Intrusive memories of trauma in the laboratory: Methodological developments and future directions

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Structured Abstract

Purpose of the review: Intrusive memories are those that spring to mind unbidden, e.g., sensory recollections of stressful/traumatic events. We review recent methods to monitor intrusions of a stressor within the laboratory, which open up additional approaches for experimental psychopathology research on intrusive symptom development, persistence and mitigation.

Recent findings: Recent studies suggest three main methodologies after viewing a trauma film by which to monitor intrusions in the laboratory: during post-film rest periods, after exposure to trigger cues, and while performing an ongoing task. With these approaches, factors (e.g., psychological or pharmacological) that may influence the frequency of occurrence of intrusions can be tested.

Summary: We highlight methodological considerations to guide experimental design using intrusion monitoring in the laboratory, which complement monitoring approaches in daily life (e.g., diaries). Such designs confer greater experimental control for trauma film studies and open novel research avenues, which may inform intervention development to mitigate problematic intrusive memory symptoms.

Keywords: intrusive memories; trauma; PTSD; involuntary memory; mental imagery

1. Introduction

Research on intrusive memories, or more simply intrusions, has expanded over the last decade, owing to an increased recognition of their role in emotional psychopathology (1,2). In the context of treatment and prevention research for mental health, intrusions have been recently highlighted as intervention targets in their own right (3), and also as intermediate clinical targets which may possibly 'knock out' further clinical symptoms (1,2). There is a demand for innovative approaches to reduce intrusive cognitions across psychopathology, requiring tailored methods to track and study intrusion development, persistence and mitigation. Alongside the often-used intrusion monitoring approaches in everyday life (e.g. with a diary), intrusion monitoring in the laboratory allows for additional approaches to be explored.

1.1. The clinical phenomena

Intrusive memories are those that spring to mind unbidden, e.g., sensory recollections of stressful or traumatic events (4). These are common following psychological trauma (5), representing a core symptom of post-traumatic stress disorder (PTSD) and acute stress disorder (ASD) (6). For instance, a trauma survivor after a gun assault may repeatedly experience a vivid mental image of 'a gun put to the head' (7). Intrusive manifestations are distinct from voluntary retrieval, for example, when the same trauma survivor is asked to deliberately recall details of the attack to participate in a court case and describe what happened during the trauma (8).

1.2. Experimental psychopathology: The trauma film paradigm

Experimental psychopathology (9), or more generally experimental medicine, is an important approach for innovation in the prevention and treatment of mental health difficulties, particularly at preclinical stages of intervention development. The approach aims

to model clinical processes under controlled laboratory conditions. For a better understanding of the impact of psychological trauma (e.g., ASD and PTSD), an ideal experimental psychopathology model would be able to simulate both exposure to trauma and the hallmark symptom - intrusive memories of the traumatic event.

The trauma film paradigm emerged as an experimental model of intrusions generated in response to a laboratory stressor in the 1960's, initially pioneered by Horowitz (10) and Lazarus (11). The paradigm involves participants watching film footage depicting stressful/ potentially traumatic events (i.e., modelling exposure to trauma), which are powerful enough to induce intrusions of the film in everyday life for up to several days outside the laboratory (i.e., modelling intrusive symptoms) (12) (Figure 1). Interestingly, the paradigm could also facilitate translational links with other human and non-human models such as fear conditioning paradigms, as similar aspects of emotional responding can be assessed across paradigms, e.g., psychophysiological outcomes (8).

[Insert Figure 1]

The trauma film paradigm provides a platform to test proof-of-concept innovative interventions to for example reduce or increase the frequency of occurrence of intrusions, evaluate risk factors for intrusion development, and explore mechanisms by which interventions could worsen stress symptoms (13–16). Findings from the laboratory using this paradigm are already beginning to be translated to real-life settings, with early promising results. For instance, a behavioural protocol (a memory reminder cue followed by the computer game Tetris) was used in the laboratory soon after exposure to a trauma film with nonclinical volunteers. Such protocol was hypothesised to interfere with the (re)consolidation of memories (by competition with cognitive resources), which would otherwise become intrusive (13,17,18). Compared to a control condition, the intervention protocol was found to reduce intrusions as monitored in a one-week diary (18). The same protocol used with

patients following a road traffic collision (19) or an emergency caesarean section (20) also led to fewer intrusions for the one-week period post-trauma compared to control protocols.

1.1.1. Monitoring intrusive memories in daily life

The most common approach for assessing intrusions in the trauma film paradigm is to sample them in everyday life (Figure 1). Typically, participants return to their daily lives after viewing the film and record the intrusions they experience, such as using pen-and-paper (13,21) or electronic diaries (22,23). The primary benefit is the ecological validity of real-life monitoring (12). However, sampling in everyday contexts does come with some drawbacks, including possible non-compliance with completion and variability in the contexts experienced by individuals in their everyday lives (e.g., daily activities or environmental cues).

1.1.2. Monitoring intrusive memories in the laboratory

A complementary approach to diaries is monitoring intrusions in the laboratory. Lab-based assessments of intrusions have been used since the early trauma film studies in the 1970's (10) and increasingly over the last decade (12) (Figure 1). Unlike diaries, intrusion monitoring in the laboratory can provide additional experimental control over the retrieval context for trauma film studies. For example, contextual factors such as environmental cues and/or the attentional state of the participant while intrusions arise can be controlled for, potentially reducing inter-individual variability. Moreover, those contextual factors can also be directly manipulated, so their impact on intrusion retrieval (and how such context might interact with the effect of the primary factor of interest) can be tested. Despite such advantages, a review of methods to monitor intrusions (of an experimental trauma) within the laboratory is currently lacking.

2. Aim and scope

We aim to summarise recent methodological developments using the trauma film paradigm that allow for monitoring of intrusive memories in the laboratory. To this end, we selectively reviewed the relevant literature in the last decade (12), focussing on studies that had a) induced intrusions using stressful films, b) studied the frequency of occurrence of intrusions, and c) assessed intrusions both within a laboratory setting and in daily life to allow comparisons.

3. Methodological variations in monitoring intrusive memories in the laboratory

Mirroring the use of the clinical term *peri-trauma* to refer to the period during the traumatic event, we will use the term *peri-intrusion* to refer to the period during which intrusions are monitored and assessed (Figure 1). Three key parameters were identified that have been used to simulate the peri-intrusion window in the laboratory: a) whether a definition of intrusions was provided to participants before or after the peri-intrusion window; b) whether or not triggering cues were presented; and c) whether or not an ongoing task was included. Different combinations of these parameters yielded three main intrusion-monitoring methodologies in the laboratory (Table 1): 1) intrusions that occur during post-film rest periods (three studies), 2) those occurring in the context of triggering cues (ten studies), and 3) those that occur while participants are performing an ongoing task (four studies).

[Insert Table 1]

3.1. Intrusive memories during a post-film rest period

One method for sampling intrusions in the laboratory is during periods of quite rest, typically with eyes closed for roughly 2 to 5 min. A definition of an intrusive memory is given to participants prior to the post-film rest period and they are instructed to specifically monitor intrusions as they happen in real-time (Table 1). Using this approach, Wilksch and Nixon (24) assessed intrusions during a 5-min peri-intrusion period, first immediately after a

trauma film and then one week later in a separate laboratory session. For each peri-intrusion period, participants were instructed to lift a finger when an intrusion occurred, and lower their finger when the intrusion had gone. These periods were videotaped and later analysed. Individuals with a tendency to interpret intrusive symptoms more negatively, compared to those who did not, reported subsequently more laboratory intrusions (both rest periods) and everyday intrusions (one-week diary completed between both sessions).

A 5-min peri-intrusion period was also employed by Hawkins and Cougle (25). Soon after the film, participants completed a free recall task and a recognition memory task regarding the content of the trauma film, and then used a tally counter to monitor intrusions during the peri-intrusion period. Individuals who underwent acute nicotine administration prior to film viewing, compared to a placebo lozenge group, reported more laboratory intrusions within the first session but not in a subsequent one-week diary.

Clark et al. (26) assessed the neural correlates of intrusive memory *retrieval* using functional magnetic resonance imaging (fMRI). Immediately after watching a film in the fMRI scanner, participants were asked to press a button if they experienced an intrusion of any scene from the film while remaining in the scanner for 6 min (peri-intrusion period). To minimise experimental demands, they were told not to worry if they did not experience any intrusions. Brain activation related to intrusion key presses was compared to brain activation associated with random key presses generated by a separate group of participants who did not watch the film. Experiencing an intrusion was associated with brain activity in frontal regions, but most notably in the left inferior frontal gyrus, an area also implicated in the initial *encoding* of specific film scenes that subsequently intruded, as indicated by intrusion descriptions in a one-week diary.

3.2. Intrusive memories after exposure to trigger cues

Although intrusions usually appear to spring to mind unbidden, clinical theories propose that these are often triggered by reminders that have sensory-perceptual overlap with the initial encoded event (27,28). Drawing from these perspectives, a number of trauma film studies have sampled intrusions while exposing participants to reminder cues from the trauma film (Table 1). For example, Schaich et al. (29) asked participants to undergo two 3-min rest periods after film viewing: a first one without any cues (uncued rest), and a second one after exposure to nine visual stills (presented for 10 sec each) taken directly from the film (cued rest). Participants estimated the total number of intrusions experienced at the end of each rest period, and also for every evening for the subsequent seven days in daily life. Intrusion count in the laboratory was reported by collapsing both rest periods. Higher *trait* rumination was found to be associated with more frequent intrusions both in the laboratory and daily life for individuals who trained to use abstract processing (focussing on meanings) but not concrete processing (focussing on the events) *before* film viewing.

A similar approach using retrospective assessments was adopted by two additional studies, with findings reported instead separately for uncued and cued rest periods. For cued rest, Ehring et al. (30) used auditory cues and visual stills from scenes of the original source of the film footage which did not overlap with the scenes shown to the participants. Participants were assigned to one of three guided thinking tasks immediately after the film: abstract, concrete or distraction, and then underwent the uncued rest followed by the cued rest. For cued rest, the concrete thinking group reported fewer intrusions than the distraction group, with the abstract group lying numerically in the middle. However, no significant group differences in intrusion frequency were reported for uncued rest or in daily life (three days post-film), suggesting that concrete thinking may modulate the ability of cues (at least in the laboratory) to trigger intrusions. In contrast, Morina et al. (21) reported a similar pattern of results for intrusions in both uncued and cued rests. Participants underwent 2-min rest periods

twice, once immediately after the film (uncued), and followed by another after exposure to seven still pictures from the film (cued). Higher trait mental imagery vividness was associated with more frequent laboratory intrusions (in both rest periods) and also more intrusions in a five-day diary, suggesting that the level of trait imagery vividness is a potential risk marker for increased intrusions after a stressor.

Using a Memory Trigger Task, Wegerer et al. (31) developed an innovative approach to trigger intrusions within the same session as film viewing. After watching a trauma film, participants listened to three types of sound landscapes: 1) embedded with an auditory cue associated with the trauma film (conditioned cue), 2) embedded with an auditory cue not associated with the film (unconditioned cue), or 3) not embedded with auditory cues (no-cue control). After each landscape, participants retrospectively estimated the total number of intrusions. The conditioned cue elicited more intrusions in the laboratory, as well as higher skin conductance levels and anxiety ratings, compared to the unconditioned cue or no-cue control. A higher negative rating to the conditioned cue was also associated with more intrusions in daily life (estimated in each of the subsequent three evenings). This study illustrates the advantage of sampling intrusions in the laboratory to investigate concurrent correlates of emotional responding, including psychophysiological outcomes.

Marks and Zoellner (32) also developed a novel method to assess intrusive memories. Participants initially watched a trauma film in the laboratory, and two days later returned for an extinction manipulation. At 24h after the manipulation, participants received a phone interview: they first estimated the overall number of intrusions experienced over the last 24 hr pre-interview; they were then presented with a Fear Renewal Task, during which they closed their eyes and paid attention to a 25-sec audio clip directly obtained from the film; at the end of the clip, participants estimated the number intrusions experienced both during and after the audio clip. The number of intrusions post-manipulation was collapsed across all the above

monitoring stages. It was found that an extinction intervention led to more intrusions than did control procedures. This study showcased a creative solution to provoke intrusions under experimental control (via telephone) while minimising the burden of returning to the laboratory.

All the above studies relied on retrospective estimates by participants. To assess intrusions throughout the peri-intrusion window, various studies have employed the Intrusion Provocation Task (IPT). Here, participants are first presented with film-related visual cues, which consist of film stills of neutral scenes from the film (e.g., stills that do not depict the 'worst' moments, e.g., the car collision). They are then instructed that they can think freely without restrictions for 2 min during a rest period. Participants then indicate each intrusion occurrence as they happen, via keyboard button presses or tally markers on paper. All of the following studies used the IPT one week after the film in a second laboratory session. Malik et al. (33) found that young people with a high incidence of hypomanic experiences, compared to controls, reported more intrusions in the IPT as well as in a one-week daily sampling of intrusions via text message. Lang et al. (34) found that a positive appraisal training after a film led to fewer intrusions reported in the IPT and in a one-week diary compared to a negative appraisal training. In two experiments, James et al. (13) found that a behavioural protocol (film reminder cue before a 10-min gap followed by Tetris game play at 24 hr post-film) led to fewer intrusions both in the IPT and in the one-week diary compared to control protocols (reminder-only, Tetris-only or no-task controls). A subsequent study by James et al. (35) found that a similar behavioural protocol administered *before* film viewing did not influence intrusions (in either the IPT or a one-week diary), suggesting temporal constraints of this type of interventions such that it may be effective if delivered after but not before trauma exposure.

3.3. Intrusive memories while performing an ongoing task

The third approach to assess intrusions in the laboratory is during ongoing tasks as opposed to pure rest periods, potentially creating a situation more akin to when intrusions occur alongside other activities in everyday life. Typically, a definition of an intrusion is given to the participants after watching the trauma film and they are then instructed to notice intrusions while performing the ongoing task. Each intrusion is indicated in real-time via keyboard button presses or a tally counter (Table 1). For example, Verwoerd et al. (36) assessed laboratory intrusions while participants were also instructed to actively focus on their breathing during a 3-min period. Participants who were trained to direct their attention away from film reminders after viewing the film, relative to those who received a control training, reported fewer laboratory intrusions after the training within the same session, as well as in a subsequent three-day diary.

Marks et al. (37) assessed laboratory intrusions while participants performed a concurrent 4-min digit task. This task involved a random series of two-digit numbers being presented on a computer screen, which participants were instructed to read out loud. Simultaneously, participants indicated each intrusion occurrence with a hand-held clicker. The study explored the effect of a visuospatial task (versus no task) during film viewing on intrusions but found no effect of condition on either laboratory intrusions (30 min post-film) or daily life intrusions in a one-week diary. However, it was found that participants who reported having psychotic-like experiences in daily life, compared to those that did not, reported more laboratory and diary intrusions, suggesting that psychotic-like experiences may confer vulnerability to intrusion development.

Two additional studies manipulated the type of ongoing task to directly examine their impact on the number of intrusions concurrently experienced as well as those experienced later. For the peri-intrusion periods, participants were asked to close their eyes, and then lift a finger when an intrusion occurred and lower the finger when the intrusion was gone (similar

to the approach used in studies with pure resting periods). These periods were videotaped and scored later. Intrusions were monitored in the first session and in a later session at one week after the film, but this second time without performing the ongoing tasks. A one-week intrusion diary was completed in daily life between sessions. Using such an approach, Nixon et al. (38) assessed intrusions while participants performed one of the following ongoing tasks soon after the film: suppressing any film-related thoughts, suppression while also holding one of three cognitive loads (hyperventilation, visuospatial load or verbal load) or no suppression at all. Findings showed there were no significant group differences on the number of laboratory or diary intrusions. In a second study (39), participants underwent the intrusion assessment after viewing the film (and completing a word-stem task and dot-probe task with film-related information) while simultaneously performing similar tasks to the first study: suppressing any film-related thoughts, holding a verbal cognitive load, both suppression and holding a cognitive load, or neither. Again, findings showed no significant group differences on intrusion frequency immediately after the film or at one week. However, individuals who performed both suppression and holding a cognitive load during the first 5-min period subsequently reported instead more diary intrusions.

4. Conclusions

A review of the literature of recent studies using the trauma film paradigm has revealed three main methodologies to monitor intrusive memories within the laboratory: 1) during post-film rest periods, 2) after exposure to triggering cues, or 3) while performing ongoing tasks. A primary focus of this research to date is testing associations between relevant factors (e.g., psychological or pharmacological) before, during or soon after trauma and the frequency of intrusions at a later time point, treating intrusions as an outcome. Thus, we first discuss key methodological considerations to guide experimental design using intrusion monitoring in the laboratory and treating intrusions as an outcome, complementing

monitoring approaches in daily life (e.g., diaries). We then argue that intrusion monitoring in the laboratory is yet to be fully exploited, and can be leveraged for novel avenues in experimental psychopathology research, including research into the context in which intrusions arise and the impact of intrusions themselves.

4.1. Methodological considerations

One consideration is when the peri-intrusion window occurs in relation to other tasks within the full experimental design. In some studies, the period for intrusion monitoring may be preceded by tasks (e.g., word-stem task) that provide reminders about the film and that could potentially act as triggers for intrusions. It is important that these unintended triggers do not inadvertently lead to intrusion 'over-provocation', i.e., a ceiling effect that could mask the association with the primary factor of interest. More critically, tasks that elicit voluntary memory (e.g., free recall and/or recognition) may activate a 'voluntary' retrieval mode, potentially making it more difficult to ascertain if the intrusions subsequently reported were indeed 'involuntary' (25). Voluntary retrieval of film content itself can also modulate intrusions (40,41). Thus, it is preferable to administer such film-related tasks *after* the peri-intrusion window whenever possible, or consider a counter-balanced design. A more rigorous but also laborious approach is to use a between-subject design where each group is administered one type of memory test only. Researchers may also be cautious about eliciting verbal descriptions after the occurrence of each intrusion within the laboratory – while this may provide richer descriptions of the intrusion content, it may also act as a form of additional 'voluntary' retrieval that can inadvertently influence the subsequent rate of intrusions.

Another consideration is the use of rest periods versus ongoing tasks during the peri-intrusion window. Rest periods are easy to implement. However, ongoing tasks could increase experimental control over the retrieval phase, e.g., equating attentional instructions

across participants (36,37). If such tasks are considered, then it is important that these are not extremely taxing as the development of intrusions could be impeded all together, leading to a floor effect. Studies reviewed here typically used tasks with low attentional demands such as breathing (36) and digit monitoring (37).

Real-time monitoring of intrusions is generally preferred, as retrospective estimates may suffer from memory biases. With a clear a priori definition of intrusive memories, monitoring can become relatively simple for the participant, who can then easily distinguish intrusions from related processes (e.g. intrusive versus voluntary memories) (13,33–35). However, retrospection may be preferable in some designs where uninterrupted performance on a primary task is needed (e.g. task with reaction time measures). In such cases, retrospection biases should be minimised with appropriate durations of monitoring, e.g., most studies in this review used no more than 3 to 5 min of monitoring before participants reported retrospective estimates (21,29–31).

It is also important to consider the timing of intrusion monitoring in the laboratory, which could take place within the first session (e.g., immediately after, or after a short period) or in a subsequent session (Figure 1). Such timing should be informed by mechanistic theory of how the primary variable of interest relates to emotional memory over time. For instance, if the impact of an intervention on memory takes time to emerge, e.g., due to consolidation (42) or reconsolidation processes (43), effects on intrusion monitoring immediately after the intervention would not be expected, so later monitoring periods would also be needed to track such potential time-dependent effects.

Finally, we must carefully evaluate the distinction between ‘uncued’ versus ‘cued’ intrusions. While clinical proposals suggest a primary role of sensory-perceptual cues in the development of intrusive symptoms (32,33), the assumption that such cues are necessary to sample intrusions in the laboratory has been little researched. Interestingly, one may argue

that the occurrence of intrusions during 'uncued' rest periods indicate that overt cues are not always necessary to provoke intrusions. However, triggers may also arise from testing participants in the same context as film viewing (e.g., same room, researcher and/or apparatus including brain-imaging apparatus) or from other tasks (containing trauma-related information) within the experimental design, as described previously. It remains to be established whether or not (and which) triggers are important to sample intrusions, and whether those triggered specifically by sensory-perceptual cues are the most relevant to the clinical phenomena. Thus, it may be important to assess intrusions and their associated triggers whenever possible, as these may inform the potential mechanisms of putative intervention

4.2. Future directions

The main value of using laboratory monitoring compared to diaries in trauma film studies is the additional control over *retrieval* processes that pertain to intrusions. This opens up numerous new research directions. First, we can design experiments that elucidate the role of retrieval/contextual factors on the development and persistence of intrusions as specified by clinical and theoretical models of intrusions (27,28,44,45). These include the role of different trigger cues (31) as described above, and the role of ongoing activities (38,39). Building on the studies reviewed here, a greater understanding of such retrieval processes could inform more precise parameters for designing intrusion-monitoring methods.

A second use of laboratory monitoring is to assess the causal impact of intrusions on other processes. Emerging research suggests intrusions impacts on daily functioning (3), yet most experimental psychopathology research focuses on the impact of other variables on intrusions (12) rather than the impact of intrusions themselves. Experimentally-induced intrusions in the laboratory could be used to assess their impact on other cognitive processes, e.g., concentration (46). Concurrent physiological correlates of intrusion retrieval can also be

assessed dynamically in real-time throughout the peri-intrusion window in the lab, including peripheral physiology, e.g., skin conductance and heart rate (31), and neurophysiology, e.g., fMRI (26) and electroencephalography (47,48).

A third use of laboratory monitoring is to make better comparisons with tests of voluntary memory (e.g., free recall or recognition). It is desirable to reduce intrusions without interfering with voluntary memory of an event, e.g., for legal accounts (8), and thus it is important to assess the impact of interventions on both memory types. Tests of voluntary memory are typically performed in the laboratory, whereas intrusions are mostly assessed outside of the laboratory (12). Having laboratory methods to monitor intrusions means both memory types can be assessed in tandem while matching potential confounds, e.g., similar amount of triggering cues and attentional focus across test types.

One observation from this review is that in some studies (25,29,38), a primary variable of interest shows significant associations with the number of laboratory intrusions only or instead with only the number of daily intrusions. One reason may be due to the limited statistical power. Another reason may be due to methodological differences in, for example retrieval delays (laboratory intrusions typically cover early time periods whereas diary intrusions cover later periods) (25,26) or availability of coping strategies (one may be more likely to engage in suppression in the laboratory but distraction in daily life) (24). More research is needed to understand differences and similarities between both sampling contexts. Such research would also benefit from better establishing the psychometric properties of both monitoring methodologies.

Finally, monitoring intrusions in the laboratory also offers practical advantages for future experiments. A trauma film study typically requires two sessions separated by usually a one-week diary. Instead, a study design can that consider trauma film and intrusion monitoring within a single session, could reduce potential participant burden, avoid dropouts,

and speed up data collection. Such single-session experiment also opens up the possibility of inducing and then dampening intrusions by the end of the session, which may facilitate research with clinical populations where the importance of intrusive imagery is becoming increasingly recognised (49,50).

4.3. Limitations of the trauma film paradigm

Viewing trauma films in the laboratory is not the same as experiencing real-life trauma. Unlike studies with patients who typically have retrospective biases, the use of an experimental trauma allows for prospective controlled design. Studying intrusive symptoms using this approach can minimise also clinical and ethical concerns compared to symptom provocation in trauma-exposed individuals or patients. Nevertheless, experimental psychopathology findings should be complemented with prospective studies of real-life trauma, such as in individuals who are at high-risk of trauma exposure (e.g., paramedics and journalists).

In recent years there has also been increased recognition of the role of indirect media exposure of traumatic events on psychopathology in civilians (51,52), as well as in the professional context, e.g., a police officer reviewing video footages of child trafficking (6). The trauma film paradigm provides a model to study the impact of viewing trauma more broadly. However, it does not aim to simulate media-based exposure that is repeated and prolonged per se.

Reports of intrusions to trauma films reply on self-report accounts, potentially susceptible to demand characteristics. However, this issue also applies to studies with patients with ASD/PTSD, who are asked to self-report their intrusive symptoms during assessment and/or throughout interventions. While this issue requires further investigation, the increasing inclusion of intrusion-monitoring methods in the laboratory could allow for the development

of sensitive behavioural/physiological (and potentially more objective) markers of intrusive symptoms.

4.4. Final remarks

Methodologies to monitor intrusive memories within the laboratory in studies using the trauma film paradigm have rapidly gained traction in the last few years, bringing intrusions 'out of the wild' and 'into the lab'. We have identified three such methodologies, which complement existing approaches for real-life monitoring (e.g., via diaries) and open up novel research possibilities. These methodological developments may further advance research on intervention development for psychopathology in which intrusive memories are problematic.

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Conflicts of Interest

Dr. Lau-Zhu reports studentship from The Cambridge Commonwealth, European and International Trust during the conduct of the study. Professor Holmes reports grants from Lupina Foundation, salary support from Karolinska Institutet, grants from UK Medical Research Council, during the conduct of the study; sits on the Board of Trustees, for the charity MQ transforming mental health; and receives occasional travel reimbursement and honoraria for invited conference talks. Dr. Porcheret reports grants from the Wellcome Trust.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as: * of importance and ** of major importance

1. Holmes EA, Mathews A. Mental imagery in emotion and emotional disorders. Clin Psychol Rev. 2010;30(3):349–62.

2. Brewin CR, Gregory JD, Lipton M, Burgess N. Intrusive images in psychological disorders: characteristics, neural mechanisms, and treatment implications. Psychol Rev. 2010;117(1):210–32.

3. James EL, Visser RM, Lau-Zhu A, Porcheret K, Horsch A, Holmes EA, et al. Intrusive memories of trauma: a target for prevention? New data and a guided review. Under Rev. 2017;

4. **Pearson J, Naselaris T, Holmes EA, Kosslyn SM. Mental imagery: Functional mechanisms and clinical applications. Trends Cogn Sci. 2015;19(10):590–602. **A theoretical synthesis of the cognitive neuroscience of mental imagery including its relevance to clinical applications on intrusive memories**

5. Bryant RA, O'Donnell ML, Creamer M, McFarlane AC, Silove D. Posttraumatic intrusive symptoms across psychiatric disorders. J Psychiatr Res. 2011;45(6):842–7.

6. American Psychiatric Association. Diagnostic and statistical manual of mental disorder. Fifth. Arlington, VA: American Psychiatric Association; 2013.

7. Holmes EA, Grey N, Young K a D. Intrusive images and "hotspots" of trauma memories in Posttraumatic Stress Disorder: an exploratory investigation of emotions and cognitive themes. J Behav Ther Exp Psychiatry. 2005;36(1):3–17.

8. *Visser RM, Lau-Zhu A, Henson RN., Holmes EA. Multiple memory systems,

multiple time points: How neuroscience can inform interventions to control the expression of unwanted emotional memories. Philos Trans R Soc Lond B Biol Sci. 2017;In press. **A theoretical overview on translational research across animal and human models to advance research on emotional memories including their intrusive expressions**

9. Zvolensky MJ, Lejuez CW, Stuart GL, Curtin JJ. Experimental psychopathology in psychological science. Rev Gen Psychol. 2001;5(4):371–81.

10. Horowitz MJ. Intrusive and repetitive thoughts after experimental stress. A summary. Arch Gen Psychiatry. 1975;32(11):1457–63.

11. Lazarus RS. A laboratory approach to the dynamics of psychological stress. Adm Sci Q. 1963;8(2):192.

12. James EL, Lau-Zhu A, Clark IA, Visser RM, Hagenaars MA, Holmes EA. The trauma film paradigm as an experimental psychopathology model of psychological trauma: intrusive memories and beyond. Clin Psychol Rev. 2016;47:106–42.

13. **James EL, Bonsall MB, Hoppitt L, Tunbridge EM, Geddes JR, Milton AL, et al. Computer game play reduces intrusive memories of experimental trauma via reconsolidation-update mechanisms. Psychol Sci. 2015;26(8):1201–15. **The most comprehensive symthesis of all studies using the trauma film paradigm in the last decade illustrating the numerous wasy the paradigm can be used**

14. Woud ML, Postma P, Holmes EA, Mackintosh B. Reducing analogue trauma symptoms by computerized reappraisal training - considering a cognitive prophylaxis? J Behav Ther Exp Psychiatry. 2013;44(3):312–5.

15. Hagenaars MA, Arntz A. Reduced intrusion development after post-trauma imagery rescripting; an experimental study. J Behav Ther Exp Psychiatry. 2012;43(2):808–14.

16. Porcheret K, Holmes EA, Goodwin GM, Foster RG, Wulff K. Psychological effect of an analogue traumatic event reduced by sleep deprivation. Sleep. 2015;38(7):1017–25.

17. Holmes EA, James EL, Coode-Bate T, Deeprose C. Can playing the computer game "Tetris" reduce the build-up of flashbacks for trauma? A proposal from cognitive science. PLoS One. 2009;4(1):e4153.

18. Lau-Zhu A, Holmes EA, Butterfield S, Holmes J. Selective association between Tetris game play and visuospatial working memory: A preliminary investigation. Appl Cogn Psychol. 2017;31(4):438–445.

19. **Iyadurai L, Blackwell SE, Meiser-Stedman R, Watson PC, Bonsall MB, Geddes JR, et al. Preventing intrusive memories after trauma via a brief intervention involving Tetris computer game play in the emergency department: a proof-of-concept randomized controlled trial. Mol Psychiatry. 2017;doi: 10.1038/mp.2017.23. **One of the first early-stages translation of an intervention protocol from the laboratory using the trauma film paradigm into a real-world setting**

20. Horsch A, Vial Y, Favrod C, Harari MM, Blackwell SE, Watson P, et al. Reducing intrusive traumatic memories after emergency caesarean section: A proof-of-principle randomized controlled study. Behav Res Ther. 2017;94:36–47.

21. Morina N, Leibold E, Ehring T. Vividness of general mental imagery is associated with the occurrence of intrusive memories. J Behav Ther Exp Psychiatry. 2013;44(2):221–6.

22. Bisby JA, Brewin CR, Leitz JR, Curran VH. Acute effects of alcohol on the development of intrusive memories. Psychopharmacology (Berl). 2009;204(4):655–66.

23. Kleim B, Graham B, Bryant R a, Ehlers A. Capturing intrusive re-experiencing in trauma survivors' daily lives using ecological momentary assessment. J Abnorm

504 Psychol. 2013;122(4):998–1009.

505 24. Wilksch SR, Vandervord Nixon RD. Role of prior negative cognitions on the
506 development of intrusive thoughts. Aust J Psychol. 2010;62(3):121–9.

507 25. Hawkins KA, Cougle JR. The effects of nicotine on intrusive memories in
508 nonsmokers. Exp Clin Psychopharmacol. 2013 Dec;21(6):434–42.

509 26. *Clark IA, Holmes EA, Woolrich MW, Mackay CE. Intrusive memories to traumatic
510 footage: the neural basis of their encoding and involuntary recall. Psychol Med.
511 2016;46(3):505–18. **One of the few studies investigating the neural correlates of
512 intrusive memory retrieval**

513 27. Brewin CR, Dalgleish T, Joseph S. A dual representation theory of posttraumatic stress
514 disorder. Psychol Rev. 1996 Oct;103(4):670–86.

515 28. Ehlers A, Clark DM. A cognitive model of posttraumatic stress disorder. Behav Res
516 Ther. 2000 Apr;38(4):319–45.

517 29. Schaich A, Watkins ER, Ehring T. Can concreteness training buffer against the
518 negative effects of rumination on PTSD? An experimental analogue study. J Behav
519 Ther Exp Psychiatry. 2013;44(4):396–403.

520 30. Ehring T, Szeimies A-K, Schaffrick C. An experimental analogue study into the role of
521 abstract thinking in trauma-related rumination. Behav Res Ther. 2009;47(4):285–93.

522 31. *Wegerer M, Blechert J, Kerschbaum H, Wilhelm FH. Relationship between fear
523 conditionability and aversive memories: Evidence from a novel conditioned-intrusion
524 paradigm. PLoS One. 2013 Jan;8(11):e79025. **One of the few studies investigating
525 the psychophysiological correlates of intrusve memory retrieval**

526 32. *Marks EH, Zoellner LA. Attenuating fearful memories: Effect of cued extinction on

intrusions. Emotion. 2014;14(6):1143–54. **A study devising a creative use of delivering trigger cues to sample intrusive memories via telephone interviews**

33. Malik A, Goodwin GM, Hoppitt L, Holmes EA. Hypomanic experience in young adults confers vulnerability to intrusive imagery after experimental trauma: Relevance for bipolar disorder. Clin Psychol Sci. 2014;2(6):675–84.

34. Lang TJ, Moulds ML, Holmes EA. Reducing depressive intrusions via a computerized cognitive bias modification of appraisals task: developing a cognitive vaccine. Behav Res Ther. 2009;47(2):139–45.

35. James EL, Lau-Zhu A, Tickle H, Horsch A, Holmes EA. Playing the computer game Tetris prior to viewing traumatic film material and subsequent intrusive memories: Examining proactive interference. J Behav Ther Exp Psychiatry. 2016;53:25–33.

36. Verwoerd J, Wessel I, de Jong PJ. Fewer intrusions after an attentional bias modification training for perceptual reminders of analogue trauma. Cogn Emot. 2012;26(1):153–65.

37. Marks EM, Steel C, Peters ER. Intrusions in trauma and psychosis: Information processing and phenomenology. Psychol Med. 2012;42(11):2313–23.

38. Nixon RDV, Cain N, Nehmy T, Seymour M. Does post-event cognitive load undermine thought suppression and increase intrusive memories after exposure to an analogue stressor? Memory. 2009;17(3):245–55.

39. Nixon RDV, Cain N, Nehmy T, Seymour M. The influence of thought suppression and cognitive load on intrusions and memory processes following an analogue stressor. Behav Ther. 2009;40(4):368–79.

40. Krans J, Näring G, Holmes EA, Becker ES. Tell me more: Can a memory test reduce analogue traumatic intrusions? Behav Res Ther. 2009 May;47(5):426–30.

551 41. Jobson L, Dalgleish T. Cultural differences in the relationship between intrusions and
552 trauma narratives using the trauma film paradigm. PLoS One. 2014;9(9):e106759.

553 42. McGaugh JL. The amygdala modulates the consolidation of memories of emotionally
554 arousing experiences. Annu Rev Neurosci. 2004;27:1–28.

555 43. Nader K, Schafe GE, Le Doux JE. Fear memories require protein synthesis in the
556 amygdala for reconsolidation after retrieval. Nature. 2000;406(6797):722–6.

557 44. Conway MA. Sensory-perceptual episodic memory and its context: Autobiographical
558 memory. Philos Trans R Soc Lond B Biol Sci. 2001;356(1413):1375–84.

559 45. Berntsen D. Involuntary autobiographical memories: An introduction to the unbidden
560 past. Cambridge University Press; 2009.

561 46. Holmes EA, Ghaderi A, Eriksson E, Lauri KO, Kukacka OM, Mamish M, et al. "I
562 can"t concentrate': A feasibility study with young refugees in sweden on developing
563 science-driven interventions for intrusive memories related to trauma. Behav Cogn
564 Psychother. 2017;45:97–109.

565 47. Waldhauser GT, Braun V, Hanslmayr S. Episodic memory retrieval functionally relies
566 on very rapid reactivation of sensory information. J Neurosci. 2016;36(1).

567 48. Noreika V, Canales-Johnson A, Koh J, Taylor M, Massey I, Bekinschtein TA.
568 Intrusions of a drowsy mind: neural markers of phenomenological unpredictability.
569 Front Psychol. 2015;6:202.

570 49. Di Simplicio M, Renner F, Blackwell SE, Mitchell H, Stratford HJ, Watson P, et al.
571 An investigation of mental imagery in bipolar disorder: Exploring "the mind's eye."
572 Bipolar Disord. 2016;18(8):669–83.

573 50. Ozsivadjian A, Hollocks MJ, Southcott J, Absoud M, Holmes EEA, Absoud Michael,

et al. Anxious imagery in children with and without autism spectrum disorder: An investigation into occurrence, content, features and implications for therapy. Journal of Autism and Developmental Disorders. 2016;1–11.

51. Holman EA, Garfin DR, Silver RC. Media's role in broadcasting acute stress following the Boston Marathon bombings. Proc Natl Acad Sci U S A. 2014;111(1):93–8.

52. Silver RC, Holman EA, Andersen JP, Poulin M, McIntosh DN, Gil-Rivas V. Mental- and physical-health effects of acute exposure to media images of the september 11, 2001, attacks and the iraq war. Psychol Sci. 2013;24(9):1623–34.

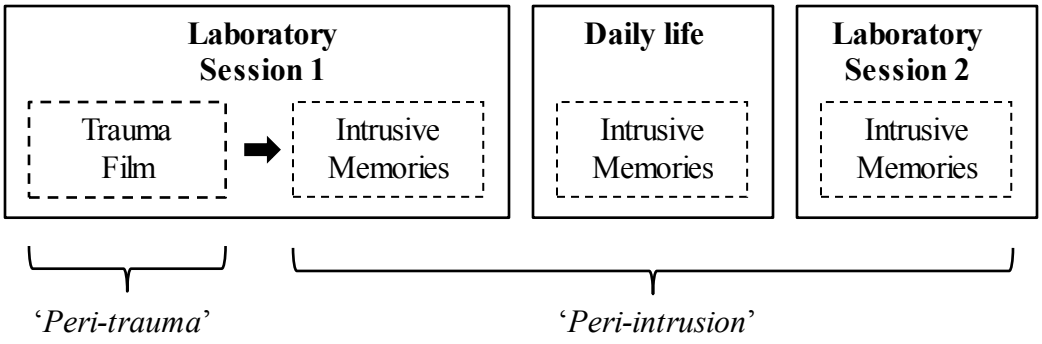

Figure 1. Basic procedure of a typical study using the trauma film paradigm. Trauma film (i.e., film with traumatic content) is presented in the laboratory (session 1); intrusive memories are typically monitored in daily life (e.g., over several days via diary). Recent studies, as shown in the current review, have also included methods to monitor intrusive memories in the laboratory (over several minutes). Intrusive memory monitoring in the laboratory can take place within the same session as the film and/or at a later session. 'Peri-trauma' means during viewing of the film, and 'peri-intrusion' means during monitoring of intrusive memories.

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Table 1. A selective review of studies where both viewing of a trauma film and monitoring of intrusive memories took place within the laboratory

Study	*N*	Design	IV of primary interest	Timing of IV	Intrusive memory sampling in the laboratory (DV: Frequency of occurrence of intrusions)				
					Peri-intrusion duration	Estimation method by the participant	Trigger cues	Ongoing task	Timing of the peri-intrusion period within the experimental design
Type 1: Rest periods									
Wilksch & Nixon, 2010	49	Correlational	Prior negative cognitions	-	5 min	Real-time	-	-	Day 1: Soon after film & Day 8
Hawkin & Couglas, 2013	54	Experimental	Acute nicotine administration	Before film	5 min	Real-time	-	-	Day 1: Soon after film
Clark et al., 2016	35	Experimental	Button presses associated with intrusions	After film	6 min	Real-time	-	-	Day 1: Soon after film
Type 2: Trigger cues									
Schaich et al., 2013	66	Experimental	Abstract/concrete processing	Before film	5 min	Retrospective	Visual	-	Day 1: Soon after IV
Ehring et al., 2009	101	Experimental	Abstract/concrete processing and distraction	After film	5 min	Retrospective	Visual and auditory	-	Day 1: Soon after film
Morina et al., 2013	67	Correlational	Trait general use of imagery	-	2 min	Retrospective	-	-	Day 1: Soon after film
Wegerer et al., 2013	66	Experimental	Conditioned and unconditioned cues	After film	3 min	Retrospective	Auditory	-	Day 1: 30 min after film
Marks & Zoellner, 2014	148	Experimental	Extinction procedures	After film	25 s	Retrospective	Auditory	-	Day 3
Malik et al., 2014	110	Correlational	Hypomanic experiences	-	2 min	Real-time	Visual	-	Day 8
Lang et al., 2009	48	Experimental	Cognitive bias modification procedure	Before film	2 min	Real-time	Visual	-	Day 8
James et al., 2015, Exp 1	52	Experimental	Reminder plus Tetris game play procedure	After film	2 min	Real-time	Visual	-	Day 8
James et al., 2015, Exp 2	76	Experimental	Reminder plus Tetris game play procedure	After film	2 min	Real-time	Visual	-	Day 8
James et al., 2016	56	Experimental	Tetris game play procedure	Before film	2 min	Real-time	Visual	-	Day 8
Type 3: Ongoing tasks									
Verwoerd et al., 2012	45	Experimental	Attentional training	After film	3 min	Real-time	-	Focus on breathing	Day 1: Soon after IV
Marks et al., 2012	49	Correlational	Analogous psychotic experiences	-	4 min	Real-time	-	Digit monitoring	Day 1: Soon after film
Nixon et al., 2009a	120	Experimental	Thought suppression and cognitive load	After film	5 min	Real-time	-	Suppression and/or cognitive load	Day 1: Soon after film & Day 8
Nixon et al., 2009b	80	Experimental	Thought suppression and cognitive load	After film	5 min	Real-time	-	Suppression and/or cognitive load	Day 1: Soon after film & Day 8

Note. *N* = number of participants in the main analyses; IV = independent variable; DV = dependent variable. Studies are presented in the order as they appeared in the main text. Peri-intrusion means during intrusion monitoring.