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A systematic review and meta-analysis of experimental methods for modulating intrusive memories following lab-analogue trauma exposure in non-clinical populations

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Experiencing trauma leads to intrusive memories (IMs), a hallmark symptom of post-traumatic stress disorder (PTSD), which also occurs transdiagnostically. Understanding why IMs increase or decrease is pivotal in developing interventions to support mental health. In this preregistered meta-analysis (PROSPERO: CRD42021224835), we included 134 articles (131 techniques, 606 effect sizes and 12,074 non-clinical participants) to investigate how experimental techniques alter IM frequency, intrusion-related distress and symptoms arising from lab-analogue trauma exposure. Eligible articles were identified by searching eight databases until 12 December 2023. To test potential publication biases, we employed methods including Egger's test and three-parameter selection models. We employed three-level multilevel modelling and meta-regressions to examine whether and how experimental techniques would modulate IM frequency and associated outcomes. Results showed that techniques (behavioural, pharmacological, neuromodulation) significantly reduced intrusion frequency ($g = 0.16$, 95% confidence interval [0.09, 0.23]). Notably, techniques aimed to reduce IMs also ameliorated intrusion-related distress and symptoms, while techniques that increased IMs exacerbated these related outcomes, thus highlighting IM's centrality in PTSD-like symptoms. Techniques tapping into mental imagery processing (for example, trauma reminder followed by playing Tetris) reduced intrusions when administered immediately after, or at a delayed time after trauma. Although our meta-analysis is limited to symptoms induced by lab-analogue trauma exposure, some lab-based results have now generalized to real-world trauma and IMs, highlighting the promising utility of lab-analogue trauma paradigms for intervention development.

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Psychological trauma, defined as 'exposure to actual or threatened death, serious injury, or sexual violence'[1], impacts approximately half of the global population at least once in their lifetime[2]. Experiencing trauma can lead to recurrent involuntary intrusions, referred to as intrusive memories (IMs), characterized by fragmented sensory episodes from the trauma, sometimes colloquially called 'flashbacks'[1,3–6]. These intrusions, accompanied by emotional distress, can exacerbate a spectrum of symptoms associated with post-traumatic stress disorder (PTSD), such as avoidance and hyperarousal, thereby further deteriorating mental health and incurring staggering economic cost[6–9]. For example, in the United States alone, the total economic burden of PTSD was estimated to be US$232.2 million in 2018[10].

Network models suggested that for PTSD patients, IMs were among the most central symptoms[11–13]. While symptom centrality does not always directly translate into clinical relevance[14], targeting IMs could be valuable given that they are distressing in themselves and impair peoples' daily functioning[5]. This opens an intriguing question of whether techniques that reduce intrusions could also alleviate intrusion-related distress and symptoms[15], ultimately ameliorating PTSD symptoms.

The overarching goal of our preregistered meta-analysis is to examine the effectiveness of experimental techniques in modulating IMs, including intrusion frequency, intrusion-related emotional distress and symptoms (for example, sleep difficulties, emotional reactions) following lab-analogue trauma exposure among non-clinical populations. Achieving this goal can illuminate the mechanisms involved in the formation, perpetuation and alteration of IMs, paving the way for enhancing existing or developing new clinical interventions aimed at treating IMs and related symptoms. This knowledge will be valuable in supporting individuals to maintain mental health and resilience in the face of life adversity and trauma.

A plethora of experimental techniques have been studied in the laboratory for their effectiveness in modulating IMs[5,6,16–19] (Fig. 1). However, a comprehensive quantitative examination of lab-based intrusion modulation techniques has yet to be conducted. Notably, these techniques encompass a wide spectrum, ranging from behavioural (for example, cognitive, emotional, social), to pharmacological (for example, oxytocin, alcohol) and neuromodulatory (non-invasive, transcranial electrical/magnetic stimulation) manipulations. Moreover, certain techniques aim to reduce or increase IMs, whereas others target modulating associated emotional distress and intrusion-related symptoms[20–22]. While recent meta-analyses have examined the modulation of IMs[23–26], they have either focused on specific subsets of techniques (for example, sleep, cognitive techniques), or only examined selected intrusion-related outcomes (for example, frequency only). Thus, a comprehensive examination of existing intrusion modulation techniques and their impacts on intrusion-related distress/symptoms would be both valuable and timely.

To induce IMs and related symptoms among non-clinical populations, researchers often use the lab-analogue trauma paradigms that employ film clips, sounds, pictures or immersive virtual reality (VR) depicting traumatic events (for example, severe injury, death or dying)[5,16–18]. Although lab-analogue trauma exposure clearly deviates from real-world trauma exposure, viewing materials depicting traumatic events (such as real-world trauma in news media) nevertheless can elicit analogous responses such as intrusions or hyperarousal dimensionally akin to PTSD-like symptoms[17,27,28]. Furthermore, according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), actual PTSD symptoms can develop from trauma 'exposure through electronic media, television, movies, or pictures' when this exposure is 'work related'[1] (for example, police viewing film footage of a murder). This suggests that at least in some circumstances, trauma exposure via viewing film footage can lead to clinical post-traumatic stress symptoms.

Our preregistered meta-analysis aimed to achieve the following goals. First, we aimed to examine the overall effect sizes for techniques that modulate intrusion frequency, intrusion-related distress and symptoms. Moreover, by examining intrusion frequency across various measures (that is, daily diaries, lab tasks or self-report questionnaires), we sought to determine whether different measures would converge in assessing the effectiveness of various techqniues[29].

Second, we aimed to provide procedural and mechanistic insights on which categories of techniques are effective and why they are effective. According to the procedure of a technique, we categorized individual techniques into three types: (1) behavioural, (2) pharmacological and (3) neuromodulation. In terms of mechanisms underlying IMs, both the dual-representation account (DRA) and the cognitive theory of PTSD[9,30] propose that IMs arise due to excessive encoding of low-level sensory details of the trauma in conjunction with inadequate encoding of high-level verbally accessible components about the trauma[3,7,8,31]. Accordingly, to modulate IMs, techniques can tap into imagery/visuospatial processing or verbal-conceptual (for example, elaboration/contextualization) processing. More recently, the retrieval-based feedback loop model emphasized that the associated distress and negative appraisal accompanying maladaptive memory retrieval, such as involuntary intrusions, contribute to the persistence of IMs[19]. Therefore, techniques that reduce distress or change emotional processing could also potentially modulate IMs. Drawing from these theoretical frameworks that shed light on the mechanisms behind IMs, we further coded behavioural techniques into three major mechanistic categories: (1) imagery, (2) verbal and (3) emotional (see Fig. 2 for coding schema).

Third, we aimed to examine the timing of techniques being administered and when they are effective. Techniques can be administered either before, during/peri, immediately after the analogue trauma or even with a delay after trauma. Pre-trauma techniques might prove valuable for safeguarding certain professions that anticipate traumatic experiences (for example, firefighters). However, given the unpredictability of real-world trauma, post-trauma techniques, especially those effective even with a delay, may be more practical. Relatedly, neuroscientific evidence suggests that older memories are not fixed but can be updated when memory traces are reactivated[32–37]. This has prompted small-scale research into reducing long-standing intrusive memories in clinical cases of PTSD stemming from trauma many years ago[38–40]. In the current meta-analysis, within each timepoint of administration, we examined the moderation effects of Procedure- and Mechanism-relevant superordinate categories, and the effectiveness of individual techniques (for example, Trauma Reminder + Tetris, Positive vs Negative Cognitive Bias Modification (CBM), Sleep) in modulating IMs.

Compared with existing meta-analyses that focused on specific techniques in intrusion reduction[23–26], the present meta-analysis provides presumably the most comprehensive examination so far by covering 131 unique techniques aimed at modulating IMs and intrusion-related outcomes (for example, intrusion-related distress and symptoms). To facilitate future research synthesis and empirical studies, we developed a website utilizing the meta-analysis dataset, allowing researchers to analyse the data freely and interactively (https://intrusivememory.shinyapps.io/shinymeta/).

Results

Description of included experiments

This meta-analysis included 134 articles, with $n = 153$ experiments, $k = 606$ effect sizes from $N = 12{,}074$ participants ($M_{age} = 23.37$, Female = 67.92%), covering 131 unique experimental techniques that modulate IMs (frequencies, distress and symptoms; for technique coding schema and preregistered analyses, see Fig. 2; for literature search and screening PRISMA flowchart, see Fig. 3). Table 1 shows summaries of included experiments. Included articles and their detailed coding are given in Supplementary Tables 1 and 11.

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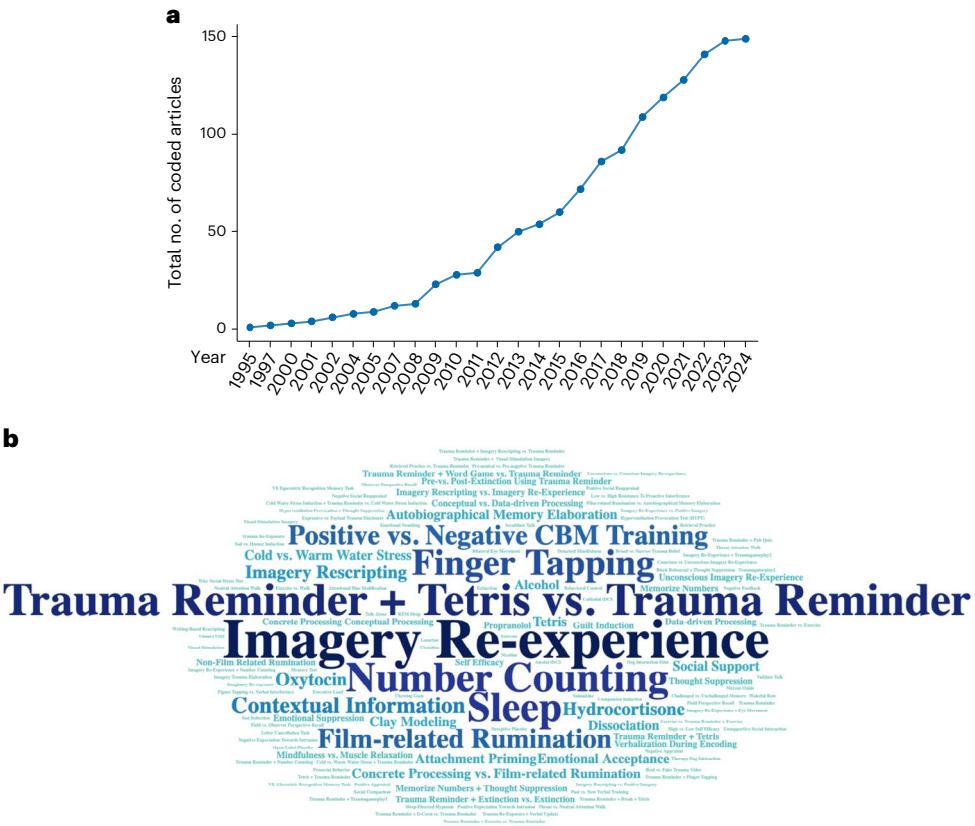

Fig. 1 | Descriptives of the coded articles. a, The total number of coded articles by year. **b**, A word cloud visualizing individual techniques identified in the meta-analysis. Larger sizes and deeper colour represent a greater number of articles investigating the corresponding technique.

Techniques significantly reduced IM frequency (preregistered)

For experiments that had measured IM frequency, techniques significantly reduced overall intrusion frequency (116 techniques, $n = 139$, $k = 370$, collected across diary-, lab- and questionnaire-based measures, Hedges' $g = 0.16$, 95% CI [0.09, 0.23], $Z = 4.59$, $P < 0.001$; Fig. 4a). We also found substantial heterogeneity ($Q(369) = 922.06$, $P < 0.001$, $I^2 = 64.34\%$, $\tau^2_{\text{experiment}} = 0.13$ at experiment level, and $\tau^2_{\text{outcome}} < 0.001$ at outcome level). Cochran's Q refers to the chi-squared statistic; I^2 is the percentage of total variances in the effect sizes that is due to heterogeneity rather than sampling error; and τ^2 is the tau-squared statistic which provides the variance estimate at the experiment and outcome levels. However, in this omnibus analysis, we did not find credible evidence that techniques would impact intrusion-related distress (Hedges' $g = 0.04$, 95% CI [−0.03, 0.11], $Z = 1.06$, $P = 0.290$) or intrusion-related symptoms (Hedges' $g = 0.07$, 95% CI [−0.01, 0.16], $Z = 1.70$, $P = 0.089$; Fig. 4a), with moderate degree of heterogeneity (Supplementary Table 2). Results remained largely consistent (except for symptoms) after excluding outliers and influential cases (Supplementary Table 2).

Examining publication biases, Egger's test revealed no significant evidence of publication bias ($Z = 1.88$, $P = 0.060$). The trim-and-fill procedure imputed 17 artificial effect sizes to adjust for potential publication biases, which resulted in a non-significant effect size, Hedges' $g = 0.07$, 95% CI [−0.01, 0.14], $Z = 1.81$, $P = 0.070$ (Fig. 4b; see Supplementary Fig. 1 and Table 3 for trim-and-fill results of different measures of intrusion frequency, and of distress and symptom outcomes). Complementing these publication biases analyses, we conducted three-parameter selection model analysis (non-preregistered), which showed a significant albeit small effect size in intrusion reduction, Hedges' $g = 0.06$, 95% CI [0.003, 0.12], $Z = 2.06$, $P = 0.039$ (Supplementary Table 4).

It is important to note that while the majority of experiments aimed to reduce intrusion frequency and associated distress/symptoms ($n = 109$), we were surprised to discover how a sizeable number of experiments instead investigated techniques aimed to do the opposite, that is, to increase intrusions and related distress/symptoms ($n = 62$; Table 1). Combining techniques predicted to decrease and increase intrusions might present a misleading picture of results. Thus, to better understand how different techniques impact intrusions and their associated distress/symptoms, we conducted additional non-preregistered analyses to examine techniques' impact on intrusions based on directional hypotheses for a decrease or increase, as stated in the original article (for hypothesis coding, see Supplementary Table 1).

Techniques aimed to reduce intrusions (non-preregistered). When techniques aimed to reduce intrusions and related outcomes, they significantly reduced overall intrusion frequency ($n = 104$, $k = 194$; Hedges' $g = 0.31$, 95% CI [0.23, 0.39], $Z = 7.78$, $P < 0.001$; Fig. 4a). We also found substantial heterogeneity ($Q(193) = 482.77$, $P < 0.001$, $I^2 = 62.83\%$, $\tau^2_{\text{experiment}} = 0.11$ at experiment level and $\tau^2_{\text{outcome}} < 0.001$ at outcome level). In addition, they significantly reduced both intrusion-related distress ($n = 44$, $k = 69$; Hedges' $g = 0.11$, 95% CI [0.03, 0.19], $Z = 2.66$, $P = 0.008$) and symptoms ($n = 35$, $k = 47$; Hedges' $g = 0.22$, 95% CI [0.12, 0.32], $Z = 4.27$, $P < 0.001$; Fig. 4a), with moderate degree of heterogeneity (Supplementary Table 2). These results remained robust against excluding outliers and influential cases (Supplementary Table 2). For related publication bias analyses (funnel plots and trim-and-fill), see Supplementary Fig. 1 and Table 3.

Techniques aimed to increase intrusions (non-preregistered). When techniques aimed to increase intrusions and related outcomes, they significantly increased overall intrusion frequency ($n = 52$, $k = 105$; Hedges'

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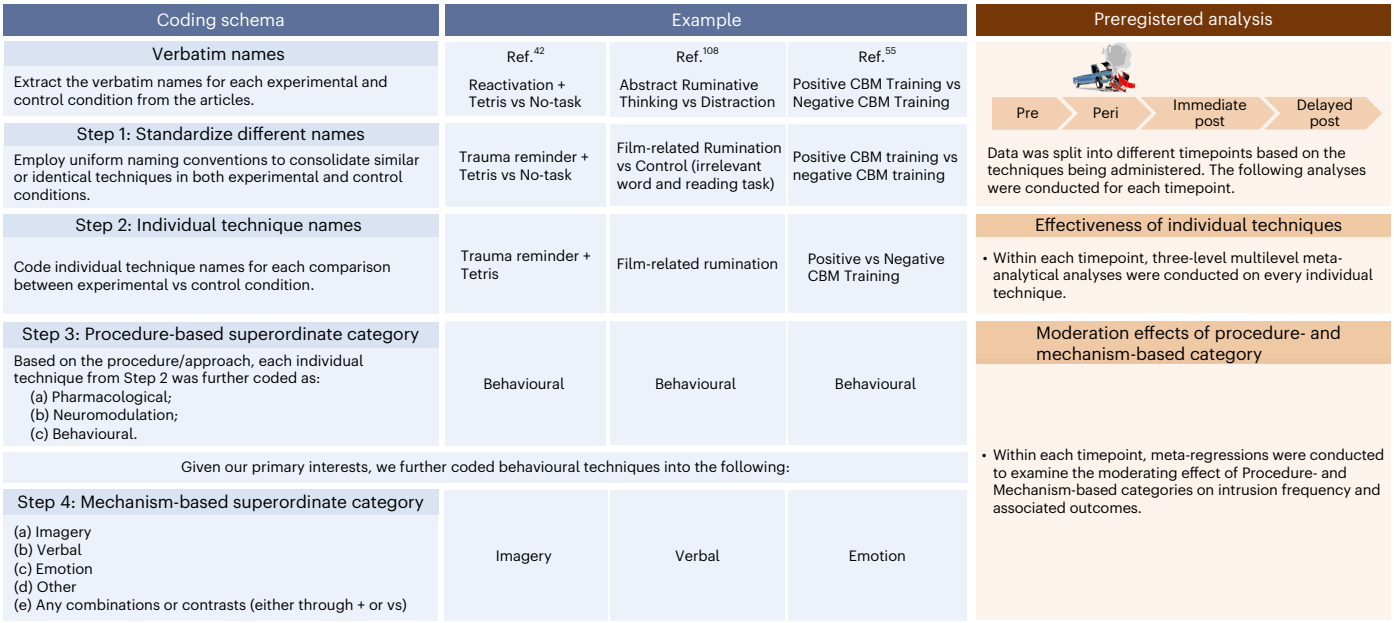

Fig. 2 | Coding schema of techniques used in the meta-analysis. Examples and corresponding preregistered analyses are presented side by side. For individual techniques in each mechanism category, see Supplementary Table 5.

$g = -0.13$, 95% CI [−0.25, −0.02], $Z = -2.24$, $P = 0.025$; Fig. 4a). Again, we found substantial heterogeneity ($Q(104) = 250.13$, $P < 0.001$, $I^2 = 63.80\%$, $\tau^2_{\text{experiment}} = 0.12$ at experiment level and $\tau^2_{\text{outcome}} = 0.02$ at outcome level). In addition, they significantly increased intrusion-related distress ($n = 26$, $k = 46$; Hedges' $g = -0.14$, 95% CI [−0.25, −0.03], $Z = -2.57$, $P = 0.010$; Fig. 4a) and symptoms ($n = 24$, $k = 30$; Hedges' $g = -0.19$, 95% CI [−0.37, −0.01], $Z = -2.04$, $P = 0.041$). Results were largely consistent (except for symptoms) after excluding outliers and influential cases (Supplementary Table 2). For related publication bias analyses (funnel plots and trim-and-fill), see Supplementary Fig. 1 and Table 3.

Timing of technique administration (preregistered)

We coded timepoint of technique administration relative to trauma occurrence, including pre, peri, immediate post (that is, within 24 h post trauma) and delayed post (that is, more than 24 h post trauma). First, using meta-regression, we examined whether Procedure- and Mechanism-based categories as moderators would modulate intrusion frequency, distress and symptoms (Fig. 5, see Supplementary Table 1 for categorizations of each article/technique, see Supplementary Table 5 for mechanism-based techniques). Full results from these timepoint-based moderation analyses are provided in Supplementary Table 6.

Second, employing three-level multilevel meta-analysis, we calculated the effect sizes of individual techniques (Fig. 5). Considering the robustness of results, we report and plot results from individual techniques with a minimum of 3 experiments (for results of all individual techniques, see Supplementary Table 7).

Pre. When administered before analogue trauma exposure, Procedure significantly modulated overall intrusion frequency ($Q(2) = 11.43$, $P = 0.003$; Fig. 5). Specifically, administration of Pharmacological techniques significantly increased overall intrusion frequency ($n = 6$, $k = 12$; Hedges' $g = -0.40$, 95% CI [−0.67, −0.13], $Z = -2.94$, $P = 0.003$). In contrast, Behavioural and Neuromodulation techniques did not significantly alter overall intrusion frequency ($P > 0.128$). Within Behavioural techniques, the Mechanism moderator (Imagery, Emotion, Verbal) did not significantly impact overall intrusion frequency ($Q(2) = 5.11$, $P = 0.078$). When examining individual techniques, no technique (with $n \geq 3$) significantly altered overall intrusion frequency ($P > 0.063$; Fig. 5).

Peri. Because only Behavioural techniques were administered during analogue trauma exposure, the Procedure moderation analysis was not conducted. Within Behavioural techniques, the Mechanism moderator significantly modulated overall intrusion frequency ($Q(3) = 26.07$, $P < 0.001$). Specifically, Imagery and Emotion techniques significantly reduced overall intrusion frequency with medium effect sizes (Imagery: $n = 11$, $k = 17$; Hedges' $g = 0.47$, 95% CI [0.25, 0.70], $Z = 4.18$, $P < 0.001$; Emotion: $n = 3$, $k = 10$; Hedges' $g = 0.37$, 95% CI [0.05, 0.69], $Z = 2.24$, $P = 0.025$). When examining individual techniques, concealed Finger Tapping (of a complex pattern) during trauma exposure significantly reduced overall intrusion frequency with a medium effect size ($n = 7$, $k = 12$; Hedges' $g = 0.57$, 95% CI [0.31, 0.84], $Z = 4.25$, $P < 0.001$). No other individual techniques (with $n \geq 3$) significantly modulated intrusion frequency.

Immediate Post. When administered immediately after analogue trauma exposure, Procedure did not modulate overall intrusion frequency ($Q(1) = 0.01$, $P = 0.925$; Behavioural, $n = 77$, $k = 226$; Pharmacological, $n = 3$, $k = 4$; there were no Neuromodulation techniques at this timepoint). Within the Behavioural category, the Mechanism moderator (Imagery, Verbal, Emotion, etc.) did not significantly moderate intrusion frequency ($Q(5) = 6.43$, $P = 0.266$). When examining individual techniques, the Trauma Reminder + Tetris (vs Trauma Reminder alone) significantly reduced overall intrusion frequency with a large effect size ($n = 11$, $k = 21$; Hedges' $g = 0.80$, 95% CI [0.66, 0.93], $Z = 11.59$, $P < 0.001$). Other techniques (with $n \geq 3$) that significantly reduced overall intrusion frequency were: Sleep ($n = 8$, $k = 9$; Hedges' $g = 0.26$, 95% CI [0.10, 0.43], $Z = 3.07$, $P = 0.002$); Imagery Re-experience + Eye Movement ($n = 3$, $k = 3$; Hedge's $g = 0.49$, 95% CI [0.13, 0.85], $Z = 2.67$, $P = 0.008$) and Imagery Re-experience + Number Counting ($n = 3$, $k = 3$, Hedge's $g = 0.56$, 95% CI [0.12, 1.00], $Z = 2.51$, $P = 0.012$, see Fig. 5).

Delayed Post. When administered at a delayed time (that is, more than 24 h) after analogue trauma exposure, Procedure did not modulate overall intrusion frequency ($Q(1) = 0.97$, $P = 0.325$; Behavioural, $n = 9$, $k = 31$; Pharmacological, $n = 1$, $k = 2$; there were no Neuromodulation techniques at this timepoint). Within the Behavioural techniques, the Mechanism moderator was not significant ($Q(1) = 0.39$,

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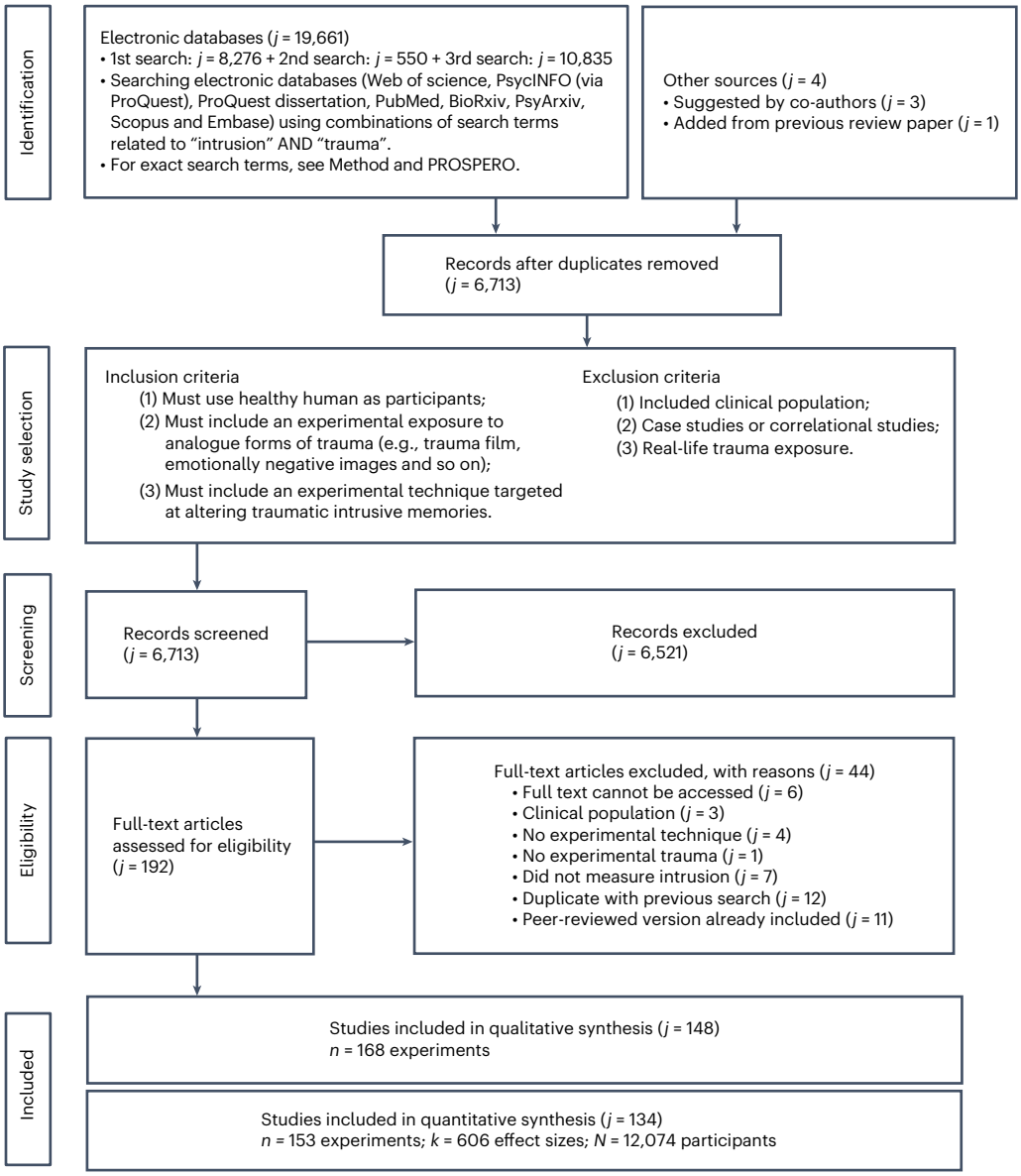

Fig. 3 | A PRISMA flowchart of literature search and screening.

$P = 0.534$). Examining individual techniques with $n \geq 3$, only Trauma Reminder + Tetris (vs No-Task control) technique significantly reduced overall intrusion frequency with a large effect size ($n = 3, k = 6$; Hedges' $g = 0.77$, 95% CI [0.07, 1.48], $Z = 2.14$, $P = 0.032$).

Impact on intrusion-related outcomes (preregistered). Neither Procedure nor Mechanism significantly modulated intrusion-related distress or symptoms at any of the four timepoints of technique administration ($P > 0.09$).

Regarding individual techniques (Fig. 6), at Pre trauma, the Positive vs Negative CBM Training showed a large effect size in distress reduction ($n = 3, k = 5$; Hedges' $g = 0.65$, 95% CI [0.38, 0.92], $P < 0.001$). At Immediate Post timepoint, the Trauma Reminder + Tetris (vs Trauma Reminder alone) showed a medium effect size in reducing intrusion-related symptoms ($n = 4, k = 4$; Hedges' $g = 0.37$, 95% CI [0.09, 0.64], $P = 0.009$), and the Imagery Re-experience + Number Counting technique showed a medium-to-large effect size in intrusion-related symptoms reduction ($n = 3, k = 3$; Hedges' $g = 0.56$, 95% CI [0.23, 0.89], $P < 0.001$).

Mode of intrusion measurement (preregistered). The mode of measurement of IMs (for example diary-, lab-, or questionnaire-based) did not significantly modulate overall intrusion frequency ($P = 0.316$; see Supplementary Table 8).

In addition to the above preregistered analyses within each timepoint of technique administration, we conducted preregistered moderation analyses, including (1) across the whole dataset, whether demographic and experiment-related factors would moderate the overall intrusion frequency and associated outcomes (Supplementary Table 8); (2) within Procedure- and Mechanism-based categories, whether different timepoints may moderate the effectiveness (Supplementary Tables 9 and 10). Internal bias assessments are provided in Supplementary Table 11.

Discussion

In this preregistered systematic review and meta-analysis, we synthesized 606 effect sizes from the 131 techniques that aimed to modulate intrusive memories (IMs, intrusion frequency, distress and symptoms) arising from lab-analogue trauma exposure. Overall, all techniques

Table 1 | Summary statistics for the studies included in the meta-analysis

Summary statistics	
n (Total experiments)	153
k (Total effect sizes)	606
N (Total sample sizes)	12,074
Demographic information	
Age, mean (s.d.)	23.37 (3.47)
Gender	
Male, *N* (%)	3,873 (32.08%)
Female, *N* (%)	8,201 (67.92%)
Countries/Regions	
England, *n* (%)	50 (32.68%)
the Netherlands, *n* (%)	29 (18.95%)
Australia, *n* (%)	24 (15.69%)
Germany, *n* (%)	19 (12.42%)
USA, *n* (%)	14 (9.15%)
Others, *n* (%)	17 (11.11%)
Experimental design	
Between-participant, *n* (%)	145 (94.77%)
Within-participant, *n* (%)	8 (5.23%)
Experimental hypothesis directions[a]	
Intrusion increase, *n*	62
Intrusion decrease, *n*	109
Unspecified, *n*	38
Null, *n*	2
Intrusion outcomes	
Intrusion frequency, *n*	139
Intrusion-related distress, *n*	66
Intrusion-related symptoms, *n*	56

[a]Note that the total number of experiments (*n* = 153) did not align with the sum of experiments stemming from various hypothesis directions (*n* = 211). This disparity arose because some experiments entailed more than two conditions and tested multiple hypothesis directions.

combined significantly reduced intrusions (g = 0.16, 95% CI [0.09, 0.23]), possibly owing to the fact that the majority of the experiments (n = 109) aimed to reduce intrusions. Notably, when we explored these techniques hypothesized in the original papers to reduce IMs, they not only reduced intrusion frequency (g = 0.31, 95% CI [0.23, 0.39]) but also alleviated intrusion-related distress (g = 0.11, 95% CI [0.03, 0.19]) and symptoms (g = 0.22, 95% CI [0.12, 0.32]). Conversely, techniques that aimed to increase IMs indeed increased intrusion frequency (g = −0.13, 95% CI [−0.25, −0.02]) as well as distress (g = −0.14, 95% CI [−0.25, −0.03]) and symptoms (g = −0.19, 95% CI [−0.37, −0.01]). Thus, modulating IMs has generalized impact on intrusion frequency, intrusion-related distress and symptoms. These results highlight IM's centrality in PTSD-like symptoms[11–13] and suggest that targeting IMs in an intervention may benefit other aspects related to psychopathology[15].

Our meta-analysis provides various insights regarding when and which techniques are effective in modulating IMs. Notably, certain post-trauma techniques (that is, those administered after lab-analogue trauma exposure) that tap into mental imagery processes were among the most effective techniques, showing large effect sizes in intrusion frequency reduction even when administered after a delay. More specifically, at both post-trauma timepoints (immediate and delay), playing Tetris following a trauma reminder was effective in reducing intrusions (Immediate: g = 0.80, 95% CI [0.66, 0.93]; Delay: g = 0.77, 95% CI [0.07, 1.48]) as well as in alleviating intrusion-related symptoms when administered immediately post trauma. In particular, benefits observed when techniques administered after a delay are consistent with hypotheses derived from a memory reconsolidation account, which posits that even older memories can be updated when reactivated[33,41]. In the context of trauma, a brief trauma reminder may reactivate part of the trauma memory traces (for example, a hotspot), rendering it labile and susceptible to interference[32,42,43]. Playing a game such as Tetris that occupies visuospatial perceptual processing is then hypothesized to interfere with the visuoperceptual nature of IMs, rendering them less likely to be triggered and re-occur[44–46].

When administered during analogue trauma exposure, an imagery technique: concealed Finger Tapping of complex patterns was found to also significantly reduce intrusion frequency. Complex spatial Finger Tapping is thought to compete for limited visuospatial working memory resources during mental imagery processing, thereby reducing imagery vividness[44]. Therefore, it is hypothesized to disrupt the encoding of visuoperceptual details of trauma content, leading to reduced IMs[47,48]. Together, these findings are consistent with the dual-representation account (DRA)[30,49] and the Cognitive model of PTSD[9] that emphasize heightened visuoperceptual processing of trauma memory to lead to intrusive memories, and specifically disrupting visuoperceptual processing during encoding would reduce the likelihood of occurrence of sensory-driven intrusions.

The DRA also proposes that contextualizing trauma memories should reduce IMs. Contextualization is thought to help integrate trauma memories into one's autobiographical memory, allowing such memories to be more susceptible to inhibitory control processes mediated by the prefrontal cortex, ultimately decreasing the frequency of IMs[30]. However, in our meta-analysis, the experimental technique Contextual Information processing, which provides additional contextual information about trauma material, did not significantly modulate intrusion frequency when administered during trauma exposure (Fig. 5)[50]. In fact, when administered before trauma exposure, this technique increased IMs, although this analysis included only two effect sizes (see Supplementary Table 7). There may be differences between this technique and that intended by DRA; nevertheless, this raises questions for trauma treatment about whether and in which circumstances to consider using contextual information processing or another form of the technique[50,51].

Although recent work shows promising results for Imagery Rescripting[23], our findings suggest that administering an analogue version of Imagery Rescripting immediately post trauma did not yield credible evidence favouring intrusion reduction, despite the highly comparable effect sizes to a previous meta-analysis[23] (Hedges' g = 0.29, 95% CI [−0.08, 0.65] in our meta-analysis vs Hedges' g = 0.31, 95% CI [0.03, 0.59] in the previous meta-analysis[23]). This discrepancy could be due to different analytical approaches: while the previous meta-analysis[23] combined both immediate and delayed post-trauma Imagery Rescripting, our meta-analysis distinguished between these two timepoints of administration and thus included fewer datasets for each timepoint. Nevertheless, given the highly comparable effect sizes in intrusion reduction, future research should further examine the effectiveness of Imagery Rescripting in lab and clinical settings.

PTSD and IMs models propose that changing emotional processing, particularly the negative (re)appraisal or distress associated with trauma, may also reduce IMs[9,19]. Our meta-analysis examined Emotion techniques, including Positive vs Negative CBM Training and Emotional Reappraisal/Acceptance/Suppression[22,52–54]. For example, Positive CBM Training aims to shift individuals away from negative reappraisal styles regarding experiencing IMs[21]. Our findings indicated that when implemented before trauma exposure, Positive CBM Training reduced subsequent intrusion-related distress[54,55], and it did not impact on IM frequency. When administered after the trauma, Positive CBM Training did not yield any significant results (Fig. 6)[21,56]. Interestingly, one clinical

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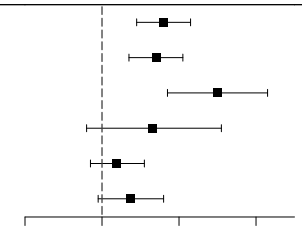
a Aggregate effect sizes for different outcomes and hypothesis directions

Outcome	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Overall intrusion frequency	10,765	139	370	0.16 [0.09, 0.23]	<0.001
Diary-based intrusion frequency	8,985	121	248	0.14 [0.07, 0.21]	<0.001
Lab-based intrusion frequency	2,859	39	79	0.3 [0.17, 0.43]	<0.001
Questionnaire-based intrusion frequency	1,715	17	43	0.13 [−0.04, 0.31]	0.137
Intrusion-related distress	5,690	66	136	0.04 [−0.03, 0.11]	0.290
Intrusion symptoms	4,730	55	100	0.07 [−0.01, 0.16]	0.089

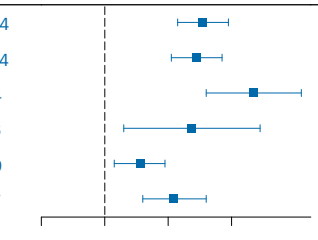
All direction



N: number of participants
n: number of experiments
k: number of effect sizes

Outcome	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Overall intrusion frequency	8,069	104	194	0.31 [0.23, 0.39]	<0.001
Diary-based intrusion frequency	6,619	89	134	0.29 [0.21, 0.37]	<0.001
Lab-based intrusion frequency	2,052	28	34	0.47 [0.32, 0.62]	<0.001
Questionnaire-based intrusion frequency	1,291	13	26	0.27 [0.06, 0.49]	0.012
Intrusion-related distress	3,881	44	69	0.11 [0.03, 0.19]	0.008
Intrusion symptoms	3,026	35	47	0.22 [0.12, 0.32]	<0.001

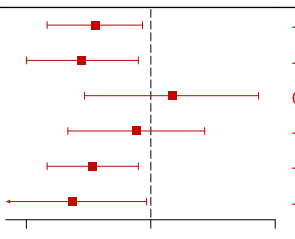
Decrease



N: number of participants
n: number of experiments
k: number of effect sizes

Outcome	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Overall intrusion frequency	4,097	52	105	−0.13 [−0.25, −0.02]	0.025
Diary-based intrusion frequency	3,611	47	63	−0.17 [−0.30, −0.03]	0.015
Lab-based intrusion frequency	1,357	16	32	0.05 [−0.16, 0.26]	0.620
Questionnaire-based intrusion frequency	487	6	10	−0.04 [−0.20, 0.13]	0.671
Intrusion-related distress	2,190	26	46	−0.14 [−0.25, −0.03]	0.010
Intrusion symptoms	2,198	24	30	−0.19 [−0.37, −0.01]	0.041

Increase



N: number of participants
n: number of experiments
k: number of effect sizes

b Funnel plot for different hypothesis directions

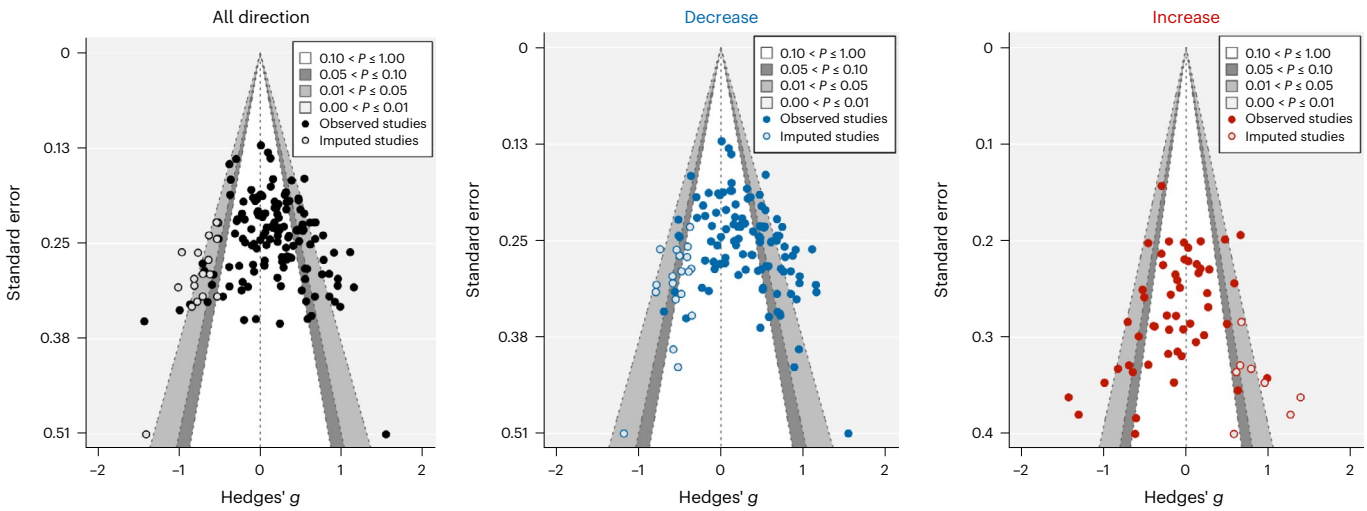


Fig. 4 | Results of the main analysis. a, Overall effect sizes for all techniques and for techniques that were hypothesized to decrease/increase the intrusions. Hedge's *g* and *P* values were extracted from the three-level multilevel meta-analytical modelling (two-sided *z*-tests). Forest plots represent the mean effect sizes, with error bars representing 95% confidence intervals. **b**, The contour-enhanced funnel plots examining publication biases. Imputed studies were calculated using the trim-and-fill method.

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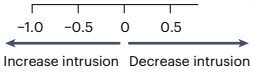
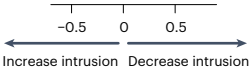
Outcome: Overall intrusion frequency

Timepoint of technique administration	Pre					Peri				
Analysis	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Moderation Analysis: Procedure-based Category				Q_M = 11.43	0.003					
Behavioural	753	13	25	0.14 [−0.04, 0.33]	0.128	NA	NA	NA	NA	NA
Pharmacological	489	6	12	−0.4 [−0.67, −0.13]	0.003	NA	NA	NA	NA	NA
Neuromodulation	118	1	2	0.23 [−0.38, 0.83]	0.464	NA	NA	NA	NA	NA
Moderation Analysis: Mechanism-based Category				Q_M = 5.11	0.078				Q_M = 26.07	<0.001
Imagery	120	2	3	0.31 [−0.19, 0.80]	0.223	750	11	17	0.47 [0.25, 0.70]	<0.001
Verbal	80	2	2	−0.4 [−0.90, 0.10]	0.114	933	13	24	−0.16 [−0.35, 0.03]	0.093
Emotion	291	5	9	0.22 [−0.10, 0.54]	0.178	227	3	10	0.37 [0.05, 0.69]	0.025
Verbal vs Imagery	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Imagery vs Verbal	NA	NA	NA	NA	NA	50	1	1	0.58 [−0.24, 1.39]	0.166
Verbal + Imagery	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Imagery + Verbal	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Individual Techniques										
Trauma Reminder + Tetris vs Trauma Reminder	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Trauma Reminder + Tetris	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sleep	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Imagery Re-experience + Eye Movement	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Imagery Re-experience + Number Counting	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Imagery Re-experience	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Film-related Rumination	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Positive vs Negative CBM Training	147	3	6	0.27 [−0.23, 0.77]	0.284	NA	NA	NA	NA	NA
Imagery Rescripting	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Autobiographical Memory Elaboration	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Finger Tapping	NA	NA	NA	NA	NA	360	7	12	0.57 [0.31, 0.84]	<0.001
Number Counting	NA	NA	NA	NA	NA	396	7	11	−0.17 [−0.62, 0.29]	0.471
Contextual Information	NA	NA	NA	NA	NA	244	4	8	−0.2 [−0.47, 0.07]	0.142
Dissociation	NA	NA	NA	NA	NA	128	3	4	−0.01 [−0.61, 0.59]	0.973
High-dose Alcohol	194	3	3	−0.22 [−0.74, 0.30]	0.404	NA	NA	NA	NA	NA
Low-dose Alcohol	194	3	3	−0.49 [−1.01, 0.03]	0.063	NA	NA	NA	NA	NA

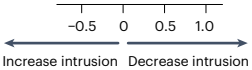
N: Number of Participants
n: Number of Experiments
k: Number of Effect Sizes





Timepoint of technique administration	Immediate post					Delayed post				
Analysis	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Moderation Analysis: Procedure-based Category				Q_M = 0.01	0.925				Q_M = 0.97	0.325
Behavioural	6,042	77	226	0.23 [0.15, 0.31]	<0.001	1,018	9	31	0.26 [−0.02, 0.54]	0.069
Pharmacological	340	3	4	0.21 [−0.23, 0.65]	0.35	65	1	2	−0.19 [−1.05, 0.67]	0.66
Neuromodulation	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Moderation Analysis: Mechanism-based Category				Q_M = 6.43	0.266				Q_M = 0.39	0.534
Imagery	2,933	37	96	0.31 [0.18, 0.43]	<0.001	837	8	27	0.27 [−0.05, 0.59]	0.104
Verbal	1,135	15	53	0.16 [−0.02, 0.34]	0.076	140	2	2	0.44 [−0.14, 1.02]	0.136
Emotion	1,023	10	16	0.01 [−0.24, 0.26]	0.928	NA	NA	NA	NA	NA
Verbal vs Imagery	107	2	2	0.36 [−0.27, 1.00]	0.264	NA	NA	NA	NA	NA
Imagery vs Verbal	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Verbal + Imagery	200	2	6	0.35 [0.02, 0.67]	0.038	NA	NA	NA	NA	NA
Imagery + Verbal	575	7	9	0.18 [−0.09, 0.45]	0.199	NA	NA	NA	NA	NA
Individual Techniques										
Trauma Reminder + Tetris vs Trauma Reminder	607	11	21	0.8 [0.66, 0.93]	<0.001	NA	NA	NA	NA	NA
Trauma Reminder + Tetris	NA	NA	NA	NA	NA	273	3	6	0.77 [0.07, 1.48]	0.032
Sleep	552	8	9	0.26 [0.10, 0.43]	0.002	NA	NA	NA	NA	NA
Imagery Re-experience + Eye Movement	250	3	3	0.49 [0.13, 0.85]	0.008	NA	NA	NA	NA	NA
Imagery Re-experience + Number Counting	250	3	3	0.56 [0.12, 1.00]	0.012	NA	NA	NA	NA	NA
Imagery Re-experience	880	8	9	0.11 [−0.09, 0.32]	0.285	NA	NA	NA	NA	NA
Film-related Rumination	370	5	16	−0.23 [−0.78, 0.33]	0.42	NA	NA	NA	NA	NA
Positive vs Negative CBM Training	341	3	4	0.16 [−0.12, 0.44]	0.27	NA	NA	NA	NA	NA
Imagery Rescripting	319	3	5	0.29 [−0.08, 0.65]	0.123	NA	NA	NA	NA	NA
Autobiographical Memory Elaboration	315	3	6	0.03 [−0.15, 0.21]	0.741	NA	NA	NA	NA	NA
Finger Tapping	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Number Counting	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Contextual Information	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Dissociation	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
High-dose Alcohol	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Low-dose Alcohol	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

N: Number of Participants
n: Number of Experiments
k: Number of Effect Sizes



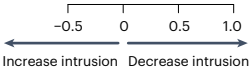


Fig. 5 | Results of the moderation analysis and analysis on individual techniques. Effectiveness of Procedure and Mechanism superordinate categories, and individual techniques within each timepoint of technique administration. For individual techniques, the figure shows results with a minimum of 3 experiments within each timepoint ($n \geq 3$). Overall moderation effects and effect sizes for each level within a moderator were estimated through the meta-regression. Effect sizes for each individual technique were estimated through three-level multilevel modelling. Forest plots represent the mean effect sizes, with error bars representing 95% confidence intervals.

study indicated that Positive CBM Training may alleviate symptoms in PTSD patients[57]. Future research is warranted to investigate the translational value of emotion-modulation techniques.

In addition to techniques hypothesized to tap into single mechanisms or processes, we also coded techniques that tackled multiple mechanisms (for example, imagery and verbal processing, cognitive

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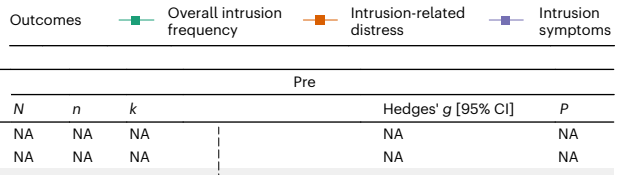
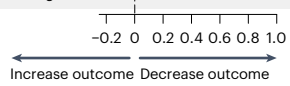


Pre

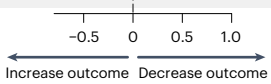
Individual techniques	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Trauma Reminder + Tetris vs Trauma Reminder	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Trauma Reminder + Tetris	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Sleep	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Imagery Re-experience + Eye Movement	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Imagery Re-experience + Number Counting	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Imagery Re-experience	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Film-related Rumination	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Positive vs Negative CBM Training	147	3	6	0.27 [−0.23, 0.77]	0.284
	147	3	5	0.65 [0.38, 0.92]	<0.001



N: Number of Participants
n: Number of Experiments
k: Number of Effect Sizes

Immediate post

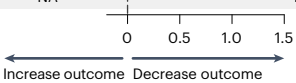
Individual techniques	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Trauma Reminder + Tetris vs Trauma Reminder	607	11	21	0.8 [0.66, 0.93]	<0.001
	267	4	4	0.37 [0.09, 0.64]	0.009
Trauma Reminder + Tetris	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Sleep	552	8	9	0.26 [0.10,0.43]	0.002
	367	6	6	0.12 [−0.10, 0.34]	0.286
	295	5	5	0 [−0.45, 0.45]	0.998
Imagery Re-experience + Eye Movement	250	3	3	0.49 [0.13, 0.85]	0.008
	250	3	3	0.26 [−0.06, 0.58]	0.114
Imagery Re-experience + Number Counting	250	3	3	0.56 [0.12, 1.00]	0.012
	250	3	3	0.56 [0.23, 0.89]	<0.001
Imagery Re-experience	880	8	9	0.11 [−0.09, 0.32]	0.285
	319	3	3	0.37 [−0.03, 0.76]	0.067
	236	3	4	−0.14 [−0.63, 0.36]	0.593
Film-related Rumination	370	5	16	−0.23 [−0.78, 0.33]	0.42
	199	3	12	−0.14 [−0.30, 0.03]	0.108
Positive vs Negative CBM Training	341	3	4	0.16 [−0.12, 0.44]	0.27
	341	3	4	−0.09 [−0.30, 0.13]	0.423



N: Number of Participants
n: Number of Experiments
k: Number of Effect Sizes

Delayed post

Individual techniques	*N*	*n*	*k*	Hedges' *g* [95% CI]	*P*
Trauma Reminder + Retris vs Trauma Reminder	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Trauma Reminder + Tetris	273	3	6	0.77 [0.07, 1.48]	0.032
	273	3	3	0.31 [−0.16, 0.78]	0.19
Sleep	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Imagery Re-experience + Eye Movement	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Imagery Re-experience + Number Counting	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Imagery Re-experience	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Film-related Rumination	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA
Positive vs Negative CBM Training	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA



N: Number of Participants
n: Number of Experiments
k: Number of Effect Sizes

Fig. 6 | Multiple outcomes (intrusion frequency, distress, symptoms) of individual techniques. Individual techniques with more than 2 outcomes and with each outcome having a minimum of 3 experiments ($n \geq 3$) within each timepoint. Three-level multilevel modelling was applied to each individual technique and each outcome within each timepoint. *P* values were obtained using two-sided *z*-tests. Forest plots represent the mean effect sizes, with error bars representing 95% confidence intervals.

and emotional processing). For example, in one article using a dual-task intervention, simultaneous Imagery Re-experience and Number Counting significantly reduced intrusions and intrusion-related symptoms when administered immediately post trauma[58]. These results raise the possibility of combining imagery and verbal processing (for example, number counting and word games[43]) in reducing IMs. Another technique found to be effective and that taps into multiple mechanisms is post-trauma Sleep[24–26]. Sleep may facilitate the integration of trauma memories into one's autobiographical memory scheme[59,60], help restore cognitive control[61–63] and alleviate affective responses[64,65]. Such results open interests in new avenues to explore composite interventions that address multiple processing types simultaneously[66].

One strength of our meta-analysis is that we included Pharmacological and Neuromodulation techniques aimed at modulating IMs. Despite the relatively low number of experiments and the diversity of Pharmacological techniques tested (for example, Alcohol, Nicotine, Oxytocin), results showed that Pharmacological techniques administered pre-trauma significantly increased intrusions. These findings provide valuable insights informing risk factors that may exacerbate traumatic intrusions. Specifically, certain drugs (Nicotine and Oxytocin) may increase intrusions via emotion-relevant mechanisms, such as increasing physiological arousal[67,68] and heightening sensitivity to emotional cues[69,70]. Heightened arousal and sensitivity may promote preferential encoding of low-level sensory details of the trauma, resulting in sensory-driven intrusions[9]. Despite the significant overall effect in increasing intrusions, the low number of experiments per timepoint prevents us from drawing strong conclusions regarding the effectiveness of specific Pharmacological techniques.

Regarding Neuromodulation techniques, research suggests that non-invasive brain stimulation could temporally inhibit or activate neural activity implicated in visual-perceptual processing[71], cognitive control[72] and emotion regulation[73], that are highly relevant for IMs. Specifically, a study employed transcranial direct current stimulation (tDCS) to stimulate the left dorsolateral prefrontal cortex to enhance cognitive control before analogue trauma exposure. Despite the hypothesis that the tDCS would reduce IMs via enhanced cognitive control, results showed that there was no significant effect of tDCS on IMs[74]. Another study found that after viewing a trauma film, disrupting neural activity of the occipital cortex through repetitive transcranial magnetic stimulation (rTMS) reduced emotional intensity of intrusions, although not intrusion frequency[75]. Building on the current meta-analysis, one future avenue is to test whether combining techniques involving both Behavioural/Imagery and Neuromodulation/Pharmacological techniques could improve the effectiveness of specific techniques.

The ecological validity of the lab-analogue trauma exposure paradigm, its limitations and the translational values of our meta-analysis should be discussed. First, lab-analogue trauma exposure (for example, films, images, VR) clearly deviate from real-world trauma exposure in many ways, including self-involvement, emotional intensity, actual threat likelihood and so on. In addition, analogue trauma typically only induces short-lived trauma symptoms that tend to subside within a week, contrasting with the potential severe and long-lasting effects often observed after real-life trauma, and such limitations are further discussed elsewhere[17]. We note that our meta-analyses only included experiments conducted in lab settings with non-clinical populations, cautioning against generalization to real-life trauma experiences and clinical populations. However, it is worth noting that repeated or extreme 'indirect' trauma exposure via media (including film), if work related, has been included within the diagnostic criterion for a traumatic event in DSM-5 (ref. 1, p. 271). Studies have shown that indirect exposure to trauma via media can induce acute stress symptoms resembling PTSD-like symptoms[27,28]. Clearly, we are not equating analogue lab trauma to real trauma, rather that the phenomenon of intrusive memories after witnessing aversive experiences is a continuum.

Recent studies have provided some evidence indicating that intrusion modulation techniques developed in the laboratory may also prove effective in clinical settings. For example, in clinical randomized controlled trials, imagery techniques (for example, Trauma Reminder + Tetris) significantly reduced the number of intrusions arising from real-life trauma such as traumatic childbirth, motor vehicle accidents, or work-related trauma in healthcare staff[15,76–80]. Consistent with our lab-based meta-analysis showing that similar imagery techniques can reduce intrusions even after a delay, it appears that imagery techniques may at times be effective for traumatic events that occurred weeks or months earlier[15,80] (see also refs. 39,40,81 for smaller case studies on older traumatic memories). A clinical meta-analysis revealed a medium effect size of $g = 0.49$, 95% CI [0.18, 0.80] in real-world intrusion reduction using the Trauma Reminder + Tetris technique[38], smaller than that reported in our meta-analysis ($g = 0.77$, 95% CI [0.07, 1.48] for Trauma Reminder + Tetris administered at the delayed post-trauma timepoint). The lower effect size is expected, given that clinical studies typically involve heterogeneous participants and trauma types, and are less well controlled than in laboratory settings.

It is important to think carefully about the relationship between studies in the laboratory and clinical settings. The lab studies usually only test post-trauma techniques administered up to 4 days after analogue trauma exposure. The similar pattern of findings with clinical samples, at longer time intervals of intervention administration post-trauma than lab studies, inspires cautious optimism about possibilities to modulate intrusive memories being on a continuum. It may also help alleviate concerns about a different pattern of results emerging (for example, increased IMs) should the time interval be extended. Considering concerns about safety is particularly important given the clinical controversy over critical incident stress debriefing, which in meta-analyses has been shown to worsen symptoms of PTSD after real trauma[82,83]. Collectively, while in their early days, similarities in the pattern of results that seem to be emerging between lab and clinical studies support the potential of using lab-analogue trauma paradigm[17] for modelling IMs as a treatment development target. In the future, new techniques could be developed for use either as stand-alone interventions, or to complement existing evidence-based interventions or treatments[84].

Limitations of the current work should be discussed. One limitation is that while our classification of techniques based on their hypothesized mechanisms was informed by existing research and theories, the precise underlying neurobiological mechanisms remain unknown. Understanding the neurobiological mechanisms through which such techniques operate could not only empirically validate their proposed mechanisms but also help identify the conditions under which they are most effective. Another limitation is that we have only focused on IMs in relation to post-traumatic stress conditions such as PTSD, neglecting the relevance of IMs in other disorders (for example, depression, anxiety, bipolar, obsessive-compulsive disorders) and related symptoms such as intrusive thoughts, rumination or excessive worry[30,85–90]. Based on our results, future research should examine whether similar techniques can reduce IMs and intrusion-related symptomatology in these other mental disorders. Third, preregistered experiments are rare (with exceptions[20,53]), and this may in part be due to the age of some included studies. Based on effect sizes provided by the current and other meta-analyses[23,26], future research should conduct preregistered and well-powered studies to improve the evidence base regarding the effectiveness of specific techniques. This is of particular importance, as mentioned above, given the small number of studies in certain subgroups when techniques are divided by timepoint. Lastly, we preregistered that we would perform three-level multilevel meta-analyses for each outcome individually, instead of conducting multivariate analyses[91]. Multivariate analyses could be advantageous as it allows researchers to examine various types of outcome (for example, intrusion frequency, distress and symptoms) in a single analysis, accounting

for correlations between outcomes. Future meta-analyses can consider utilizing these advanced multivariate analyses.

To conclude, our meta-analysis provides a comprehensive coverage of the experimental techniques on the modulation of intrusive memories arising from lab-analogue trauma exposure. Via examining 131 unique techniques' effectiveness in modulating intrusions and related symptoms, based on the timepoint of administration, our findings bear both theoretical and translational implications. To facilitate the use of this meta-analysis, we have developed a website so that researchers may interactively analyse this rich dataset to guide future research (https://intrusivememory.shinyapps.io/shinymeta/). Considering that intrusive memories are a transdiagnostic symptom for mental disorders beyond PTSD, such as in depression, anxiety, suicidal thoughts, among others[30,88], we hope that our findings can stimulate research in developing innovative interventions targeting at intrusive memory modulation across different psychological disorders.

Methods

We followed the Methodological Expectations of Cochrane Intervention Reviews (MECIR)[92] in performing our systematic review and meta-analysis, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[93] in reporting the meta-analysis. This project has been preregistered in the PROSPERO database (07 January 2021; ID: CRD42021224835). All article information, data and calculated effect sizes can be found in Supplementary Table 11. Data and scripts are available in the Open Science Framework[94]. Deviations from preregistered plans are stated below in relevant Methods sections.

Literature search

A literature search was conducted on titles, abstracts and keywords in online databases including Web of Science, PsycINFO (via ProQuest), ProQuest Dissertation, PubMed, BioRxiv, PsyArxiv, Scopus and Embase with keywords referring to intrusive memories and trauma. The exact keywords using Boolean operators are (intrusion* OR "intrusive memor*" OR re-experience* OR "unwanted memor*" OR flashback* OR "involuntary memor*" OR "mental imagery") AND ("emotional memor*" OR "experimental* trauma*" OR "analogue trauma*" OR stress*). Search keywords and fields may vary on the basis of different requirements of the search engines (the exact search words and fields can be found in PROSPERO). As in the preregistration, we initially planned to obtain additional publications through (1) citations from recent review articles (both forward and backward citations), (2) listservers such as Society for Research in Psychopathology and (3) email soliciting unpublished data from all authors published on the captioned topic for meta-analysis. Yet, considering the feasibility and time cost, in actual practice, we obtained additional publications through citations from recent review articles. Unpublished dissertations and preprints were included, with attempts to weigh against publication bias. No date-of-publication criterion was defined. The first literature search was conducted on 15 December 2020, the second update search on 27 April 2022, and the third update search on 12 December 2023. The third search included two additional databases following a reviewer's suggestions: Scopus and Embase.

Inclusion/exclusion criteria

Articles were included on the basis of the following criteria: experimental studies including (1) healthy participants, (2) experimental exposure to analogue forms of trauma (for example, trauma film, emotionally negative images and so on) and (3) experimental technique(s) (including behavioural, pharmacological/substance-related and neuromodulation techniques) targeted at altering the frequency of traumatic intrusive memories. To examine the preregistered outcome intrusion-related symptoms, we additionally included articles and experiments that exclusively examine intrusion-related symptoms.

Articles were excluded if they: (1) included clinical populations, (2) were not experimental studies (for example, correlational studies or case studies) or (3) used non-lab, real-world trauma exposure (for example, real-world motor accident).

Article selection and data extraction

Study selection followed PRISMA guidelines: in the screening phase, titles, keywords and abstracts of the studies identified through literature searches (j = 19,661) were screened by two reviewers (M.M.V., S.Z.) to identify potentially relevant studies that meet the aforementioned inclusion/exclusion criteria, resulting in 192 articles.

In the eligibility phase, the full texts of these publications (j = 192) were assessed for eligibility by three reviewers independently: M.M.V. and S.Z. assessed all articles, while L.S. assessed a random 7.81% of the articles (j = 15). Inter-rater reliability was substantial to almost perfect: 1st search M.M.V. and S.Z.: Cohen's κ = 0.95; 99.27% agreement; 2nd search M.M.V. and S.Z.: Cohen's κ = 1; 100% agreement; 3rd search M.M.V. and S.Z.: Cohen's κ = 1; 100% agreement; M.M.V./S.Z. and L.S.: Cohen's κ = 0.64; 93.75% agreement. Disagreement was reconciled by a fourth team member (X.H.) to reach a consensus. In total, 148 articles[20–22,42,43,45,47,48,50,52–56,58,59,69,70,74,75,95–221] were eligible and included in the qualitative synthesis and for subsequent data extraction.

Using a standardized Excel form, data for each study were extracted by two independent raters (M.M.V., S.Z.) according to the coding guidebook (see ref. 94). The 148 eligible articles were divided equally between the two raters, with 33.78% of the articles (j = 50) coded by both raters to obtain inter-rater reliability (M.M.V. and S.Z.: Cohen's κ ranged from 0.82 to 1 for primary information). An additional 8.11% of articles from each rater (total j = 12) were coded by L.S. for cross-validation (M.M.V./S.Z. and L.S.: Cohen's κ = 1). Any discrepancy was discussed among co-authors to reach a consensus. Following the completion of coding, the data were evenly divided and subjected to a thorough review by six research interns. Typos or errors identified by the interns were corrected by M.M.V. and S.Z.

Study coding followed our preregistration: (1) study/sample characteristics (for example, within-/between-participant design; demographics), (2) specific experimental technique and its comparison condition, (2) nature of the experimental trauma exposure (for example, film, images), (4) frequency and measurement of trauma intrusions (descriptive and inferential statistics), (5) descriptive and inferential statistics of additional outcomes (for example, emotional distress), (6) information on risk of bias (that is, based on the internal bias assessment on the quality of the study; see below for the details of internal bias assessment), (7) publication status (published/unpublished) and (8) timepoint of technique administration relative to analogous trauma onset (for example, pre vs peri vs immediate post vs delayed post).

Due to the heterogeneity brought by involving a comprehensive range of techniques, we identified the key experimental techniques and corresponding control conditions based on each study. The control condition could be a no-task condition or an alternative task condition, for example, Trauma reminder + Tetris (experimental condition) vs No-task/Buffer task of music listening (control condition); Sleep (experimental condition) vs Wakefulness (control condition); Oxytocin (experimental condition) vs Placebo (control condition) and so on. If more than 2 experimental conditions were present, experimental and control conditions were identified according to the study. Comparisons were made between each experimental condition and control condition. In the absence of a control condition, we coded the contrast made between the two experimental techniques.

Furthermore, considering that different techniques were hypothesized to either increase or decrease intrusion, we coded the predicted direction of intrusion change for each experiment (non-preregistered). A 'Decrease'/'Increase' direction means that compared with the control condition, the experimental condition was hypothesized to decrease/increase the intrusion frequency, respectively. In some cases, the

authors did not specify the direction or they hypothesized that the two conditions would not differ; here we coded the direction as 'Unspecified' and 'Null', respectively.

We preregistered to report results on the overall intrusion frequency on the basis of one, or more than one of these measures: diary-, lab- or questionnaire-based intrusion frequency. We preregistered to assess intrusion-related emotional distress and intrusion symptoms as measured by the intrusion subscale from the Impact of Event Scale (revised, IES/IES-R[222,223]) or other similar questionnaires (for example, symptom questionnaire[99]). Due to insufficient data from the included studies/experiments measuring intrusion vividness, we decided to exclude this measure even though we intended to include this outcome in our preregistration.

To assess the quality of each eligible study, an internal bias assessment was conducted, adapting from ref. 224. Disagreement was reconciled through discussion to reach a consensus. Specifically, quality assessment was done by coding each study as to whether it provides information on the following 11 aspects. Each aspect was coded as either 0 for 'not provided', or 1 for 'yes', or 0.5 for partial information reported. Details can be found in the coding guidebook:

(1) Sample characteristics (age, gender)
(2) Randomization procedures
(3) Participants inclusion criteria
(4) Data exclusion criteria
(5) Technique/intervention procedures
(6) Outcome measure and mode of measurement
(7) Comparable baseline trauma experiences between conditions
(8) Inter-rater reliability for intrusion scoring (only for studies using intrusion diary)
(9) Analysis plan
(10) Whether it is a peer-reviewed publication
(11) Mood/distress check for experimental trauma induction

The assessment scores for each study can be found in Supplementary Table 11.

Data synthesis and analyses

Effect sizes for each outcome were standardized to Hedges' *g* using the standardized mean difference (SMD) method[225], utilizing information provided in the article (for example, raw mean/s.d./s.e., *t*-score, Cohen's *d* and so on). The calculation was achieved using custom functions and packages on R, including metafor[226,227] and esc[228]. The SMDs were derived from differences between the experimental conditions and the control/alternative experimental conditions on our outcome measures, including the intrusion frequency, intrusion-related distress and intrusion-related symptoms arising from the lab-analogue trauma exposure. Higher values of Hedges' *g*s or SMDs with positive signs indicate positive outcomes, such that the experimental condition was associated with fewer intrusions, and lower levels of distress or symptoms than the control/alternative experimental condition. Lower values of Hedges' *g*s or SMDs with negative signs indicate negative outcomes, such that the experimental condition was associated with more intrusions, and higher levels of distress or symptoms than the control/alternative experimental condition.

To compare the effectiveness of different categories of techniques, we developed a hierarchical coding schema to categorize similar techniques (Fig. 2). Specifically, on the basis of each entry of experimental and control conditions, we developed the following steps, from extracting verbatim names to superordinate categorization (see detail below and in Fig. 2). From Steps 2 to 4, each entry was coded by two raters (M.M.V. and S.Z.) independently: Cohen's κ ranged from 0.57–0.79. Any inconsistency was reconciled by a third rater (X.H.).

(1) Verbatim names of the experimental and control conditions were extracted from the original article.
(2) Step 1: Standardize names for similar or identical experimental and control conditions across different experiments/articles.
(3) Step 2: Individual technique names. Code technique names for the experimental vs control condition contrasts. For example, Sleep vs No Sleep comparisons were coded as Sleep; Trauma Reminder + Tetris vs No-Task comparisons were coded as Trauma Reminder + Tetris. Note that in the absence of a control condition, we coded the contrast between two experimental conditions as the technique in this step. For instance, Trauma Reminder + Tetris vs Trauma Reminder comparisons were coded as Trauma Reminder + Tetris vs Trauma Reminder to acknowledge the importance on the inclusion of trauma reminders; Positive CBM Training vs Negative CBM Training was coded as Positive vs Negative CBM Training[21]. Similarly, Imagery Rescripting vs Imagery Re-experience was coded as Imagery Rescripting vs Imagery Re-experience. This approach aids in distinguishing between various types of comparisons during the aggregation of their effect sizes in the corresponding analyses.
(4) Step 3: Procedure-based superordinate category. We coded each individual technique into one of the following categories: (i) Behavioural, (ii) Neuromodulation, (iii) Pharmacological based on their administration procedure. Given that most of the techniques are behavioural, we further coded the behavioural techniques into Mechanism-based superordinate category (see step 4).
(5) Step 4: Mechanism-based superordinate category. According to the specific mental processes the techniques target, we coded each Behavioural individual technique into one of the following categories: (i) Imagery, that tap into visuospatial or visuoperceptual processing (for example, imagery rescripting/re-experience, data-driven processing, finger tapping and so on); (ii) Verbal, that tap into verbal processing (for example, rumination, conceptual processing, number counting and so on); (iii) Emotion (for example, emotional suppression, guilt induction, stress induction, positive cognitive bias modification and so on); (iv) Others, when techniques may tap into unspecified or multiple mechanisms (for example, sleep, self-efficacy, exercises and so on); (v) any combinations or contrasts (for example, Imagery + Verbal, Imagery vs Verbal). Note that in our Mechanism-based moderation analysis, we excluded the category of 'Others' and any combinations with 'Others', considering the heterogeneity of techniques in this category.

We additionally coded two superordinate categories on the basis of the task characteristics of each Behavioural individual technique: (1) Direct vs Indirect involvement of trauma content: on the basis of whether the techniques directly vs indirectly target the trauma memory, we coded those involving direct engagement of trauma content as Direct and others that do not require direct confrontation as Indirect; and (2) Task vs Instruction: on the basis of each technique's modality, we classified techniques into Task category if a technique required participants to perform a concrete task entailing external action (for example, finger tapping, viewing a humour inducing film, listening to a meditation recording, ingesting a pharmaceutical drug). For techniques that required participants to adopt a specific style of thinking and did not involve any external action, we coded them into Instruction category (for example, elaboration, abstract processing, mentally rehearsing, thought suppression). In cases where the experimental and comparison groups employed different modalities of techniques, we coded the comparison with 'vs' in the middle (for example, Task vs Instruction). Results related to these two superordinate categories are reported in Supplementary Table 8.

Following our preregistration, we coded the timepoint of technique administration, and examined the effectiveness of individual techniques and the moderation effect of superordinate categories

of techniques within each timepoint. Specifically, we coded the timepoint as Pre, Peri, Immediate Post, or Delayed Post relative to the onset of analogue trauma exposure. Techniques that were administered within the same day after the experimental trauma were categorized as Immediate Post, and techniques administered at least 24 h after the trauma exposure were categorized under Delayed Post. Techniques that were used in multiple timepoints were coded with '+', for example, Peri + Immediate Post.

Main analyses

We used 'rma.mv' from the metafor package[227] to calculate overall effect sizes (that is, main analyses). In addition to calculating effect sizes using the whole dataset, we further divided the data into different hypothesized directions considering each experiment/technique's hypothesis in modulating intrusion frequency (Decrease, Increase and Unspecified). These analyses were conducted on both overall intrusion frequency (aggregating across diary-, lab- and questionnaire-based intrusion frequency) and on individual measurement. A three-level multilevel meta-analytical approach[229,230] was used to model three levels of variance: (1) variances due to sampling error, (2) within-study variances among multiple effect sizes from the same experiment and (3) variances due to between-study heterogeneity. To measure heterogeneity, we reported Cochran's Q as results of chi-squared analyses and I^2 as the percentage of total variances across effect sizes that is due to heterogeneity rather than sampling error or chance; τ^2 provides the variance estimate at the experiment and outcome levels. We next repeated the analyses on other preregistered outcomes: intrusion-related distress and intrusion-related symptoms.

Publication bias analyses

We conducted publication bias analyses on each of the outcomes using: (1) contour-enhanced funnel plots, which were used to display the presence of publication bias[231], (2) Egger's test, which was used to quantify the funnel plot assessment findings[232], calculated by using the standard errors of the effect sizes as a predictor in the meta-regression. (3) Trim-and-fill method, to impute artificial effect sizes that are missing due to the impact of publication bias on literature search findings, and then calculate corrected effect sizes[233], and (4) non-preregistered three-parameter selection model analysis[234].

Moderation analyses

We used 'rma.mv' from the metafor package[227] to conduct moderation analyses on intrusion frequency, intrusion-related distress and intrusion-related symptoms. Following our preregistration, to examine the effectiveness of different superordinate categories within each timepoint of technique administration, we split data into different timepoints of technique administration (Pre, Peri, Immediate Post, Delayed Post, and so on), then we conducted meta-regressions within each timepoint using the following two moderators: Procedure- and Mechanism-based superordinate category.

We next examined whether the timepoint of technique administration may moderate the effectiveness within specific superordinate categories (that is, Procedure- and Mechanism-based). Similarly, we split data into different superordinate categories and conducted meta-regressions.

Furthermore, across the entire dataset, we conducted meta-regressions using the following moderators (reported in Supplementary Table 8):

(1) Procedure-based superordinate category
(2) Mechanism-based superordinate category
(3) Direct/Indirect involvement of trauma content
(4) Task- vs Instruction-based techniques
(5) Time of techniques being administered (for example, Pre, Peri, Post and so on, non-preregistered)
(6) Nature of experimental trauma exposure (for example, film, images, and so on)
(7) Nature of comparison condition (passive (no-task) or active (alternative task) control)
(8) Study design (within- vs between-participant)
(9) Mode of intrusion measurement (for example, intrusion diary and so on)
(10) Neuroimaging or psychophysiological measures included (yes vs no)
(11) Publication status (published vs unpublished)
(12) Gender
(13) Age
(14) Country/Region
(15) Continent

Analyses of individual techniques

In addition, we preregistered to examine the effectiveness of individual techniques (coded in Step 2, Fig. 2) within each timepoint of technique administration (for example, Pre, Peri, Immediate Post, Delay Post). We conducted three-level multilevel modelling to calculate the effect sizes of each individual technique within different timepoints of administration.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Data are available on OSF at https://osf.io/phu7w/ (ref. 94).
A website was developed for researchers to use the dataset to implement analyses (https://intrusivememory.shinyapps.io/shinymeta/).

Code availability

Codes are available on OSF at https://osf.io/phu7w/ (ref. 94).

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Author contributions

M.M.V. and S.Z. conceptualized the project, conducted investigations and formal analysis, curated data, developed the methodology and software, performed validation and visualization, wrote the original draft, and reviewed and edited the manuscript. L.S. conducted investigations, formal analysis and validation, and reviewed and edited the manuscript. E.A.H. conducted formal analysis, and reviewed and edited the manuscript. J.H. and M.H.C. conducted formal analysis and validation, and developed software. X.H. conceptualized the project, conducted investigations and formal analysis, curated data, performed validation, wrote the original draft, reviewed and edited the manuscript, administered and supervised the project, and acquired funding.

Competing interests

E.A.H.'s salary was partly funded by the Wellcome Trust (223016/Z/21/Z) via consultancy to P1vital Products Ltd for a different study. E.A.H. also receives funding from the Oak Foundation (OCAY-18-442) and Rannís The Icelandic Research Fund. E.A.H. developed the imagery-competing task intervention for intrusive memories, and know-how and training in using it over the past 20 years (ANEMONE). E.A.H. receives book royalties from Guildford Press and Oxford University Press, receives occasional honoraria for conference keynotes and clinical workshops and is on the Board of Trustees of the MQ Foundation. L.S. is an employee of Tobii AB since 2023. The remaining authors declare no competing interests.

Additional information

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