

EDITORIAL

Analog Flashbacks

Commentary on Porcheret et al. Psychological effect of an analogue traumatic event reduced by sleep deprivation. *SLEEP* 2015;38:1017–1025.

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In the growing field of research on sleep and emotion regulation, an interesting dichotomy has arisen between findings suggesting that sleep following traumatic events could, via sleep-dependent memory processes, detrimentally strengthen and perpetuate traumatic memories,^{1–3} and those that suggest that post-trauma sleep disruption contributes to emotional dysregulation and psychopathology.^{4–9} These findings have led to conflicting speculation that sleep should either be curtailed on the night following the traumatic event^{2–4} or that correcting sleep disturbance should be treated as an essential first step in preventing subsequent anxiety symptoms.^{7,9} In this issue of *SLEEP*, Porcheret and colleagues report that a night of total sleep deprivation (TSD) following presentation of series of emotionally disturbing film clips (e.g., suicide) reduced the rate at which spontaneous memories of these films intruded into participants' consciousness over the subsequent 6 days.¹⁰ The authors suggest that these intrusive memories are analogous to those that occur in posttraumatic stress disorder (PTSD) and hypothesize that sleep deprivation following an actual trauma might reduce the consolidation of such intrusive memories expressed symptomatically in PTSD as flashbacks, dissociation, and nightmares.¹⁰

These alternate approaches to preventing PTSD symptoms are, of course, not mutually exclusive, since a single night's TSD could immediately be followed by efforts to optimize sleep quality. Evidence exists that sleep disturbances during the weeks and months immediately following a traumatic event may be especially important in the development of PTSD.^{4–7} Similarly, sleep difficulties preceding traumatic experiences increase risk of later PTSD.^{11,12} However, because memory consolidation¹³ and processing of emotional memories¹⁴ during sleep are ongoing processes, it is possible that a single night's TSD would produce only a small effect. Evidence that brief peri-traumatic interventions may not prove effective comes from negative findings in pharmacological interventions that were intended to weaken initial consolidation of traumatic memories. For example, trials that used propranolol immediately post trauma to block noradrenergic facilitation of fear consolidation, although initially promising,¹⁵ did not produce a clinically significant effect in a larger sample.¹⁶ Nonetheless, reports of reduced PTSD in traumatized children initially

treated with opiates,¹⁷ as well as positive results in reconsolidation-blockade studies using propranolol^{18,19} suggest that pharmacological interventions designed to weaken traumatic memories continue to hold promise. Thus a TSD intervention might also do so and should be tested in clinical samples. Before attempting an actual peri-traumatic TSD trial, more easily accomplished paradigms might first be tried, such as reconsolidation blockade or a retrospective chart review comparing individuals kept awake incidentally following a traumatic stressor to those who slept.

Another caveat when considering a single night of TSD as prophylactic treatment for trauma-memory intrusion is the above-noted phenomenon of reconsolidation, whereby retrieved memories temporarily re-enter a labile state.²⁰ Whereas such lability offers the opportunity for modification or even elimination of an unwanted memory,^{21,22} it also presents the possibility for retrieved fear memory to re-stabilize, generalize, or even worsen. Therefore, reconsolidation blockade sessions might need to be added to the above-envisioned compound therapy. An important additional consideration in any research on preventive strategies for PTSD is that a history of trauma preceding the index event is extremely common²³ and may greatly increase the risk of developing symptoms²⁴ and complicate treatments focused exclusively on a single event.

Because of the difficulties involved in controlled peri-trauma research, experimental paradigms that reproduce elements of the human response to trauma in healthy individuals are very important for exploratory studies of potential clinical interventions.^{10,25} Such paradigms are additionally important because experimental manipulations in humans cannot ethically induce levels of stress shown to produce PTSD-like effects in rats.²⁶ The use of analog-trauma films to elicit intrusive memories has had a particularly productive history in work by Emily Holmes and colleagues.^{10,27,28} For example, this group has characterized individual differences in vulnerability to such intrusions^{29,30} and developed techniques for inhibiting their occurrence.^{31,32} These researchers also showed that memories that later elicited intrusions produced greater activation of limbic structures when encoded during trauma films,³³ conditions also known to enhance voluntary recall of emotional over neutral material.^{34,35} Such limbic activation at encoding may thus also explain intrusions following an actual traumatic stressor. Surprisingly however, in several studies, intrusion frequency was unrelated to measures of recall and recognition.^{10,36} Therefore, such analog intrusions, as well as the traumatic memories they model, must differ in fundamental ways from the voluntary recall of declarative memory, which is the form of emotional memory usually tested in sleep-dependent memory consolidation protocols.¹³

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Kuriyama et al.¹ performed a similar study in which they showed prevention, by TSD, of the generalization of fear from a trauma film to a neutral one. Fear generalization is also characteristic of PTSD.³⁷ However, it should be noted that neither of these studies necessarily show impact on a pathological process, and the phenomena observed might or might not be the same as those that become dysregulated in psychopathology. One potential confound in the study by Porcheret and colleagues¹⁰ is a possible salience effect at memory encoding,^{38,39} the consolidation of which might itself also be sleep-dependent⁴⁰ and lead to enhanced involuntary recall. For example, one might see similar effects if the pre-intervention film showed highly arousing but pleasantly valenced stimuli, and this would be an important experimental control in future studies using TSD manipulations.

Another important consideration when interpreting the effects of sleep on emotional memory processes is their apparent sensitivity to small differences in experimental procedures. For example, Kuriyama et al.⁴¹ replicated their previous finding when participants were told to recall events of the trauma film. However, they then found that TSD produced more rather than less generalization of fear when participants performed an active memory suppression procedure following their initial exposure.⁴¹ Generalization and sensitization phenomena are more nuanced aspects of emotional memory that can be affected by sleep and TSD even when the actual strength of a memory is unaffected.⁴² Moreover time-of-day and morningness-eveningness along with possible gender interactions,^{42–44} in addition to sleep itself,^{45–48} can affect the extinction of conditioned fear. Therefore, standardized paradigms, such as used by Porcheret et al.¹⁰ are necessary to dissect these more subtle influences by selective manipulation of specific factors in otherwise identical protocols.

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