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Losing memories during sleep after targeted memory reactivation

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ABSTRACT

Targeting memories during sleep opens powerful and innovative ways to influence the mind. We used targeted memory reactivation (TMR), which to date has been shown to strengthen learned episodes, to instead induce forgetting (TMR-Forget). Participants were first trained to associate the act of forgetting with an auditory forget tone. In a second, separate, task they learned object-sound-location pairings. Shortly thereafter, some of the object sounds were played during slow wave sleep, paired with the forget tone to induce forgetting. One week later, participants demonstrated lower recall of reactivated versus non-reactivated objects and impaired recognition memory and lowered confidence for the spatial location of the reactivated objects they failed to spontaneously recall. The ability to target specific episodic memories for forgetting during sleep has implications for developing novel therapeutic techniques for psychological disorders such as PTSD and phobias.

1. Introduction

Modifying memories during sleep used to be a dream; today numerous studies show the impact of targeting sensory details during slow wave sleep. Although targeted memory reactivation (TMR) has been used to enhance consolidation of multiple types of memory, episodic material has been a particular focus. It is generally assumed that such hippocampally-dependent memories are stabilized within the brain via spontaneous reactivation during non-rapid eye movement (NREM) sleep through a coordinated dialogue of slow wave oscillations, sleep spindles, and sharp-wave ripples (Born, Rasch, & Gais, 2006; Diekelmann & Born, 2010; Inostroza & Born, 2013; Wilson & McNaughton, 1994). Given that spontaneous reactivation exists during slow wave sleep (SWS), a window of opportunity exists to target these memories by reactivating their specific sensory elements. Reactivating the sensory elements of newly learned material, such as associated sounds or odors, has been demonstrated to strengthen memory for cued items as compared to uncued control items (Antony, Gobel, O'Hare, Reber, & Paller, 2012; Diekelmann, Biggel, Rasch, & Born, 2012; Diekelmann, Buchel, Born, & Rasch, 2011; Fuentemilla et al., 2013; Oudiette, Antony, Creery, & Paller, 2013; Rasch & Born, 2007; Oudiette & Paller, 2013; Rasch, Buchel, Gais, & Born, 2007; Rudoy, Voss, Westerberg, & Paller, 2009; Rihm, Diekelmann, Born, & Rasch, 2014; Schönauer, Geisler, & Gais, 2014; van Dongen et al., 2012). But what about losing or erasing memories, as explored in the movies Inception and Eternal Sunshine of the Spotless Mind? In sleep, as noted, reactivating a memory can strengthen it, but it remains unclear if reactivated memory traces can be modified in such a way that they are weakened or completely erased.

During wakefulness, reactivating a memory returns it to a susceptible state. Once destabilized, the memory trace goes through a period of reconsolidation during which it must be re-stabilized (Nader, Schafe, & LeDoux, 2000; Hupbach, Gómez, Hardt, & Nadel, 2007; Walker, Brakefield, Hobson, & Stickgold, 2003). During this reconsolidation period it is prone to interference, which can arise in various ways, including the presentation of new information or the administration of a pharmacological agent. During SWS, Rasch and Born (2007) theorized that when a memory trace is reactivated, it goes through a similar destabilization and re-stabilization journey; however, given the lack of competing environmental information during sleep, the most likely outcome is that the trace is re-stabilized. We linked the sensory reactivation of a specific memory with the concomitant reactivation of a separately trained forget tone during sleep to see if we could capitalize on this trace destabilization and induce memory loss for the reactivated memory item and its details.

Rudoy et al. (20009) trained participants on objects in specific locations paired with associated sounds. For example, participants saw a cat in the lower right-hand quadrant and heard the sound meow. During SWS, the experimenters replayed sounds for some objects at 5-s intervals (cued objects) while not cueing the remaining object sounds (uncued control objects). Following the period of sleep, participants more accurately located reactivated cued objects compared to non-reactivated control ones on the grid, demonstrating strengthening after reactivation of a targeted memory. In a reversal of this logic, we asked

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Table 1
Study objects including timing, description, and proportion used.

Object	Sound description	Length of audio file (ms)	Proportion of times objects were cued for reactivation or control
Apple	Apple crunch during a bite	1340	0.02
Arrow	An arrow hitting a dartboard	1520	0.04
Ball	Ball bouncing	2750	0.03
Camera	Camera clicking	2410	0.01
Car	Car engine revving	2330	0.03
Coins	Coins dropping	1790	0.03
Cork	Cork popping	1130	0.03
Door	Door opening	3280	0.04
Drum	Drums banging	3020	0.03
Fan	Fan whirring	2280	0.03
Flute	Flute playing	3190	0.06
Frying Pan	Frying pan sizzling	3020	0.04
Golf Club	Golf club swing	2280	0.05
Spray Paint	Spray paint sound	2470	0.02
Hands	Clapping	2380	0.04
Matchstick	Matchstick striking	2280	0.03
Pencil	Pencil writing	3120	0.04
Saw	Saw cutting	2000	0.04
Shoe	Shoes walking	2660	0.03
Soda	Soda can opening	1650	0.06
Sprinkler	Sprinkler going	2560	0.03
Straw	Slurping through a straw	1650	0.03
Teakettle	Teakettle whistling	2750	0.03
Toilet	Toilet flushing	2610	0.04
Typewriter	Type writer clicking	2720	0.04
Washing Machine	Washing Machine going	2750	0.04
Whip	Whip Cracking	1060	0.05
Zipper	Zipper zipping	2160	0.04
		Avg = 2327 ms SD = 615 ms	Total = 1.0

Note: A list of objects and their associated sounds used in the study and the proportion of times they were included as TMR-F or control objects across all participants. Objects selected more often than others (e.g. soda, flute, golf club) occurred at encoding strengths in the middle range more often than other objects.

whether it is possible to lose parts of, rather than strengthen, a memory by presenting a 'forget' signal during the targeted sleep-reactivation period. There is evidence to show that directing forgetting during wakefulness reduces the processing of preceding information (Fawcett & Taylor, 2008; Zacks, Radvansky, & Hasher, 1996) and leads to a reduction in hippocampal activity, which is associated with reduced memory performance (Ludowig, et al., 2010). For this study, we trained participants to associate an auditory tone with an explicit 'forget' instruction. Then in a second, separate task, we trained participants on objects presented with their associated sounds in specific quadrants of a display. After Rudoy et al., we replayed the sounds associated with particular object-location pairings during SWS. Unlike prior studies, we reactivated the forget tone during the interval between each object sound. We then compared the retention of reactivated cued objects to non-reactivated uncued control objects one week later. Thus, we investigate whether presenting a trained forget tone during the targeted reactivation of a specific memory during sleep (TMR-forget) will alter sleep-dependent processing, inducing the loss rather than the strengthening of long-term memory.

2. Methods

2.1. Participants

A total of 24 students (18 females; Age *M* = 20.17 years, *SD* = 1.82 years, range 18–26 years) were recruited from the University of Arizona to participate in this study, as approved by the Institutional Review Board at the University of Arizona. We computed a power analysis based on a comparable study (Rudoy et al., 2009) with an effect size = .75, α err prob = .05, and power (1-β err prob) = .8 to identify the number of subjects necessary for achieving a similar effect size. The analysis indicated n = 16. Given our exclusion criteria and anticipating a likely need to exclude subjects, we chose a sample size of 25 to ensure a sufficient sample size. Prior to participation, we administered oral and written consent. Participants were monetarily compensated. The inclusion criteria for data were as follows: (1) the median strength of object learning at encoding must be 75% or lower, (2) participants must not awaken and consciously hear the sound files during SWS, (3) participants must not know the methodology prior to participation, and (4) participants must have all 5 objects reactivated fully such that each reactivation file (containing repeats of the cued object and forget-tone) is played in its entirety twice (see Targeted Memory Reactivation Sound Files section for details). We chose these criteria because strongly encoded memories can be harder to reactivate (Wang, Oliveria Alvares, & Nader, 2009), and second, if participants hear the reactivated sounds at night or explicitly know the methodology, their data are likely tainted. We eliminated participants due to incomplete reactivation of all 5 objects (2 participants), conscious arousal and explicit knowledge of sound reactivation (2 participants), and equipment failure (1 participant). We removed one participant post hoc based on recall scores 2 standard deviations above the mean. 18 participants' data were included in the final analyses. One subject had 5 reactivated objects compared to 4 control objects, as compared to all other subjects who had 5 reactivated objects compared to 5 control objects that matched in encoding strength and location.