31/08/2023

A systematic review and meta-analysis of the effectiveness of experimental techniques in altering intrusive memories of lab-analogue trauma

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Abstract

Experiencing trauma can lead to intrusive memories, a hallmark symptom of post-traumatic stress disorder and transdiagnostic feature of stress-related disorders. Understanding why intrusions increase or decrease is pivotal in developing effective interventions to safeguard mental wellness following trauma. Building on lab-analogue trauma paradigms, we conducted a pre-registered (PROSPERO: CRD42021224835) meta-analysis to investigate the effectiveness of experimental techniques in either reducing or increasing intrusion frequency (e.g., assessed with a daily diary), intrusion-related distress and symptoms. Aggregating data from 126 articles examining 118 techniques with 584 effect sizes and 11,132 participants, we found that techniques hypothesized to reduce intrusion frequency significantly decreased intrusion frequencies, intrusion-related distress and symptoms (g = 0.11— 0.49). Moreover, techniques hypothesized to increase intrusions significantly increased intrusion frequencies and their associated distress (g = -0.15 — -0.19). Moderator and focal analyses showed that behavioral techniques tapping into imagery-based processing (e.g. playing Tetris following trauma reminder) were most effective in reducing intrusion frequency and symptoms (g = 0.22 — 0.68). However, those targeting verbal-based processing (e.g., rumination, adding contextual information) significantly increased intrusions, albeit to a small degree (g = -0.29 — -0.30). We further supplement the meta-analysis with a website that allows researchers to analyze the dataset to facilitate research synthesis and future endeavor. While techniques that reduce intrusions can inform the development of evidence-based interventions to reduce intrusions in real life, techniques that may (inadvertently) increase intrusions underscore vulnerabilities factors and thus can inform preventive measures.

Traumatic events, such as natural catastrophes, wars, physical/emotional abuse, and even pandemics, can incur a devastating physical and mental toll. Trauma, defined as “exposure to actual or threatened death, serious injury, or sexual violence” (American Psychiatric Association, 2013), impacts approximately half of the world’s population at least once in lifetime, costing approximately $4.2 trillion dollars in the US alone in 2019 (Peterson et al., 2021; US Dept. of Veterans Affair, 2018). In particular, experiencing trauma can lead to recurrent involuntary intrusions (intrusive memories) consisting of fragmented episodes from the trauma, sometimes colloquially called “flashbacks” (Ehlers et al., 2004; Hoppe et al., 2022; Hustvedt, 2012; Kanstrup et al., 2021; Singh et al., 2022). Oftentimes, experiencing intrusions and their accompanying emotional distress could perpetuate a spectrum of symptoms related to post-trauma stress disorder (PTSD) such as avoidance and hyperarousal, thereby further deteriorating mental health (Brewin, 2014; Brewin & Holmes, 2003; Ehlers & Clark, 2000; Singh et al., 2021). Therefore, understanding why intrusive memory occur, and how they can be reduced is critical for maintaining well-being and resilience when facing trauma and life adversity (McNally, 2012; Visser et al., 2018).

A plethora of experimental techniques have been used to modulate intrusive memories (Fig. 1 for an overview, for narrative reviews, see Holmes & Bourne, 2008; Iyadurai et al., 2019; James et al., 2016; Marks et al., 2018; Singh et al., 2020; Visser et al., 2018). Recent research and meta-analyses suggest that certain techniques could reduce intrusions (Asselbergs et al., 2023; Davidson & Marcusson-Clavertz, 2023; Larson et al., 2023; Schäfer et al., 2023). For instance, examining cognitive techniques in intrusion reduction (Asselbergs et al., 2023), results showed that both visuospatial interference and imagery rescripting techniques were significant in reducing the number of intrusions. However, a comprehensive examination of techniques in intrusion modulation has never been conducted. Notably, existing intrusion modulation techniques encompass a wide spectrum, including cognitive, social, emotional, pharmacological, and neuromodulatory manipulations, among others. Moreover, these techniques not only aim to reduce or increase intrusions, but also modulate intrusion-related emotional distress and subjective symptoms (e.g., sleep troubles, emotional reactions). While intrusion reduction research bears direct clinical implications, identifying any factors that increase intrusions can reveal maladaptive psychological mechanisms contributing to excessive intrusions and related mental disorder. This knowledge can aid identify and protect vulnerable populations, and the development of preventive measures even before trauma occurs. It can also inform which techniques not to use after trauma, where there might be a risk of symptoms worsening. Thus, a comprehensive quantitative synthesis of existing intrusion modulation techniques would be valuable and is in urgent need.

To bridge this gap, we conducted a systematic review and meta-analysis of studies that experimentally modulates intrusions elicited by lab-analogue trauma among non-clinical samples. Lab-analogue trauma (i.e., experimental trauma) can be generated through film clips, images, sounds or immersive virtual reality (VR) depicting various types of traumatic events, to induce intrusive memories to the experimental trauma, and other trauma-related symptoms (e.g., Holmes & Bourne, 2008; Iyadurai et al., 2019; Lau-Zhu et al., 2019; Zeng et al., 2021; for a review, see James et al., 2016). Although lab-analogue trauma exposure deviates from real-world trauma, simulated trauma (such as viewing real world trauma in the media) nevertheless elicits analogous traumatic responses such as intrusions or hyperarousal akin to PTSD-like symptoms (Holman et al., 2014; James et al., 2016; Silver et al., 2013).

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Our meta-analysis aimed to achieve the following goals: First, to calculate the effect sizes of individual techniques in either reducing or increasing intrusion frequencies and intrusion-related outcomes (e.g., distress, symptoms). Second, to categorize techniques into theory-driven and procedure-relevant superordinate categories for moderator analyses (see Fig. 2 for schematic flow chart of categorization). Third, to group highly homogenous techniques together to implement focal analyses, which greatly reduce the heterogeneity of techniques compared to moderator or overall analysis that would involve a variety of different techniques. Fourth, to evaluate the risk bias of included studies and conduct publication bias analyses. Lastly, to facilitate future research synthesis and empirical studies, we developed a website using the meta-analysis dataset for researchers to freely and interactively analyze the data for their own research purposes (http://117.78.42.83).

We first examined the effectiveness of behavioral, pharmacological, and neuromodulation techniques based on the experimental procedures. Next, given that the majority of techniques are behavioral, we coded behavioral techniques according to their hypothetical mechanisms, based on influential theoretical accounts of intrusive memories. According to the prominent dual representation account and cognitive model of PTSD (e.g., Brewin et al., 2010;

Ehlers & Clark, 2000), intrusive memories 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 (see also Brewin et al., 1996; Brewin, 2014; Ehlers & Clark, 2000; Ehlers et al., 2004). Based on these accounts, at least two different types of techniques (visuospatial or low-level perceptual processing vs. verbal-conceptual or elaboration/contextualization processing) could modulate intrusions. Recently, the retrieval-based feedback loop model emphasizes that maladaptive retrieval processes contributed to the persistence of intrusions (Marks et al., 2018). Specifically, involuntary intrusions, together with their accompanied distress, and negative appraisal of the trauma, would form a feedback loop that increases future intrusions. Therefore, manipulating retrieval or reducing distress of intrusions would lead to their reduction.

Based on these theoretical accounts, we coded whether techniques target at imagery- (e.g., Tetris, imagery rescripting), verbal-based processing (e.g., elaboration, number counting), or emotional processing (e.g., emotion regulation, mood induction). We also coded techniques that may target multiple processes, such as sleep or exercise that may simultaneously impact emotion, memory, cognitive control, etc., as Others. We additionally coded techniques that combined or contrasted any of the aforementioned categories (e.g., trauma reminder + number counting was coded as imagery + verbal).

In addition to coding these mechanism-based techniques, we considered important procedural variants of techniques. First, timing: techniques can be administered either *before*, *during/peri*, *immediately after/post* the trauma or even after a *delay*. Specifically, pre-trauma techniques aim to protect people from developing trauma-related symptoms before the actual trauma, and can be particularly helpful for professionals anticipating trauma, including first responders, firefighters, soldiers in war zones, among others. However, given the unpredictability of trauma, post-trauma techniques may be most promising and practical to help victims in the early aftermath of trauma. Furthermore, when missing the early intervention window, techniques that are effective after a delay is also important. Notably, neuroscientific evidence suggests that even remote, consolidated memories can be updated when memory traces are reactivated again via re-exposure to cues (Dudai, 2012; Nader et al., 2000; Phelps & Hofmann, 2019; Schafe et al., 2001; Scully et al., 2017; Visser et al., 2018).

Second, we considered whether the techniques would directly engage with the trauma memory or not. While some techniques (e.g., re-exposure, imagery rescripting) necessitate people to directly engage trauma memory (Dunn et al., 2009; Zetsche et al., 2009), other techniques (e.g., playing Tetris, sleep, mindfulness training) do not require people to confront with trauma memories in detail. Because direct and detailed confrontation with trauma can be debilitating and associated with treatment drop-outs, the utilization of indirect techniques may be highly valuable for real-world trauma survivors who may not wish to talk about the trauma in detail. However, to date, the distinction between the effectiveness of direct vs. indirect techniques has never been tested.

Third, we coded whether the techniques require explicit behavioral output or whether they only give instructions. Task-based techniques would require participants to actively perform specific behaviors (e.g., finger tapping, verbal counting, playing Tetris). In contrast, instruction-based techniques operate solely through verbal instructions about “how to think”. For example, participants can be asked to adopt a data- or conceptual-driven processing style (Segovia et al., 2016), or to suppress the thoughts of trauma memories (Nixon et al., 2009), yet without any explicit behavior (for all included articles and their categorizations, see Table S1).

Given that intrusion modulation research examines techniques that either increase or reduce intrusions, we conducted both hypothesis-driven and hypothesis-free analyses. Hypothesis-driven analyses were guided by the directional hypothesis proposed in the article, i.e., whether the techniques would *increase* or *decrease* the intrusion compared to control condition. In contrast, hypothesis-free analyses would present the effect size of techniques regardless of hypotheses made in the article, to minimize potential experimenter biases. For outcome measures, we primarily focused on intrusion frequency, collecting data from all existing measurements including intrusion diary, lab-based intrusion monitoring task, and self-report intrusion frequency questionnaires. In addition, we coded intrusion-related distress levels and symptoms (e.g., sleep troubles, emotional reactions) that may reinforce the persistence of intrusions (Marks et al., 2018). This allows our meta-analysis to provide unique insights on whether techniques may have generalization effects in impacting intrusion-related outcomes.

While existing meta-analyses have focused on specific techniques in intrusion reduction (e.g., sleep or cognitive techniques; Asselbergs et al., 2023; Davidson & Marcusson-Clavertz, 2023; Larson et al., 2023; Schäfer et al., 2023), the present meta-analysis aimed to provide a more comprehensive examination by covering 118 existing techniques that either increase or reduce intrusive memories. Notably, with theory-driven and procedure-relevant classification of individual techniques, and various analyses at various levels (overall, moderator and focal analyses, hypothesis-driven/-free analyses), results can provide clearer evidence to assess the effectiveness of techniques in modulating intrusions and the related outcomes, thereby informing both theories and translational research in intrusive memories.

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Results

Description of included studies

A total of 126 articles (with n = 145 experiments and k = 584 effect sizes, from 11,132 participants (M_{age} = 23.28, Female % = 67.64%, Male % = 32.36%) were included in the meta-analyses (see Fig. 3 for PRSIMA flowchart; Table 1 for descriptive). Article coding and extracted effect sizes are available at https://osf.io/phu7w/?view_only=622642ef2c3943cbb843004ec99a1c79

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Hypothesis-driven Main Analyses

When techniques aimed to reduce intrusions:

Overall intrusion frequency. For overall intrusion frequency (n = 96, k = 181) measured across daily intrusion diary, lab-based intrusion monitoring task, and questionnaires, we found a medium effect size in intrusion reduction (Hedges' g = 0.31, 95% CI [0.23, 0.39], Z = 7.27, p < .001; Fig. 4A). We also found significant heterogeneity across studies (Q(180) = 459.59, p < .001, I^2 = 63.44%, $\tau^2_{experiment}$ = 0.12 at experiment level, and $\tau^2_{outcome}$ < 0.001 at outcome level).

Examining publication biases, Egger's test revealed that the funnel plot was significantly asymmetric, Z = 5.05, p < .001, suggesting the presence of publication bias (Fig. 4B). The trim and fill method imputed 18 artificial effect sizes to adjust for potential publication biases. The adjusted effect size remained significant, Hedges' g = 0.18, 95% CI = [0.09, 0.27], Z = 3.82, p

< .001. Results from the three-parameter selection model also showed a significant effect size in intrusion reduction, Hedges' g = 0.13, 95% CI = [0.04, 0.21], Z = 2.87, p = .004.

Diary-based intrusion frequency. When only including effect sizes on diary-based intrusion frequency (n = 82, k = 125), we found a significant small-to-medium effect size in intrusion reduction (Hedges' g = 0.29, 95% CI [0.20, 0.38], Z = 6.27, p < .001; Fig. 4A). Again, we found significant heterogeneity across studies (Q(124) = 296.19, p < .001, I^2 = 61.43%, $\tau^2_{\text{experiment}}$ = 0.12, τ^2_{outcome}< .001).

Lab-based intrusion frequency. When only including effect sizes on lab-based intrusion frequency (n = 26, k = 32), we found a significant medium effect size in intrusion reduction effect (Hedges' g = 0.48, 95% CI [0.32, 0.64], Z = 5.76, p < .001; Fig. 4A). Again, heterogeneity across experiments was significant (Q(31) = 67.33, p < .001, I^2 = 57.08%, $\tau^2_{\text{experiment}}$= 0.11, $\tau^2_{\text{outcomoutcome}}$< .001).

Questionnaire-based intrusion frequency. When only including effect sizes on questionnaire-based intrusion frequency (n = 11, k = 24), we found a significant small-to-medium effect size in intrusion reduction (Hedges' g = 0.27, 95% CI [0.03, 0.51], Z = 2.20, p = .028; Fig. 4A). The heterogeneity across experiments/outcomes was significant (Q(23) = 69.13, p < .001, I^2 = 67.99%, $\tau^2_{\text{experiment}}$ = 0.12, τ^2_{outcome}< 0.001).

Intrusion-related emotional distress. We examined the impact of intrusion reduction techniques on intrusion-related emotional distress (n = 40, k = 64). We found a significant and small effect size in distress reduction (Hedges' g = 0.11, 95% CI [0.02, 0.19], Z = 2.48, p = .013; Fig. 4A). The heterogeneity across experiment/outcomes was not significant (Q(63) = 80.05, p = .072, I^2 = 31.27%, $\tau^2_{\text{experiment}}$ = 0.03, τ^2_{outcome}< 0.001).

Intrusion-related symptoms. We examined the impact of intrusion reduction techniques on intrusion-related symptoms (e.g., sleep disturbance, emotion reaction, n = 35, k = 46). We found a significant and small effect size in reducing intrusion-related symptoms (Hedges' g = 0.23, 95% CI [0.12, 0.33], $Z = 4.28$, $p < .001$; Fig. 4A), and significant heterogeneity ($Q(45) = 75.75$, $p = .003$, $I^2 = 42.05\%$, $\tau^2_{experiment} = 0.03$, $\tau^2_{outcome} = 0.02$).

In summary, techniques targeted at intrusion reduction can effectively reduce the number of involuntary intrusions across daily diaries, lab-based computerized tasks, and questionnaires. Besides reducing intrusion frequencies, these techniques also ameliorated intrusion-related emotional distress and symptoms. Results were robust after potential outliers and influential cases were removed (Hedge's $g = 0.10$ to 0.48, *p*s < .05 see supplementary Table S2).

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When techniques aimed to increase intrusions:

Overall intrusion frequency (n = 50, k = 102). We found a significant and small effect size in intrusion increase (Hedges' $g = -0.15$, 95% CI [-0.26, -0.03], $Z = -2.52$, $p = .01$; Fig. 4A), with significant heterogeneity ($Q(101) = 234.28$, $p < .001$, $I^2 = 62.09\%$, $\tau^2_{experiment} = 0.11$ at experiment level and $\tau^2_{outcome} = 0.02$ at outcome level).

Egger's test showed that the funnel plot was significantly asymmetric, $Z = -3.01$, $p = .003$; indicating the existence of publication bias (Fig. 4B). Employing the trim and fill method, which imputed 8 artificial effect sizes, the adjusted effect size was no longer significant, Hedges' $g = -0.04$, 95% CI = [-0.18, 0.09], $Z = -0.65$, $p =.518$. However, the three-parameter selection model showed a significant effect size after adjusting for publication biases, Hedges' $g = -0.11$, 95% CI = [-0.21, -0.01], $Z = -2.25$, $p =.025$.

Diary-based intrusion frequency. When only including effect sizes on diary-based intrusion frequency (n = 45, k = 61), We found a significant and small effect size in intrusion increase (Hedges' $g = -0.19$, 95% CI [-0.32, -0.05], $Z = -2.72$, $p =.006$; Fig. 4A), and significant heterogeneity across experiments ($Q(60) = 148.60$, $p < .001$, $I^2 = 64.31\%$, $\tau^2_{experiment} = 0.14$, $\tau^2_{outcome} < 0.001$).

Intrusion-related emotional distress. We examined the impact of intrusion increase techniques on intrusion-related emotional distress (n = 25, k = 45). We found a significant small effect size in distress increase (Hedges' g = -0.15, 95% CI [-0.26, -0.03], Z = -2.51, p = .012; Fig. 4A) and significant heterogeneity across studies, ($Q(44) = 61.79$, p = .039, $I^2 = 32.21\%$, $\tau^2_{experiment} = 0.04$, $\tau^2_{outcome} < 0.001$).

However, techniques that aimed to increase intrusions did not significantly influence either lab- or questionnaire-based intrusion frequencies as well as intrusion-related symptoms (ps>.05; Fig. 4A).

Overall, techniques targeted at increasing intrusion frequency showed inconsistent findings: while they increased diary-based intrusion frequency and intrusion-related emotion distress with a small effect size, they did not change lab- or questionnaire-based intrusion frequency as well as intrusion-related symptoms. The same trend of results was obtained when potential outliers and influential cases were removed (Hedge's g = -0.17 to 0.08, see supplementary Table S2).

When techniques' effect were unspecified

With techniques that did not have a specified hypothesis on intrusion reduction or increase, the effect sizes were insignificant across different outcomes (Hedge's g = -0.01 to 0.17, ps > .061). However, after potential outliers and influential cases were removed, we found significant and small effect sizes in intrusion reduction (overall intrusion, n = 31, k = 65; Hedges' g = 0.13, p = .005; diary-based intrusions, n= 28, k = 47; Hedges' g = 0.12, p = .028).

For overall intrusion frequency following outlier removal, the Egger's test showed that the asymmetry of the funnel plot was not significant, Z = -0.53, p = .594 (see supplementary Fig. S1, Table S3). The three-parameter selection model similarly showed a significant and small effect size in intrusion reduction after adjusting for publication biases, Hedges' g = 0.13, 95% CI = [0.04, 0.22], Z = 2.83, p = .005 (see supplementary Table S5).

Hypothesis-driven Moderator Analyses

We employed meta-regression to examine how different moderators impacted changes in intrusion frequency and the associated outcomes. In the main text, we present the moderation results on overall intrusion frequency.

When techniques aimed to reduce intrusions:

Behavioral vs. Pharmacological vs. Neuromodulation: Results showed significant differences among these different procedures, $Q(2) = 6.16$, $p = .046$: Behavioral techniques were significant in intrusion reduction (n = 88, k = 170; Hedge's $g = 0.34$, 95% CI = [0.25, 0.43], Z = 7.74, $p < .001$), whereas pharmacological nor neuromodulation techniques were not.

Hypothetical mechanism(s) (Level 3a superordinate category). We coded behavioral techniques based on the hypothetical mechanisms or processing they targeted at: mental imagery (Imagery), verbal processing (Verbal), emotional processing (Emotion), multiple processes (Other). Besides, we coded combination (e.g. Imagery + Verbal) or contrasts (e.g. Imagery vs. Verbal) of the aforesaid categories (see Fig. 2). This moderator analysis was not significant, $Q(7) = 7.36$, $p = .392$ (see Fig. 5). Examining these categories separately, we found that the Imagery techniques (with the highest n = 45 and k = 94, Hedge's $g = 0.41$, 95% CI = [0.29, 0.53], Z = 6.82, $p < .001$), and the Other techniques (n = 16, k = 24; Hedge's $g = 0.31$, 95% CI = [0.12, 0.51], Z = 3.15, $p = .002$) were significant in intrusion reduction. In contrast, Emotion techniques (n = 10, k = 15) and Verbal (n = 15, k = 27) categories were not significant in intrusion reduction (*p*s > .114; see Fig. 5)

Direct vs. Indirect Involvement of Trauma Content (Level 3b superordinate category). We coded behavioral techniques based on whether they directly engage the trauma memory or not. This moderator analysis was not significant. $Q(3) = 4.67$, $p = .198$ (see Fig. 5). Examining these categories separately, we found that both Indirect and Direct techniques were significant in intrusion reduction (Indirect: n = 44, k = 82; Hedge's $g = 0.38$, 95% CI = [0.26, 0.49], Z = 6.15, $p < .001$; Direct: n = 31, k = 53; Hedge's $g = 0.22$, 95% CI = [0.08, 0.37], Z = 3.04, $p = .002$). Moreover, a combination of Direct + Indirect techniques (trauma reminder followed by Tetris playing), was significant in intrusion reduction (n = 15, k = 34; Hedge's $g = 0.48$, 95% CI = [0.28, 0.67], Z = 4.82, $p < .001$).

Task vs. Instruction (Level 3c superordinate category). We coded behavioral techniques based on whether they required behavioral output or merely gave participants instructions to change thinking/processing styles. This moderator analysis was not significant, $Q(2) = 2.08$, $p = .354$ (Fig. 5). Examining these categories separately, we found that only Task-based techniques (n =

80, k = 159; Hedge's $g = 0.35$, 95% CI = [0.26, 0.44], Z = 7.66, $p < .001$) were significant in intrusion reduction.

Timing. We coded techniques based on the timing of implementation (pre- vs. peri- vs. post-trauma). This moderator analysis was not significant, $Q(5) = 10.41$, $p = .064$ (Fig. 5). Examining these time points separately, we found that only techniques administered during (peri) or after (both immediate and delayed post) trauma exposure were effective to reducing intrusions (Peri: n = 15, k = 22; Hedge's $g = 0.40$, 95% CI = [0.18, 0.63], Z = 3.56, $p < .001$; Immediate Post: n = 55, k = 110; Hedge's $g = 0.36$, 95% CI = [0.26, 0.47], Z = 6.65, $p < .001$; Delayed Post: n = 10, k = 26; Hedge's $g = 0.31$, 95% CI = [0.07, 0.55], Z = 2.51, $p = .012$).

When techniques aimed to increase intrusions:

Behavioral vs. Pharmacological vs. Neuromodulation (Level 3 superordinate category). This moderator analysis was not significant, $Q(2) = 2.76$, $p = .251$. Examining individual categories, we found that Pharmacological and Behavioral techniques significantly increased intrusions (Fig. 6, Pharmacological: n = 4, k = 6; Hedge's $g = -0.40$, 95% CI = [-0.80, -0.01], Z = -2.02, $p = .044$; Behavioral: n = 45, k = 95; Hedge's $g = -0.13$, 95% CI = [-0.25, -0.01], Z = -2.17, $p = .030$).

Hypothetical mechanism(s) (Level 3a superordinate category). This moderator analysis was not significant, $Q(6) = 7.59$, $p = .270$ (Fig. 6). However, when examining individual categories separately, we found that the Verbal techniques significantly increased intrusion frequencies (n = 18, k = 39; Hedge's $g = -0.30$, 95% CI = [-0.50, -0.10], Z = -2.96, $p = .003$).

Direct vs. Indirect Involvement of Trauma Content (Level 3b superordinate category). This moderator analysis was not significant, $Q(3) = 0.03$, $p = .999$ (Fig. 6). Examining individual categories separately, we found that neither Direct nor Indirect techniques significantly increased intrusions (*p*s > .132).

Task vs. Instruction (Level 3c superordinate category). This moderator analysis was not significant, $Q(2) = 3.35$, $p = .187$ (Fig. 6). Examining individual categories separately, we found that Task-based techniques (n = 34, k = 69) significantly increased intrusion frequency (Hedge's g = -0.19, 95% CI = [-0.33, -0.06], Z = -2.79, p = .005).

Timing. This moderator analysis was not significant, $Q(4) = 0.85$, $p = .932$ (Fig. 6). However, after removal of outliers and influential cases, techniques implemented during (peri) the trauma exposure significantly increased intrusions (Peri: n = 17, k = 24; Hedge's g = -0.21, 95% CI = [-0.39, -0.03], Z = -2.26, p = .024).

When techniques' effect were unspecified

Apart from the mechanism moderator ($Q(3) = 12.46$, $p = .006$), we did not detect significant moderation effects.

Hypothesis-Free Moderator Analyses

Here, we present moderator analyses results in a hypothesis-free manner, i.e., regardless of the directional hypotheses made in the articles. For brevity, we report the results for overall intrusion frequency in the main text.

Behavioral vs. Pharmacological vs. Neuromodulation (Level 3 superordinate category). We found a significant moderator effect, $Q(2) = 7.52$, $p = .023$ (Fig. 7). Examining individual categories showed that the Behavioral techniques significantly reduced overall intrusion frequency with a small effect size (n = 120, k = 333; Hedge's g = 0.18, 95% CI = [0.10, 0.25], Z = 4.75, $p < .001$). None of the categories significantly increased intrusions in this hypothesis-free context.

Hypothetical mechanism(s) (Level 3a superordinate category). We found a significant moderator effect $Q(9) = 28.26$, $p = .001$ (Fig. 7). Examining individual categories showed that Imagery and Other techniques significantly reduced intrusions with a small-to-medium effect size (Imagery: n = 56, k = 139; Hedge's g = 0.30, 95% CI = [0.20, 0.40], Z = 5.97, $p < .001$; Other: n = 28, k = 55; Hedge's g = 0.20, 95% CI = [0.05, 0.34], Z = 2.67, p = .008). Note that none of the mechanism-based categories significantly increased intrusions in this hypothesis-free analysis.

Direct vs. Indirect Involvement of Trauma Content (Level 3b superordinate category). We did not find a significant moderator effect $Q(4) = 9.40$, $p = .052$ (Fig. 7). Examining individual categories separately, we found that Indirect as well as a combination of Direct + Indirect behavioral techniques significantly reduced intrusions, with a small-to-medium effect size (Indirect: n = 64, k = 143; Hedge's $g = 0.23$, 95% CI = [0.13, 0.32], Z = 4.62, $p < .001$; Direct + Indirect: n = 16, k = 42; Hedge's $g = 0.30$, 95% CI = [0.14, 0.46], Z = 3.72, $p < .001$). None of the categories significantly increased intrusions under this hypothesis-free context.

Task vs. Instruction (Level 3c superordinate category). We did not find a significant moderator effect, $Q(3) = 4.38$, $p = .223$ (Fig. 7). Examining individual categories separately, we found that the Task-based techniques (n = 107, k = 286; Hedge's $g = 0.19$, 95% CI = [0.12, 0.27], Z = 4.92, $p < .001$) significantly reduced intrusions. None of the categories significantly increased intrusions in this hypothesis-free context.

Internal bias assessment (IBA). Importantly, we implemented quality control by coding each included study based on 11 quality assessment criteria (e.g., randomization, baseline measurement of participants' trauma history; see Methods for all 11 criteria). Each study received a total IBA score between 0-11, with 11 indicating the highest quality. Using the total IBA scores as a continuous measure, we found that the total IBA scores did not significantly influence effectiveness of techniques at modulating overall intrusion frequency (Hedge's $g = 0.05$, $p = .068$).

Other Notable Findings from Moderator Analyses

We found that for Emotion techniques that aimed to reduce intrusions, they significantly reduced lab-based intrusion frequency (n = 2, k = 3, Hedge's $g = 0.53$, 95% CI = [0.05, 1.05], Z = 2.00, $p = .045$). The Emotion and Other techniques were significantly effective at reducing intrusion-related distress (Emotion: n = 9, k = 13; Hedge's $g = 0.19$, 95% CI = [0.00, 0.37], Z = 1.99, $p = .046$; Other: n = 10, k = 12; Hedge's $g = 0.20$, 95% CI = [0.02, 0.37], Z = 2.23, $p = .026$).

Under the hypothesis-free context, even though Emotion techniques did not significantly modulate overall intrusions, they significantly reduced lab-based intrusion frequency (n = 4, k = 9, Hedge's $g = 0.45$, 95% CI = [0.11, 0.78], Z = 2.63, $p = .009$).

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Non-Pre-registered Hypothesis-Free Focal analysis

Here, we present focal analyses conducted to examine the effectiveness of individual techniques at intrusion modulation. These non-pre-registered analyses were performed in a hypothesis-free manner, i.e., regardless of the proposed directional hypotheses. We report the results for overall intrusion frequency in the main text (for full results, see supplementary Table S6).

Individual Techniques (Level 2 technique name). We found that playing Tetris following trauma reminder (Trauma Reminder + Tetris) significantly reduced intrusion frequency with a large effect size (n = 9, k = 17; Hedge's g = 0.76, 95% CI = [0.51, 1.00], Z = 6.03, p < .001). Relatedly, playing Tetris where exposure to trauma reminder was controlled (i.e. both experimental and control conditions involved the exposure of trauma reminder, with only experimental conditions additionally involved Tetris) also significantly reduced intrusions with a medium-to-large effect size (n = 9, k = 16; Hedge's g = 0.58, 95% CI = [0.28, 0.88], Z = 3.83, p < .001; Fig. 8). Furthermore, finger tapping during trauma exposure significantly reduced intrusions with a medium-to-large effect size (n = 8, k = 13; Hedge's g = 0.58, 95% CI = [0.34, 0.82], Z = 4.72, p < .001). Another notable technique is sleep: sleep following trauma exposure significantly reduced intrusions with a small-to-medium effect size (n = 7, k = 8; Hedge's g = 0.26, 95% CI = [0.09, 0.44], Z = 2.91, p = .004). Lastly, we found that techniques such as emotional acceptance, imagery re-experience + eye movement/number counting also significantly reduced intrusions with a medium-to-large effect size (Hedge's *gs*: 0.49 — 0.53, *p*s < .05, see Fig. 6).

For techniques that increased intrusions, we found that presenting additional contextual information during trauma exposure significantly increased intrusions with a small-to-medium effect size (n = 6, k = 10, Hedge's g = -0.26, 95% CI = [-0.48, -0.04], Z = -2.28, p = .023; Fig. 6). Moreover, low-dose alcohol (when contrasted against high-dose alcohol) also increased intrusions albeit with low number of experiments (n = 2, k = 2, Hedge's g = -0.75, 95% CI = [-1.25, -0.24], Z = -2.88, p = .004).

Some notable techniques with relatively large sample sizes/number of effect sizes yet yielded non-significant results were imagery re-experience (n = 9, k = 10), number counting (n =

9, k = 18), rumination related to trauma content (n = 7, k = 19), positive CBM (contrasted against negative CBM; n = 6, k = 10), and imagery rescripting (n = 4, k = 6; see Fig. 6, see also Fig. 7 for a graphic summary of exemplar individual techniques that significantly modulated intrusion-related outcomes).

----- Insert Fig.6 -----

----- Insert Fig.7 -----

Discussion

In this pre-registered systematic review and meta-analysis, we synthesized 584 effect sizes from the 118 techniques in modulating intrusive memories using the lab-analogue trauma paradigm, involving 11,132 participants. We found that techniques hypothesized to reduce intrusions were effective with a small-to-medium effect size (g = 0.31); furthermore, techniques hypothesized to increase intrusions increased intrusions with a small effect size (g = -0.15). Notably, intrusion modulation techniques also influenced intrusion-related emotion distress, in the same direction as the intrusion changes. Moreover, for intrusion reduction techniques, they also ameliorated intrusion-related symptoms.

Our meta-analysis has the following strengths: First, we had a comprehensive coverage of literature gave us 118 unique techniques that either aimed to increase or reduce intrusions. Second, we implemented both theory-driven and procedure-relevant moderator analyses: hypothetical mechanisms (e.g., Imagery, Verbal, Emotion, Other), direct engagement with trauma memory or not (e.g., Direct, Indirect), required behavioral output or not (e.g., Task, Instruction), timing (e.g., Pre, Peri, Immediate and Delay Post), among others. Third, we conducted both hypothesis-driven, which considered directional hypothesis and theory-driven predictions, and hypothesis-free analyses, which overcame potential publication/experimental biases. Moreover, our focal analyses aggregated homogeneous techniques together regardless of hypothesis, thereby providing compelling evidence on individual technique's effectiveness in intrusion modulation. Lastly, we designed a website with the datasets from the current meta-analysis that allows researchers to interactively analyze the data to guide future research. We will next discuss the results from the moderator and focal analyses, and their theoretical and translational implications.

The dual-representation account of PTSD and trauma memory (Brewin, 2001; Brewin et al., 2010) proposes that disrupting the abnormal visual-perceptual processing of trauma memory would reduce sensory-driven intrusions. Supporting this account, techniques that engaged visuospatial/imagery processing were among the most effective at intrusion reduction across convergent measurements (e.g., diary, lab-based tasks). These findings were robust across both hypothesis-driven and hypothesis-free analyses (g = 0.30 – 0.68). Consistently, our hypothesis-free focal analyses suggested that playing Tetris following a trauma reminder is highly effective at reducing intrusion frequency as well as intrusion-related symptoms. Similarly, finger tapping (of a complex pattern) during trauma exposure reduced subsequent intrusions in both overall and diary-based intrusions (Andrade et al., 1997; Baddeley & Andrade, 2000; Ehlers & Clark, 2000; Hackmann et al., 2004; Holmes et al., 2004; Holmes et al., 2009; Pearson et al., 2015; Sündermann et al., 2013).

An alternative approach to modulate intrusive memory is to change the emotional processing of the trauma or individuals' emotional processing styles, such as positive vs. negative bias modification, emotional reappraisal/acceptance/suppression (Dunn et al., 2009; Espinosa et al., 2023; Woud et al., 2013, 2018). While results from both hypothesis-driven and hypothesis-free analyses showed that these techniques were not significantly effective at reducing overall intrusions, they reduced lab-based intrusions and intrusion-related emotional distress (g = 0.19 – 0.45). Examining individual emotion-related techniques, our focal analyses revealed that emotional acceptance significantly reduced overall intrusions. However, this result warrants further replications, because it was only based on 3 experiments. Overall, results from emotion-related techniques suggested emotion-related techniques bear promises in altering intrusive memories and their accompanying emotional distress (Marks et al., 2018), but their benefits beyond lab setting awaits further investigation.

In addition to techniques that tap into specific mechanisms or processes, we also examined techniques that simultaneously tackle multiple mechanisms (e.g., emotional and memory-related processing, self-regulation) to modulate intrusions. Indeed, both hypothesis-driven and hypothesis-free analyses showed that this Other category significantly reduced intrusions (g = 0.20 – 0.31). Moreover, these techniques reduced intrusion-related distress when they aimed to reduce intrusions (g = 0.20). One notable exemplar technique is post-trauma sleep. According to the cognitive account of PTSD (Ehlers & Clark, 2000), post-trauma sleep may support the integration of trauma memories within one's autobiographical memory scheme, which makes traumatic memories less disorganized and intrusive in nature (Kleim et al., 2016; Zeng et al., 2021). Furthermore, post-trauma sleep may ameliorate strongly charged emotional reactivity over time (Cellini et al., 2019; Tomaso et al., 2021; Walker & van der Helm, 2009; Zeng et al., 2021), which would dampen the hyperarousal and specific emotion associated with trauma. At the same time, sleep could restore the top-down inhibitory control functions mediated by the prefrontal cortex, which effectively prevent unwanted memories from intruding into mnemonic awareness (Harrington & Cairney, 2021; Poh et al., 2016). Notably, the effect size of sleep at intrusion reduction (g = 0.26) is consistent with recent meta-analyses that exclusively examined sleep's effect on intrusions (Davidson & Marcusson-Clavertz, 2023; Schäfer et al., 2023; Larson et al., 2023).

While research on intrusion reduction bears important clinical implications, an understanding of why some people may experience more intrusions is also significant because it informs about the maladaptive mechanisms that perpetuate or worsen intrusions. Among categories of techniques increasing intrusions, we found techniques that predominantly engage verbal processing increased overall intrusions, when these techniques were hypothesized to increase intrusions (g = -0.30). Among verbal-based techniques, focal analyses further showed that when participants were provided with additional contextual information about the trauma during trauma exposure (Krans et al., 2013; Pearson, 2012), they experienced more intrusions (g = -0.26). It shall be noted that this result seemed to be inconsistent with the notion that contextualizing trauma details within the autobiographical memory scheme may reduce their intrusiveness (Brewin et al., 2010; Ehlers & Clark, 2000). Thus, providing trauma-related contextual information during trauma encoding may not aid in contextualizing trauma. Importantly, additional trauma-related information may increase participants' arousal, personal involvement, or empathy; thereby strengthening the sensory representations of trauma (Brewin & Burgess, 2014). Alternatively, such additional trauma-related information may actually increase the available memory cues, thereby triggering more intrusive memories (Pearson, 2012).

Apart from behavioral verbal-based techniques, pharmacological techniques also increased overall intrusion frequency (g = -0.40). Subsequent focal analysis showed that Nicotine (g = -0.54), Oxytocin (g = -0.30,) and low-dose alcohol (0.36 – 0.40g/kg, vs. doubled dosage, g = -0.75) are some examples that increased overall intrusion. Specifically, low-dose alcohol may selectively impair verbally accessible trauma information, making sensory-perceptual trauma details more salient that led to increased intrusions; whereas high-dose alcohol would impair both verbally accessible as well as sensory-perceptual memory encoding systems, leading to fewer intrusions (Bisby et al., 2009). Drugs such as Nicotine and Oxytocin may influence intrusions via multiple mechanisms, such as increasing physiological arousal (Buckley et al., 2007; Eckstein et al., 2014) and heightening sensitivity to emotional cues (Hawkins & Cougle, 2013; Schultebraucks et al., 2022). Heightened arousal and sensitivity may promote preferential encoding of low-level sensory details of the trauma, resulting in sensory-driven intrusions (Ehlers & Clark, 2000).

Procedure wise, we coded 1) whether the techniques asked participants to directly confront trauma memory or not, 2) whether the techniques required explicit behavior output or not, and 3) the timing when the techniques were implemented. We found that Direct and Indirect techniques, and the combination of Direct + Indirect techniques (e.g., trauma reminders followed by playing Tetris, James et al., 2015) robustly reduced intrusions under both hypothesis-free and hypothesis-driven contexts (g = 0.26 – 0.84). Notably, the Direct + Indirect results support the memory reconsolidation account: older memories can become labile and susceptible to interference and modification when they are reactivated (Nader & Hardt, 2009; Dudai, 2015; Scully et al., 2017). When comparing between Task- and Instruction-based techniques, we found that, in the hypothesis-free context, Task-based techniques significantly reduced intrusions across multiple intrusion measurements (g = 0.18 – 0.34), while Instruction-based techniques requesting someone to change their thinking styles for example, were ineffective. In our coding, Task-based techniques required behavioral engagement (e.g., computer gameplay, finger tapping, number counting, verbal elaboration), while Instruction-based techniques merely instructed participants to adopt a specific style of thinking (e.g., rumination, thought suppression) without any behavioral output. Based on these findings, future research shall emphasize on the specific implementations of tasks to modulate intrusions.

Regarding the timing, we found that techniques administered during and post trauma exposure (both immediately and delayed after 24 hours) robustly reduced intrusions in the hypothesis-driven context (g = 0.31 – 0.63). In contrast, techniques implemented prior to trauma exposure did not yield significant results. These findings merit strong clinical and practical implications as they suggest that it is possible and important to reduce intrusion in the aftermath of trauma exposure, but less likely before the trauma.

While our meta-analysis primarily focused on intrusion frequencies, we also examined intrusion-related emotional distress and symptoms. Specifically, techniques that aimed to decrease intrusion frequency also decreased intrusion-related emotional distress and symptoms (g = 0.11 – 0.22). Similarly, techniques that aimed to increase intrusions also increased emotional distress (g = -0.15). Focal analyses examining individual techniques revealed that the Trauma Reminder + Tetris gameplay technique was most robust in reducing intrusion frequency, together with intrusion-related symptoms (Fig. 7). However, other representative techniques such as sleep and contextual information only modulated intrusion frequency (Fig. 7). Together, these findings provide insights into the specificity of intrusion modulation techniques, while presenting preliminary evidence suggesting that certain intrusion modulation techniques (e.g., Trauma Reminder + Tetris) could impact intrusion- and even PTSD-related outcomes.

Limitations and future directions shall be discussed. First, whether lab-based techniques could be translated to non-lab real-world context continues to warrant future investigation. Recent studies provided initial and promising evidence toward clinical setting: in hospital settings among individuals exposed to real-life trauma such as traumatic childbirth or motor vehicle accidents, visuospatial interference interventions (e.g., trauma reminder + Tetris playing) were similarly effective in reducing subsequent intrusions (e.g., Horsch et al., 2017; Iyadurai et al., 2018; Kanstrup et al., 2021; Singh et al., 2021). Second, while examining intrusive memories bears direct relevance to post-traumatic stress conditions such as PTSD, future research is required to gain a more comprehensive and nuanced understanding of intrusions in other disorders (e.g., depression, anxiety) and related symptoms such as intrusive verbal thoughts, rumination, or excessive worry (Arendt et al., 2021; Dalgleish & Hitchcock, 2023; Ehlers & Steil, 1995; Macatee et al., 2015). Third, future research shall consider testing the effects of other intrusion modulation techniques. One such example is retrieval suppression, a cognitive ability that voluntarily stops retrieving memories in front of their cues. Research shows that retrieval suppression could induce forgetting of unwanted memories; while PTSD, anxiety and depression patients showed deficits in retrieval suppression (Catarino et al., 2015; Mary et al., 2020; Stramaccia et al., 2021). Future research could test techniques such as retrieval suppression in reducing traumatic intrusions. Lastly but importantly, pre-registered studies are rare (e.g., Espinosa et al., 2023; Varma & Hu, 2022), though in part this may be due to the age of some included studies. Based on effect size estimates provided by the current and other meta-analyses (e.g., Asselbergs et al., 2023; Schäfer et al., 2023), future research shall conduct pre-registered, high-powered studies to present more convincing evidence regarding the effectiveness of specific techniques. Particularly, our meta-analysis identified techniques that could be appealing to therapists (e.g., imagery rescripting, imagery re-experience + eye movement, cognitive bias modifications), yet only with few numbers of studies. Future research shall consider replicating these findings with pre-registration and higher statistical power.

To conclude, we provide a comprehensive meta-analysis on how to modulate intrusion arising from lab-analogue trauma exposure. The present findings can not only inform theoretical models of intrusive memories but also provide new insights to inform how to best prevent and intervene with intrusions from a translational research perspective, as well as factors that may worsen intrusions. Given that intrusive memories can be a transdiagnostic feature for a variety of psychiatric disorders beyond PTSD such as in depression and anxiety, our results may hold useful implications for treatment innovation across various psychological disorders.

Method

This meta-analysis is prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Moher et al., 2009) and has been pre-registered in the PROSPERO database on 07 January 2021 (ID: CRD42021224835, https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=224835). A detailed PRISMA flowchart can be found in Fig. 3. All article information, data and effect sizes can be found in Table S7. Data and scripts are available in the Open Science Framework (OSF: https://osf.io/phu7w/?view_only=622642ef2c3943cbb843004ec99a1c79). Deviations from pre-registered plans are stated below in relevant method sections.

Literature search

A literature search was conducted on title, abstract and keywords with online databases including Web of Science, PsycINFO (via ProQuest), ProQuest Dissertation, PubMed, BioRxiv and PsyArxiv with key words 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 based on different requirements of the search engines (the exact search words and fields can be found in the PROSPERO). As in the pre-registration, we initially planned to obtain additional publications through 1) citations from recent review articles (both forward and backward citations) 2) listserver 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 Dec 15th,2020, and was updated till April 27th, 2022.

Inclusion/Exclusion criteria

Articles were included based the following criteria: experimental studies including 1) healthy participants; 2) experimental exposure to analogue forms of trauma (e.g., trauma film, emotionally negative images etc.); 3) experimental technique(s) (including pharmacological/substance-related and neuromodulation techniques) targeted at altering the frequency of traumatic intrusive memories.

Articles were excluded if they: 1) included clinical populations; 2) are not experimental studies (e.g., correlational studies or case studies); 3) use naturally occurring or real-life trauma exposure (e.g., real-life 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 both literature searches (n = 8,826) were screened by two reviewers (MMV, SZ) to identify potentially relevant studies which meet the aforementioned inclusion/exclusion criteria, resulting in 178 articles.

In the eligibility phase, the full texts of these publications (n = 178) were assessed for eligibility by three reviewers independently: MMV and SZ assessed all articles, while LS assessed a random 10% of the articles (n = 15). Interrater reliability is substantial to almost perfect: 1st search MMV and SZ: Cohen's κ = 0.95; 99.27% agreement; 2nd search MMV and SZ: Cohen's κ = 1; 100% agreement; MMV/SZ and LS: Cohen's κ = 0.64; 93.75% agreement. Disagreement was reconciled by a fourth team member (XH) to reach a consensus. In total, 137 articles were eligible and included in the qualitative synthesis and for subsequent data extraction.

Using a standardized excel form, data for each study was extracted by two independent raters (MMV, SZ) according to the coding guidebook (see OSF). The 137 eligible articles were divided equally between the two raters, with 38% of the articles (n = 52) coded by both raters to obtain inter-rater reliability (MMV and SZ: Cohen's κ ranges from 0.82 to 1 for primary information). An additional 5% of articles from each rater (total n = 12) were coded by LS for cross validation (MMV/SZ and LS: Cohen's κ = 1). Any discrepancy was discussed among co-authors to reach 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 MMV and SZ.

Study coding primarily involved the following aspects: 1) study/sample characteristics (e.g., within/between subject design; demographics); 2) specific experimental technique and its comparison condition; 3) nature of the experimental trauma exposure (e.g. film, images); 4) frequency and measurement of trauma intrusions (descriptive and inferential statistics); 5) descriptive and inferential statistics of additional outcomes (e.g. emotional distress); 6) information on risk of bias (i.e. 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); 8) timing of technique administration (e.g., pre vs. peri vs. immediate post vs. delayed post trauma exposure).

Due to the heterogeneity brought by involving all kinds of techniques, we identified the key experimental techniques and corresponding control condition based on each study. The control condition could be a no-task condition or an alternative task condition, e.g., Reminder cue + 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) etc. If more than 2 experimental conditions were present, experimental techniques and control conditions were identified according to the study and comparisons were made between each experimental technique and control condition. In the absence of a control condition, pairwise comparisons were conducted for different types of experimental techniques.

Furthermore, to address the issue that different techniques could lead to either an increase or decrease of intrusion frequency based on different hypotheses, we also coded the predicted direction for each study: an “Increase”/ “Decrease” direction means that compared to the control condition, the experimental condition was hypothesized to increase/decrease the intrusion frequency, respectively. In some cases, the authors did not specify the direction or hypothesized the two conditions did not differ, in which cases, we coded the direction as “Unspecified” and “Null”, respectively.

We pre-registered to assess the primary outcome: the frequency of the experimentally induced intrusive memories, as measured by intrusion diaries and lab-based intrusion monitoring tasks. We also pre-registered to assess intrusion-related outcomes, namely, intrusion-related emotional distress and intrusion symptoms as measured by the intrusion subscale from the Impact of Event Scale (-revised, IES/IES-R; Horowitz et al., 1979; Weiss & Marmar, 1997) or other similar questionnaires assessing the symptoms (e.g., symptom questionnaire; Halligan et al., 2002; Turl, 2005). For non-pre-registered outcomes, we included intrusion frequencies measured via self-report questionnaires, to provide a more comprehensive assessment of intrusion frequencies. Moreover, due to insufficient data from the included studies/experiments measuring intrusion vividness, we decided to not include it in our coding schema even though we intended to include this outcome in our pre-registration.

An internal bias assessment (IBA) was conducted to assess the quality of each eligible study. 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 aspects (coded as 0 for ‘no’ or 1 for ‘yes’, 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) Peer-reviewed publication;
11) Mood/distress check for experimental trauma induction;

The assessment scores for each study can be found in the supplementary Table S7.

Data synthesis and analyses

Effect sizes for all outcomes were standardized to Hedges' *g* based on the available information provided in the article (e.g., raw mean/SD/SE, *t*-score, Cohen's d etc.) using custom functions and packages on R, namely, *metafor* (R Core Team, 2020; Viechtbauer, 2010) and *esc* (Lüdecke, 2019).

In order to compare the efficacy of different categories of techniques, we developed a hierarchical structure to categorize similar techniques (Fig. 2). Specifically, based on each entry of experimental and control conditions, we developed four levels: Level 0 and Level 1 were coded separately for experimental and control conditions; Level 2, Level 3, Level 3a, Level 3b and Level 3c were coded based on experimental vs. control comparison. From level 2 to level 3, each entry was coded by two raters (MMV and SZ) independently: Cohen's κ ranges from 0.57-0.79. Any inconsistency was reconciled by a third rater (XH).

a) Level 0: Verbatim names of the experimental and control conditions that were used in the original article.

b) Level 1: Consistent names for similar or identical experimental and control conditions, when they were given different names in the original article.

c) Level 2 (*Individual Techniques*): Technique names for the key techniques in the experimental group vs. control group contrasts. For example, Sleep vs. No sleep comparisons were coded as Sleep; Trauma reminder + Tetris vs. Trauma reminder comparisons were coded as Tetris (while the importance on the inclusion of trauma reminders needs to be emphasized wherever applicable); Trauma reminder + Tetris vs. No task comparisons were coded as Trauma reminder + Tetris.

d) Level 3 (*Operation of Techniques*): Superordinate categories based on each technique's mechanistic operation. Specifically, we coded each level 2 technique into one of the following categories: a) Behavioral; b) Neuromodulation; c) Pharmacological.

Given our primary interests in behavioral techniques, we further coded the behavioral techniques into Level 3a: Hypothetical Mechanism, Level 3b: Direct/Indirect Involvement of Trauma Memory and Level 3c: Task vs. Instruction.

e) Level 3a (*Hypothetical Mechanism of Techniques*): Based on the specific mental processes they target , we code each Level 2 technique into one of the following categories: a) Imagery, that tap into perceptual-visual processing (e.g., imagery rescripting/re-experience, data-driven processing, finger tapping etc.); b) Verbal, that tap into verbal processing (e.g., rumination, conceptual processing, number counting etc.); c) Emotion (e.g., emotional suppression, guilt induction etc.); d) Others (e.g., sleep, self-efficacy, exercises, etc.); e) any combination or contrasts of the above, if appropriate (e.g., Direct Imagery + Indirect Imagery, Direct Imagery vs. Direct Verbal).

f) Level 3b (*Direct vs. Indirect Involvement of Trauma Content*): Based on whether the techniques directly vs. indirectly target the trauma memory, we coded those involving direct engagement of trauma content as Direct, and others don't require direct confrontation as Indirect.

g) Level 3c (*Task vs. Instruction*): Superordinate categories based on each technique's modality. We classified techniques which required participants to perform a concrete task entailing external action into Task category (e.g., finger tapping, viewing a humor inducing film, listening to a meditation recoding, ingesting a pharmaceutical drug). For techniques that required participants to adopt a specific style of thinking and did not involve any external action was classified into Instruction category (e.g., elaboration, abstract processing, mentally rehearse, thought suppression). In cases where the experimental and comparison group employed different modality of techniques, we will code both with "vs." in the middle (e.g., Task vs. Instruction).

Lastly, while we pre-registered to compare between individual techniques within each implementation timepoint (i.e., Pre vs. Peri vs. Immediate Post vs. Delayed Post relative to the onset of trauma), this would include fewer studies for each timepoint. Instead, we examined the Timing as a separate, non-pre-registered, moderator to include more data. Techniques that were administered within the same day after the experimental trauma were categorized as Immediate Post, and techniques administered following at least 24 hours delay after the experimental trauma exposure were categorized under Delayed Post. For techniques that were used in multiple time points, we will code it with "+", e.g., Peri + Immediate Post.

Main Analysis

Given that intrusion modulation research examined techniques with different hypothesis (i.e., a specific technique would either increase or decrease intrusions), we calculated overall effect sizes of experimental techniques for each intrusion modulation directions (i.e., Increase, Decrease and Unspecified). These analyses were conducted on both overall intrusions (aggregating across diary-, lab- and questionnaire-based intrusion frequencies), and on intrusion frequencies on each measurement. A three-level multilevel meta-analytical approach (Cheung, 2014; Harrer et al., 2021) was used to model three levels of variance: (i) variances due to sampling error, (ii) within-study variances among multiple effect sizes from the same experiment and (iii) variances due to between-study heterogeneity. Homogeneity Q and I^2 statistics were used to compare the variability in individual effect sizes both within-study as well as comparisons between studies.

We repeated the aforementioned analyses on two additional outcomes, namely, i) intrusion-related emotional distress; and ii) intrusion-related symptoms.

Publication Bias Analyses

We conducted publication bias analyses on each of the outcomes for hypothesis-driven datasets through: (i) funnel plots, which was used to assess the presence of publication bias, (ii) Egger's test, which was used to quantify the funnel plot assessment findings, (iii) trim and fill method, to substitute studies which are missing due to the impact of publication bias on literature search findings, and (iv) three-parameter selection model.

Moderation Analysis

We used "rma.mv" from *metafor* package (Viechtbauer, 2010) to conduct moderation analyses on intrusion frequency, intrusion-related distress and intrusion-related symptoms. Meta-regressions were conducted on both the hypothesis-driven and hypothesis-free datasets using the following moderators:

1) Operation of Techniques (Level 3 superordinate category)

2) Mechanism of Techniques (Level 3a superordinate category)
3) Direct/Indirect Involvement of Trauma Content (Level 3b superordinate category)
4) Task- vs. Instruction-based Techniques (Level 3c superordinate category)
5) Time of techniques being implemented (e.g., pre-, peri-, post-, etc., non-pre-registered)
6) Nature of experimental trauma exposure (e.g., film, images)
7) Nature of comparison condition (passive (no-task) or active (alternative task) control)
8) Study design (within vs. between-subject)
9) Mode of intrusion measurement (e.g., intrusion diary etc.)
10) Neuroimaging or psychophysiological measures included (yes vs. no)
11) Publication status (published vs. unpublished)
12) Gender
13) Age
14) Country/Region
15) Continent

In addition to these moderators, we examined IBA score as a moderator under hypothesis-free context.

Non-Pre-registered Hypothesis-Free Focal Analysis

In addition to the pre-registered analyses mentioned above, we also conducted non-pre-registered focal analysis on Level 2 (i.e., Individual Techniques) regardless of the specific hypothesis made in the articles (i.e., hypothesis-free). In other words, this focal analysis included the whole dataset (i.e., including studies with increase or decrease or unspecified or null directions). Specifically, we conducted three-level multilevel modelling to compare effectiveness of individual techniques (Level 2 technique name).

Data availability

Data and scripts are available on the OSF (link: https://osf.io/phu7w/?view_only=622642ef2c3943cbb843004ec99a1c79). A website was developed for researchers to use the dataset to implement analyses mentioned in the paper (link: http://117.78.42.83).

Author Contributions

M.M.V. and Z.S.: Conceptualization, Investigation, Formal Analysis, Data Curation, Methodology, Software, Validation, Writing - Original Draft, Writing - Review & Editing, Visualization; **L.S.:** Investigation, Formal Analysis, Validation, Writing - Review & Editing; **E.H.,** Formal Analysis, Writing - Review & Editing; **J.H.:** Formal Analysis, Software, Validation; **X.H.:** Conceptualization, Investigation, Formal Analysis, Data Curation, Validation, Writing - Original Draft, Writing - Review & Editing, Supervision, Project Administration, Funding Acquisition.

Acknowledgements

The research was supported by the Ministry of Science and Technology of China STI2030-Major Projects (No. 2022ZD0214100), National Natural Science Foundation of China (No. 32171056), General Research Fund (No. 17614922) of Hong Kong Research Grants Council. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. The authors would thank to the many researchers who contributed to this manuscript by sharing their data.

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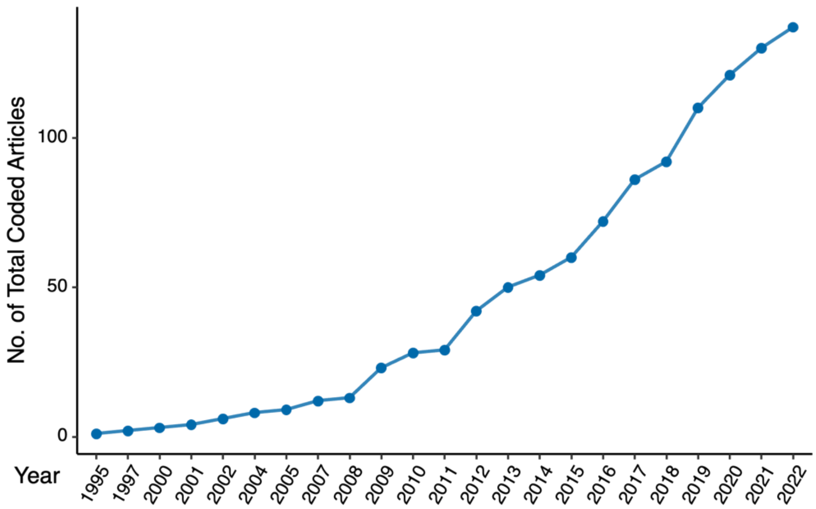
Table 1. Summary statistics for the studies included in the meta-analysis.

Summary statistics	
n (Total experiments)	145
k (Total effect sizes)	584
N (Total sample sizes)	11132
Demographical information	
Age, mean (SD)	23.28 (3.44)
Gender	
Male, N (%)	3602 (32.36%)
Female, N (%)	7530 (67.64%)
Number of Experiments by Countries/Regions	
UK, n (%)	49 (33.79%)
Netherlands, n (%)	28 (19.31%)
Australia, n (%)	24 (16.55%)
Germany, n (%)	17 (11.72%)
USA, n (%)	14 (9.66%)
Others, n (%)	13 (8.97%)
Study Design	
Between-subject, n (%)	138 (95.17%)
Within-subject, n (%)	7 (4.83%)
Study Hypothesis Direction	
Intrusion increase, n	60
Intrusion decrease, n	101
Unspecified, n	38
Null, n	2
Outcome	
Intrusion frequencies, n	131
Intrusion-related distress, n	61
Intrusion-related symptoms, n	55

Fig 1: (A) The number of total coded articles by year. (B) Visualizing individual techniques coded in the meta-analysis a word cloud, with larger fonts indicating higher numbers of articles investigating the corresponding technique.

(A) The number of articles across years coded in the current meta-analysis



(B) Cloud to visualize individual techniques (from Level 2)

Fig. 2: Coding scheme of techniques (level 0-2), and categorization of individual techniques as moderators (level 3).

Level 0: Verbatim names

We extracted the verbatim names for each experimental and control conditions from the articles.

Level 1: Unify different names

We used consistent names to unify similar or identical experimental and control conditions.

Level 2 (Focal Analysis): Individual Technique names

We coded each experimental vs. control comparison as one level 2 technique.

Level 3 (Moderator Analysis): Superordinate category

Based on the operation of the technique, each level 2 coding was further coded as:

a) Pharmacological;
b) Neuromodulation;
c) **Behavioral**.

Given our primary interests in behavioral techniques, we further coded **behavioral techniques** into following:

Level 3a: ***Hypothetical Mechanism(s) of Techniques***

a) **Imagery** (e.g., Tetris)
b) **Verbal** (e.g., Elaboration)
c) **Emotion** (e.g., Reappraisal)
d) **Other** (e.g., Sleep)
e) **Any combinations or contrasts** (either through + or vs.)

Level 3b: ***Direct vs. Indirect Involvement of Trauma Content***

Direct: Behavioral techniques that directly engage the analogue traumatic experience (e.g., Elaboration, Re-exposure).
Indirect: Techniques that do not require direct confrontation with the trauma content (e.g., Finger Tapping, Number Counting).

Level 3c: ***Task vs. Instruction of Techniques***

Task: Behavioral techniques that require participants' behavioral action and output (e.g., Elaboration);
Instruction: Techniques that give participants instructions to change processing styles, without any behavioral output (e.g., Thought Suppression).

Fig. 3. A PRISMA flow chart of literature search and inclusion

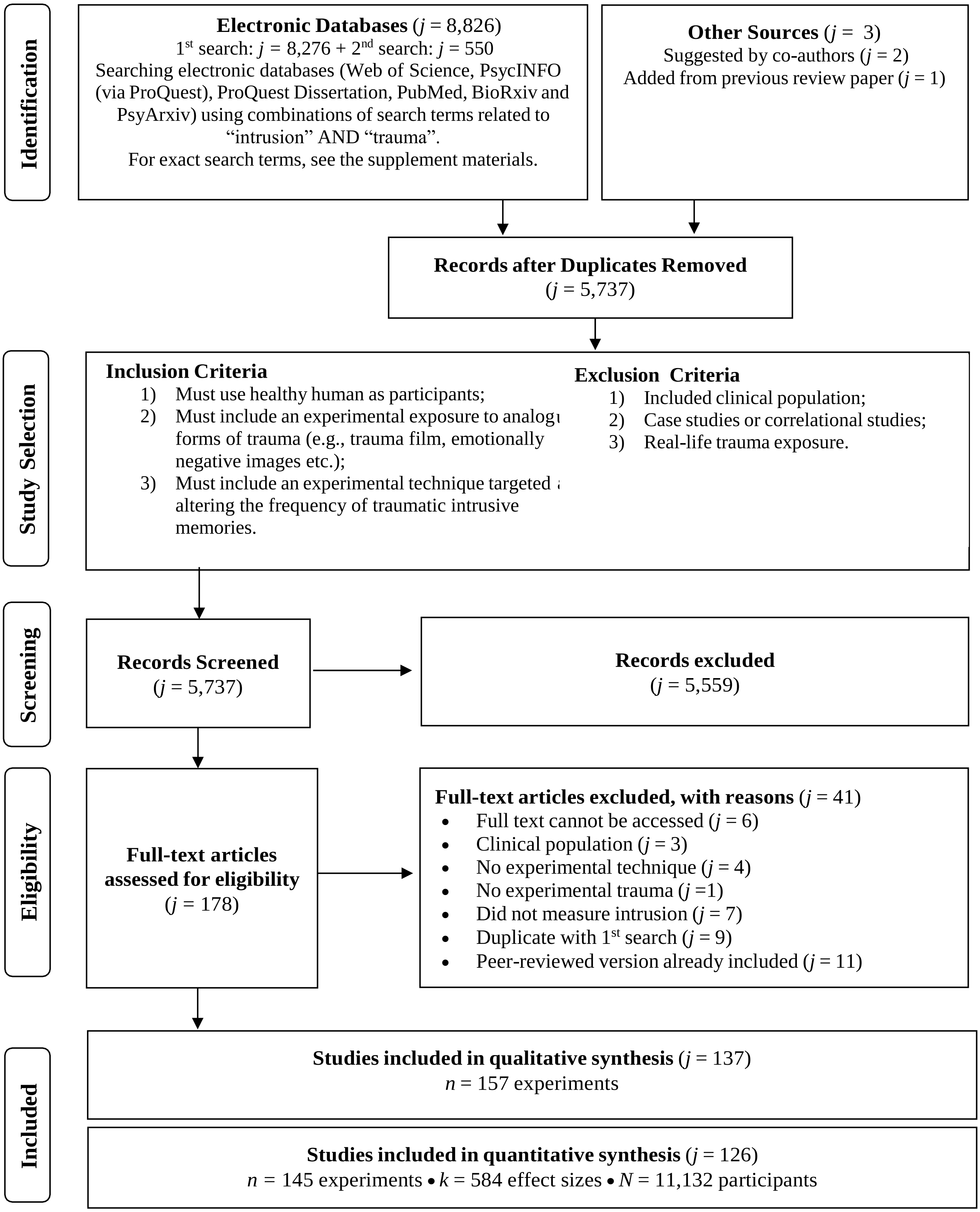
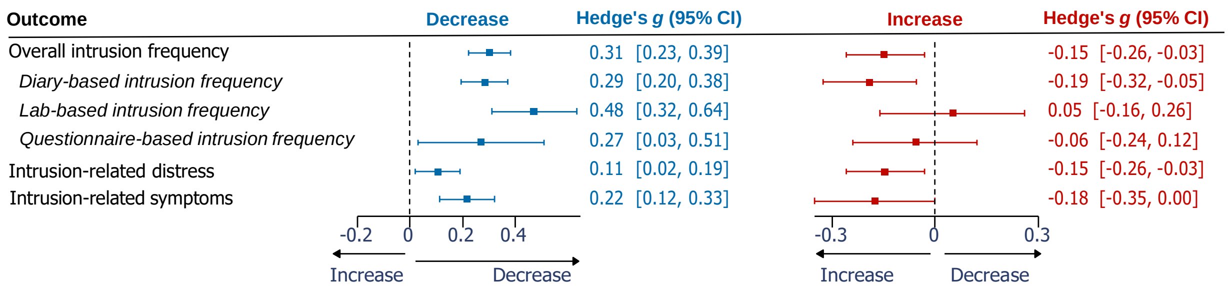
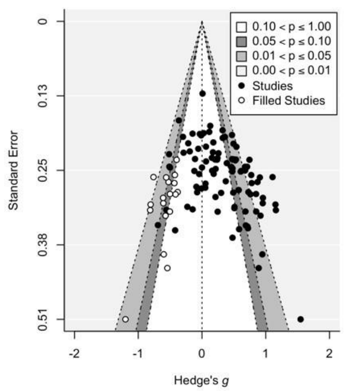


Fig. 4. (A) Overall effect sizes from hypothesis-driven main analyses considering the directional hypothesis made in the articles and (B) funnel plots.

(A) Aggregate effect sizes for different outcomes and hypothesis directions



(B) Funnel plot for overall intrusion frequency (Decrease)



(C) Funnel plot for overall intrusion frequency (Increase)

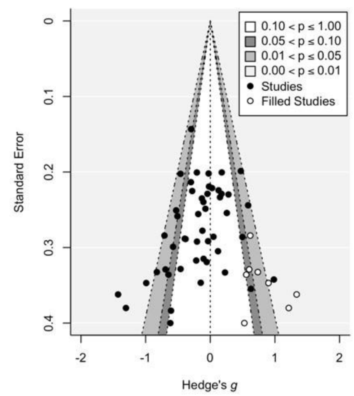


Fig. 5. Effect sizes on overall intrusion frequency from the moderator analyses in both Hypothesis-driven (blue: Decrease, red, Increase) and Hypothesis-free (All, including all effect sizes regardless of hypotheses) analyses.

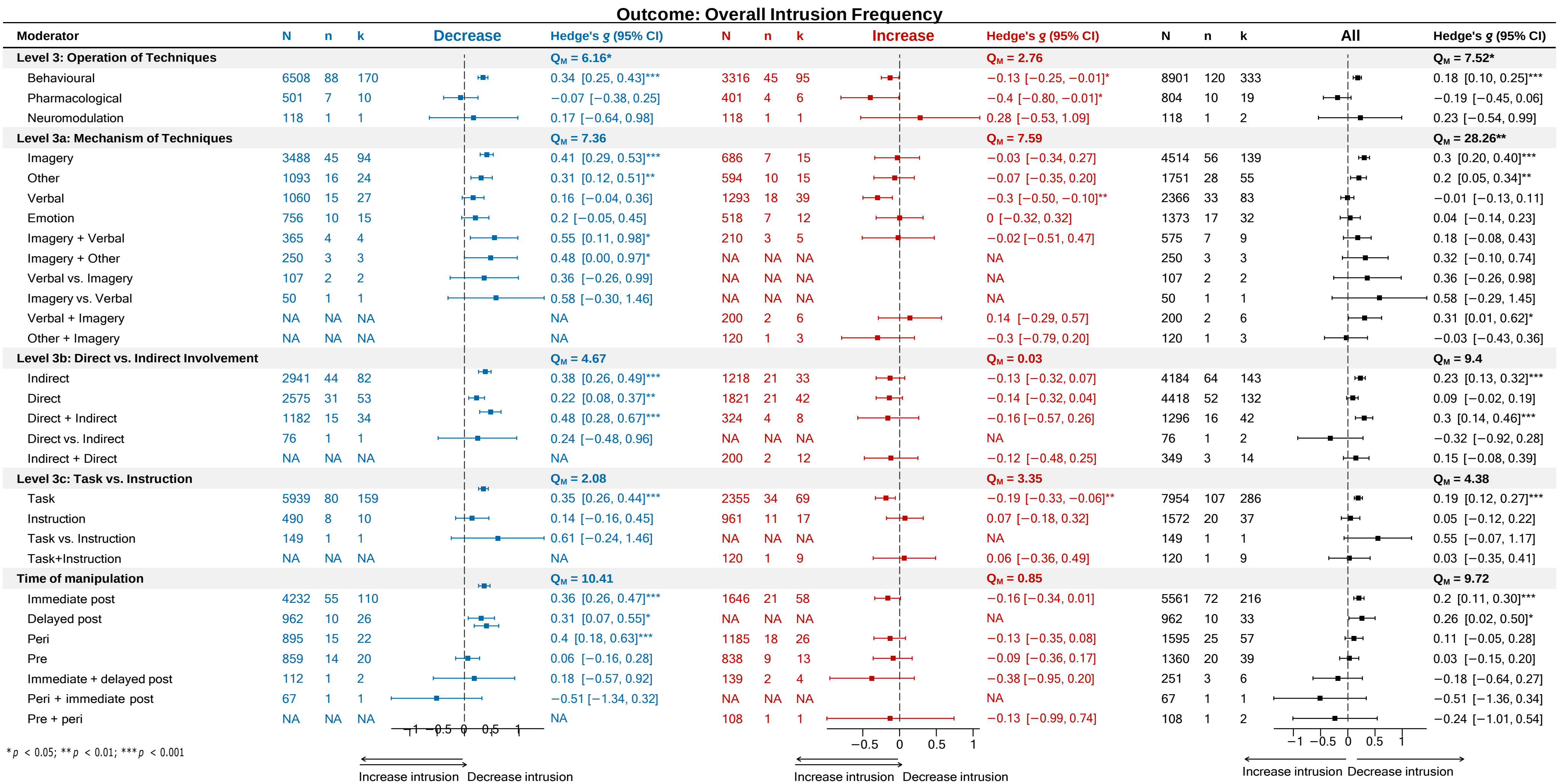


Fig. 6 Hypothesis-free focal analysis on Level 2 Individual Techniques (Note: only techniques with more than 2 articles were included)

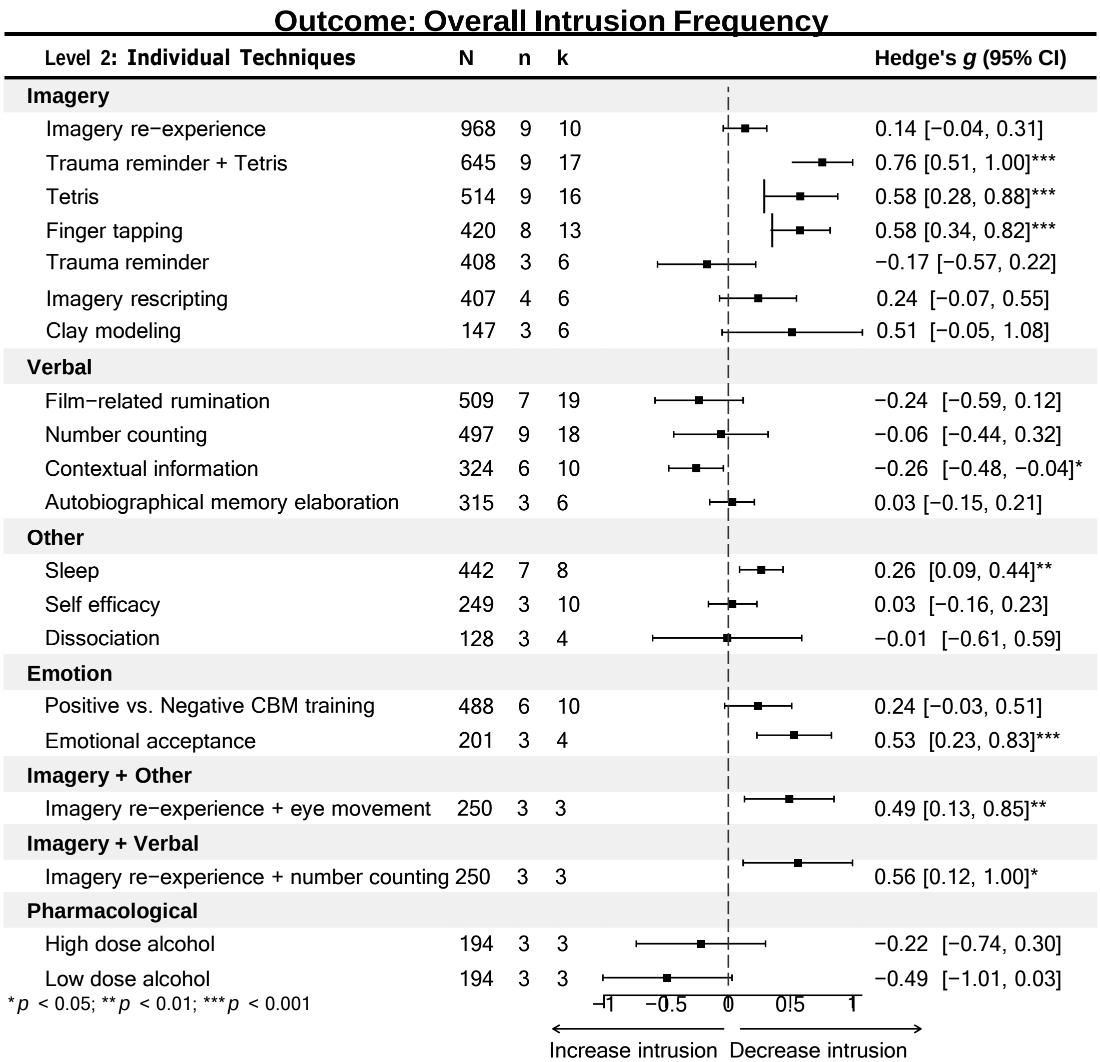


Fig. 7. Visual illustration of exemplar individual techniques (each with more than 5 articles) that significantly modulated either intrusion frequency, distress or symptoms.