% ($SD = 123\%$) from first to second half of treatment. In total, 49% of all nontargeted intrusions had a reduction of more than 50% from first to second half of treatment.

A repeated-measures ANCOVA comparing mean number of targeted versus nontargeted intrusions per week in the postintervention period (or second half of treatment for nontargeted), with mean baseline difference between targeted and nontargeted intrusions as a covariate, showed a significant effect of targeted versus nontargeted, $F(1, 14) = 12.42$, $p = .003$, $\eta^2 = 0.47$, indicating that postintervention intrusion frequency was lower for targeted compared with comparison time frame of nontargeted intrusions while controlling for baseline differences. There was a significant effect of the covariate, $F(1, 14) = 9.14$; $p = .009$; $\eta^2 = 0.40$, and a significant interaction between targeted/nontargeted condition and baseline-difference, $F(1, 14) = 10.35$; $p = .006$; $\eta^2 = 0.43$.

Mean reduction in intrusion frequency of targeted hotspots was significantly larger from pre- to postintervention period, compared with first versus second half of baseline period: 5.60 (4.84) vs. 0.99 (4.35); 95% CI [2.69, 6.54]; $t_{19} = 5.01$; $p < .001$.

To further underpin our assumption of a specific and quickly occurring intervention effect, a set of three-week-intervals was formed for each individual intrusion, and the slope of the regression line was calculated for each interval, showing the change in frequency in that interval. The regression line slopes of intervals that included an intervention session in the second week (i.e., first week: preintervention; second week: intervention; third week: postintervention) were then compared with the slopes of all other three-week-intervals in a first step. We observed a greater reduction slope around the intervention, compared with other time windows: mean −2.54 (4.50) versus −0.48 (2.94); $n_1 = 72$; $n_2 = 684$; $U = 18812$; $Z = 4.81$; $p < 10^{-5;}$ $g = 0.66$; 95% CI [0.41, 0.91]. In a next step, intervals around the intervention were com-

Table 1
Mean Number of Intrusions Per Week for (I) Each Targeted Intrusive Memory (Hotspot) at Baseline ("A," Preintervention) and Postintervention ("B") With Relative Reduction (in %), as Well as (II) Mean Number Per Week of All Nontargeted Intrusive Memories Combined, Over a Comparable Time Period ("A" = First Half of Treatment, "B" = Second Half of Treatment)

	Number of intrusive memories per week									
	Targeted memories (one column per memory/hotspot)									
	Intrusive memories showing "response" (>50% reduction)						Intrusive memories not showing "response"			Nontargeted memories
Patient code	1	2	3	4	5	6	1	2	3	mean (*SD*)
Responders										
P01										
A	7.00	11.00								4.50 (4.95)
B	.00	3.00								3.50 (1.41)
% red.	100	73								22
P02										
A	2.57	2.00	1.00							.20 (.00)
B	.33	.40	.00							.20 (.28)
% red.	87	80	100							0
P03										
A	18.17	24.57	15.60	8.00	8.50					3.00 (4.55)
B	2.00	3.00	.33	.25	.25					.00 (.00)
% red.	89	88	98	97	97					100
P04										
A	5.25	5.33								n/a
B	.00	.50								n/a
% red.	100	91								n/a
P05										
A	2.33	1.40					.25			1.06 (1.05)
B	.00	.00					.33			.41 (.57)
% red.	100	100					−33			62
P06										
A	16.50	2.33	6.33							n/a
B	.33	.00	.25							n/a
% red.	98	100	96							n/a
P07										
A	13.33	3.33	11.00							5.86 (1.82)
B	.50	.00	5.00							8.31 (2.59)
% red.	96	100	55							−42
P09										
A	.60	1.17	7.33				3.40			1.00 (.35)
B	.00	.00	.00				3.00			.29 (.48)
% red.	100	100	100				12			71
P10										
A	17.00	15.00	8.00	6.80	3.40	15.25	3.33			3.00
B	7.80	2.00	3.00	2.00	.50	6.33	2.00			1.57
% red.	54	87	63	71	85	58	40			48
P11										
A	28.67	14.00	10.00							3.07 (4.31)
B	1.00	1.00	1.00							1.07 (1.22)
% red.	97	93	90							65
P13										
A	14.50	25.00	6.00	5.50	8.83					4.62 (4.65)
B	.00	.00	.00	.00	.00					4.31 (3.14)
% red.	100	100	100	100	100					7
P15										
A	8.00	2.67	1.00				1.25			1.13 (1.61)
B	3.40	1.00	.00				2.00			.65 (1.22)
% red.	58	63	100				−60			42
P16										
A	6.00	8.00	8.50							4.80 (4.12)
B	.00	.00	.00							2.10 (2.27)
% red.	100	100	100							56
P17										
A	17.00	7.67	10.00							19.33
B	1.40	.00	.00							19.67
% red.	92	100	100							−2
P18										

(*table continues*)

Table 1 (*continued*)

	Number of intrusive memories per week									
	Targeted memories (one column per memory/hotspot)									
	Intrusive memories showing "response" (>50% reduction)						Intrusive memories not showing "response"			Nontargeted memories mean (*SD*)
Patient code	1	2	3	4	5	6	1	2	3	
A	9.00	7.00	4.00	1.00						n/a
B	2.00	.00	1.33	.00						n/a
% red.	78	100	67	100						n/a
P19										
A	5.00	1.67	6.50				3.00	.20		1.00 (.76)
B	.25	.60	2.50				2.00	1.00		.18 (.42)
% red.	95	64	62				33	−400		82
Nonresponders										
P08										
A	4.00						5.60	3.50	3.67	n/a
B	1.80						4.00	3.33	2.75	n/a
% red.	55						29	5	25	n/a
P12										
A							3.00	6.00	7.17	1.89 (1.22)
B							2.60	4.00	10.00	4.11 (1.60)
% red.							13	33	−40	−117
P14										
A	1.00	1.43	.33				14.33	20.20	5.43	12.88 (17.85)
B	.00	.00	.00				12.00	12.33	8.00	17.13 (24.22)
% red.	100	100	100				16	39	−47	−33
P20										
A	2.00						1.33	2.75		1.31 (.85)
B	.00						1.50	3.00		1.58 (1.02)
% red.	100						−13	−9		−20

Note. Targeted memories are grouped into those showing "response" (left) and "nonresponses" (right), and patients are grouped into "responders" and "nonresponders." "Patient codes" P01–P20 were assigned by the order of admission. *SD* = standard deviation, provided if there was >1 nontargeted hotspot. "Responders" = 16 patients were classified as responders (>50% of targeted intrusions showed a response), whereas the remaining four were "nonresponders." For four patients, all intrusions were targeted ("n/a" in column for nontargeted intrusive memories).

pared to other intervals only for targeted intrusions (i.e., all intervals belonging to intrusions that were *never* targeted by the intervention were left out of the analysis). Again, reduction slopes were more negative around the intervention, compared to the other time windows: mean −2.54 (4.50) versus −0.86 (3.49); $n_1 = 72$; $n_2 = 281$; U = 10281; Z = 3.19; $p = .0014$; g = 0.45; 95% CI [0.19, 0.71].

Overall Symptom Measures

Questionnaire data are provided in Supplementary Tables 2–5. At admission, all 20 patients were above the cut-off for depression (BDI-II >18), and 18 out of 20 showed at least moderate levels of anxiety (BAI >15). At discharge, 11 patients (55%) were below the cut-off for depression and 10 patients had moderate anxiety. Concerning symptoms of PTSD, seven patients out of 17 who were administered the IES-R (41%) showed a response (more than 50% reduction) in total IES-R scores, and eight (47%) showed a response in the intrusion subscale of IES-R. Hence, about half of the patients showed significant overall clinical improvement according to these criteria over the course of treatment.

For targeted intrusions, reduction in intrusion frequency was significantly positively correlated with reduction in BDI-II scores ($r = .57$; $p = .009$) and BAI scores ($r = .51$; $p = .021$), but not with reduction in IES-R total ($r = .29$; $p = .26$) or intrusion subscale scores ($r = .28$; $r = .28$). For nontargeted intrusions, there were significant positive correlations with reduction in IES-R total score ($r = .56$; $p = .039$) and IES-R intrusion subscale scores ($r = .58$; $p = .031$), but not with BDI-II ($r = .48$; $p = .063$) or BAI ($r = .44$; $p = .086$).

Within-Intervention Session Measures

There was missing data on arousal levels for two out of a total of 75 targeted intrusions. Mean arousal increased from 7.19 (*SD* = 2.78) before to 8.96 (*SD* = 1.55) after the *memory reminder* procedure across all intrusions, and decreased to 5.92 (*SD* = 2.18) after *Tetris* gameplay across all intrusions. This decrease in arousal showed a trend to be more pronounced for intrusions that showed a response (3.23 [*SD* = 1.76]) compared with nonresponding intrusions (2.41 [1.70])], using a Mann–Whitney *U* test (U = 330, z = −1.93, $p = .053$).

Mean highest gameplay *Tetris* score for intrusions considered to be "responders" was 88,525 (*SD* = 73,098), and 98,214 (*SD* = 77,355) for "nonresponders." *Tetris* scores were not significantly correlated with the decrease in arousal from before to after *Tetris* gameplay, $\rho(72) = 0.11$, $p = .34$. Relative reduction of intrusion frequency postintervention was not significantly correlated with *Tetris* scores, $\rho(72) = 0.12$, $p = .31$; arousal change during the *memory reminder* procedure, $\rho(73) = -0.004$, $p = .97$; or arousal change during *Tetris* gameplay, $\rho(73) = 0.17$, $p = .15$.

Discussion

As part of our research drive to translate basic science into clinically useful intervention techniques, we tested in a pragmatic single case series with 20 inpatients with longstanding and complex PTSD whether a novel intervention derived from cognitive science (based on the ideas of visuospatial interference and reconsolidation-update mechanisms) could help reduce the frequency of intrusive memories of trauma. This research was motivated by the potential value of offering a mechanistically driven intervention targeting intrusions as the core symptom of PTSD that could be administered by nonspecialists, without patients having to discuss extensively the distressing details of their trauma or purposefully relive traumatic events, as is required for example by exposure therapy.

Overall, the pattern of change of intrusion frequencies over the course of treatment supported our hypotheses: Targeting a specific intrusion via the intervention led to a reduction in the frequency of occurrence of that specific intrusion that was maintained for the remainder of the study. The majority of the intrusions showed a decrease in frequency after the intervention, and the majority of patients had decreases in intrusion frequency for most of their targeted intrusions. Visual inspection of the intrusion trajectories suggests a sharp decrease in frequency of specific intrusions in the 1 or 2 weeks after being targeted via the intervention, rather than a uniform nonspecific decrease in all intrusions over time, consistent with a specific effect of the intervention rather than nonspecific effects such as the passage of time or the broader inpatient treatment program. Additional analyses strengthen the hypothesis of a specific effect of the intervention with targeted intrusions having a significantly steeper decline in frequency from pre- to postbaseline than within the baseline period before the intervention. Additionally, the three-week-intervals around the intervention show a significantly steeper decline than all other three-week-intervals for the later targeted intrusions "outside" the intervention. Further, nontargeted intrusions showed a more mixed picture with varying courses of intrusion frequency and a weaker, less consistent decrease over the course of treatment, strengthening the argument of a specific intrusion-focused treatment effect. Thus, overall the data provide the multiple replications across both intrusions and participants of the specific pattern of decrease in intrusion frequency following intervention sessions that we would require to feel some confidence about the intervention at this stage of research.

Our results therefore extend work investigating the potential of visuospatial interference tasks to reduce the frequency of intrusive memories in analogue (e.g., James et al., 2015) or actual recent (Horsch et al., 2017; Iyadurai et al., 2017) trauma to older trauma memories with a complex patient sample with longstanding complex PTSD. These early stage initial results indicate that such tasks may be adapted for development as clinical applications even in a complex chronic sample.

Of the four patients classified as "nonresponders," two (P8 and P12) were diagnosed with borderline personality disorder. All four patients had been identified by clinicians as having particular difficulties with persistent dysfunctional cognitions such as a tendency to overidentify with the trauma, ambivalence toward the perpetrator and difficulties "letting the past go." These factors could potentially contribute to dampening the effect of a relatively simple and mechanistic intervention that does not itself target the cognitive and biographical complexities behind a PTSD diagnosis.

In relation to our secondary outcome measures, changes in scores for BDI-II, BAI and the total and intrusion subscale of the IES-R from admission to discharge suggest a clinical improvement in about half of the patients. The study design does not in itself provide any evidence as to whether these changes were in any way influenced by the study-specific intervention, but the relatively lower rate of "response" on overall symptom scores compared with intrusion frequency may also suggest a specific rather than generic effect of the intrusion-focused intervention (cf. Horsch et al., 2017; Iyadurai et al., 2017). At first sight, the correlations between secondary outcome measures and intrusion frequency may appear somewhat counterintuitive: The greater the reduction in intrusions after the intervention, the better patients improve for general clinical variables (BDI, BAI), though this is not seen on the specific variables (IES-R total and intrusion subscale). The reverse pattern is true for the reduction of intrusions that have never been targeted (without intervention) which correlates positively with IES-R total and intrusion subscale scores but not BDI and BAI. One possible explanation for this could be that the targeted hotspots are one important cause of negative emotions (e.g., shame, guilt) contributing to depression and anxiety scores. On the other hand, the remaining (never targeted) hotspots still exist to a certain degree preventing IES intrusion scales to drop strongly. Nevertheless, this should be investigated further in future studies.

Importantly, because the *memory reminder* plus *Tetris* intervention selectively targets intrusive memories of trauma, we do not claim that our intervention causes general improvements for patients on other PTSD symptom scales (e.g., avoidance or hyperarousal), but rather hypothesized a specific effect on the number of intrusions. Regarding all forms of clinical improvement evident in our patient sample, one has to consider, that patients were in a full inpatient treatment program for complex PTSD, which supposedly is responsible for many aspects of their improvement. A potential confound is that it is clinically plausible that at any given time point a patient may have also discussed specific trauma related themes related to a given hotspot targeted (rather than those not targeted) in their regular therapy sessions. As we do not have access to the clinical record we are not able to further check this possibility. We also note that part of our ethical approach to this study was to conduct it as a supplement to standard clinical care.

Self-reported levels of arousal mostly increased after the *memory reminder* procedure and decreased after playing *Tetris*. This is in line with clinical observations that the majority of patients reported that it was distressing to be reminded of the trauma but helpful to play *Tetris* directly afterward. We do not yet know how much memory activation is enough to initiate destabilization (i.e., to allow so called memory updating), and this is a subject of ongoing enquiry in the literature on memory consolidation (e.g., Fernández et al., 2016; Kindt & van Emmerik, 2016; Treanor, Brown, Rissman, & Craske, 2017; Visser et al., 2018): It is hard to know whether a memory has been successfully reactivated or not and this is typically inferred by the effects of the intervention procedure itself. In our experimental work we use a very modest reactivation procedure (brief presentations of scenes from a film; James et al., 2015), and it would be valuable to examine how brief a *memory reminder* is possible for much older and highly distressing clinical memories of trauma.

Importantly, there were no serious adverse events or drop-outs for our sample of 20 patients. The fact that the decrease in arousal after playing *Tetris* showed a trend to be more pronounced for later "responding" than "nonresponding" intrusions could be a first hint that an immediate measurable index related to engagement in the intervention might predict later success in decreasing intrusion frequency. The apparent lack of correlation between *Tetris* scores (performance) and clinical variables (changes in arousal, effect on intrusions) speaks for the fact that participants do not necessarily have to be "good" at playing *Tetris* in order to profit from it as part of an intervention.

Although the results support our hypothesis about the *effect* of this theory-driven intervention, this does not necessarily imply that the *mechanisms* responsible for the reduction of intrusion frequency were the ones postulated in creating this interventional procedure. We suggested that the two-step intervention procedure would first help to reactivate old trauma memories, rendering them labile, and then *Tetris* gameplay would cause visuospatial interference in order to disrupt reconsolidation of these memories, leading to a reduction in their occurrence as intrusions. We derived ideas from the results of dual-task experiments (Baddeley & Andrade, 2000), theories of PTSD (Brewin, 2014), and the results of experimental studies in animals and healthy participants, each of which contributed to individual aspects of our account combining possible memory reactivation, interference and reconsolidation-update mechanisms (Holmes et al., 2009; Holmes et al., 2010; James et al., 2015; Kindt, Soeter, & Vervliet, 2009; Kindt & van Emmerik, 2016; Kroes et al., 2014; Misanin et al., 1968; Nader et al., 2000; Schiller et al., 2010; see Introduction for a more length coverage of related findings).

The clinical and experimental literature suggest that it is unlikely that either component of our intervention in isolation would be effective: For example, it seems implausible that simply playing *Tetris* once per week would in itself lead to intrusion reductions. However, the results of our study do not in themselves provide evidence that reconsolidation mechanisms or the visuospatial nature of the cognitive interference task were involved in the effects observed, and further work such as dismantling designs would be needed to elucidate whether the actual mechanisms involved are those that were drawn on to inspire the intervention.

Although the procedure in the current study was designed to be applicable without specialist input and without requiring extensive "reliving" of the trauma by patients, in the current study for most patients the administration was carried out by trained therapists, and patients were required to write down traumatic content with a certain degree of emotional involvement (see arousal levels). As previously described in the Method section, the use of therapists to administer the procedure was based on initial safety and ethical concerns, given that this was the first application of this procedure in a complex clinical sample. However, the nature of the therapists' limited involvement, lack of need for therapist intervention during the procedure, and the fact that it was possible to transition to having the procedure conducted by a research assistant, supports the argument that therapist-administration should not be necessary in future studies. Further, given that the patients were able to go through the *memory reminder* procedure and gameplay without needing therapist intervention, and the increases in arousal were relatively small (mean of 1.77 on a 0 to 10 scale), the *memory reminder* procedure appears manageable for even these complex patients.

Further limitations to our study are that the small, mostly female, sample and specialist treatment setting limit generalizability of the results. From an experimental perspective, a stronger single case design might have included randomization of individual intrusion baseline lengths via randomly deciding which intrusion to target in each treatment session, rather than basing this decision on clinical need. However, it seems unlikely that the currently most distressing intrusion is the one most likely to suddenly decrease in frequency in subsequent weeks, and a degree of pragmatism was necessary in working in a clinical inpatient setting. Similarly, while the lack of randomization of intrusion target may limit comparability between targeted and nontargeted intrusions, from a clinical perspective in the context of a time-limited intervention it would not be appropriate to risk not targeting the intrusive memories causing patients the most distress.

In any translational work toward new techniques in psychological treatments it is essential to remain scientific and to be appropriately critical of novel findings, and seek to learn from what may and may not work (Holmes et al., 2018). These are early days and there are many aspects of the approach outlined here that could and should be scrutinized. One example is the nature of the concurrent task (see Introduction). Another is debates within the theory of memory reconsolidation (e.g., for a critical review see Treanor et al., 2017) which question the foundations of this or any other intervention approach building on reconsolidation. It is hoped that a constructive scientific debate may continue to enhance the literature and ultimately this may best advance in science when there are opportunities for face-to-face dialogue, reflection, and mutual understanding of perspectives—perhaps particularly important in interdisciplinary and clinically relevant work.

The intervention as tested in this study may be amenable to further optimization in terms of the *memory reminder* procedure, cognitive interference task, or frequency and timing of the interventions. For example, there is no theoretical reason to target only one intrusion per week (in fact, there were pragmatic deviations from this), and some memories may need repeated attempts at reactivation in order to be successfully targeted. The case series was registered with a clinical trials registry, but this registration took place between data collection and analysis (i.e., retrospective registration), and future clinical studies would benefit from prospective registration. Finally, a randomized controlled trial design with a suitable control comparison would be needed to draw strong conclusions about the overall efficacy of the intervention in reducing intrusion frequency. However, such a study would have been premature and potentially resource-inefficient in the absence of having first provided some evidence of applicability and specificity of effects in this clinical population.

In conclusion, our initial single case series with 20 patients with longstanding complex PTSD provides some encouraging evidence for the potential of a simple behavioral intervention comprising a *memory reminder* plus *Tetris* gameplay (visuospatial interference task) to reduce the occurrence of intrusive memories of trauma, and to maintain this reduction for at least the remainder of the study. These effects were found despite the longstanding nature of most of the trauma symptoms and the limited therapist input or patient time required for the procedure. These early but encouraging results therefore warrant further replication and testing against a control condition in for example a randomized controlled trial design. Pending such further research, this novel intervention could help develop an affordable, easy-to-use, and widely available treatment tool to target intrusive memories after trauma.

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Received September 14, 2017
Revision received May 16, 2018
Accepted July 7, 2018 ■