

# Mesmerizing Memories: Brain Substrates of Episodic Memory Suppression in Posthypnotic Amnesia

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DOI 10.1016/j.neuron.2007.11.022

## SUMMARY

Two groups of participants, one susceptible to posthypnotic amnesia (PHA) and the other not, viewed a movie. A week later, they underwent hypnosis in the fMRI scanner and received a suggestion to forget the movie details after hypnosis until receiving a reversal cue. The participants were tested twice for memory for the movie and for the context in which it was shown, under the posthypnotic suggestion and after its reversal, while their brain was scanned. The PHA group showed reduced memory for movie but not for context while under suggestion. Activity in occipital, temporal, and prefrontal areas differed among the groups, and, in the PHA group, between suggestion and reversal conditions. We propose that whereas some of these regions subserve retrieval of long-term episodic memory, others are involved in inhibiting retrieval, possibly already in a preretrieval monitoring stage. Similar mechanisms may also underlie other forms of functional amnesia.

## INTRODUCTION

For items in memory to be retrieved and guide behavior properly, suppression of some memory representations seems to be as important as the expression of others (Hasher and Zacks, 1988; Levy and Anderson, 2002; Schnider, 2003; Racsmay and Conway, 2006; Gilboa et al., 2006; Bjork, 2007). Indeed, when memory suppression fails, mnemonic-guided behavioral interactions with ongoing reality fail as well (Schnider, 2003; Gazzaley et al., 2005). However, despite intriguing data on postulated processes and manifestations of memory suppression that emerged in recent years from laboratories and clinics alike (Conway and Fthenaki, 2003; Schnider, 2003; Anderson et al., 2004), relatively little is known of the brain mechanisms that subserve such suppression.

Three major types of experimental approaches reign in the discipline of memory suppression. One involves manipulation of learned material in healthy individuals, so that items to be recalled are either incidentally or intentionally blocked (Bjork

et al., 1968; Rosen and Engle, 1998; Levy and Anderson, 2002; Racsmay and Conway, 2006). Another involves investigation of pathological conditions in which normal memory suppression occurs by definition, such as psychogenic or functional amnesia (Markowitsch, 1999), or is postulated to occur, such as spontaneous confabulation (Schnider, 2003). Still another approach bridges the worlds of cognitive research and the clinic. It addresses certain memory deficits that occur with aging (Hasher and Zacks, 1988; Gazzaley et al., 2005) or following posthypnotic suggestion (Kihlstrom, 1997).

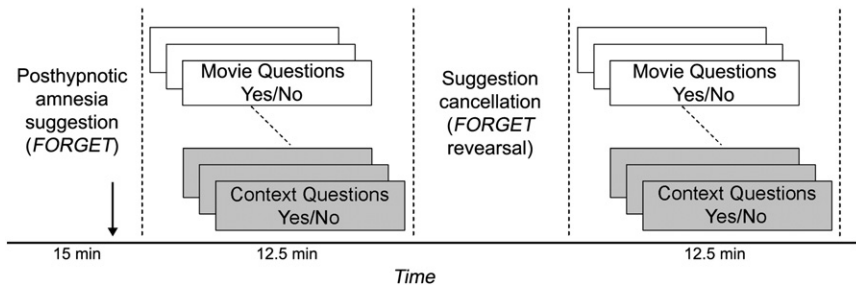
The present work uses hypnosis as a tool to tap into memory suppression in the brain. Hypnosis was known to healers and their clients since the dawn of history and was harnessed into the service of western medicine in the past 200 years, following the observations of Franz Mesmer, James Braid, and their followers (Braid, 1845; Gauld, 1995). It is considered in folk psychology as an altered state of consciousness. The majority of scientific treatments do not refute this intuition, but differ on the type of alteration, its manifestations in nonhypnotic states, and the conceptual framework and semantics used to define it. Formally, the phenomenon refers to a psychosocial situation, mental state, mental or neuronal process, and behavioral procedure (Hilgard, 1975; Kihlstrom, 1997; Kirsch, 1998; Wagstaff, 1998). The psychosocial situation is of a person, the hypnotized subject, who acts on suggestion from another, the hypnotist. In self-hypnosis, both roles are played by the same brain. The state, as noted above, is that of altered consciousness, commonly described as dissociative. The latter notion has evolved over the years to encompass different mental faculties, which might also become dissociated in the absence of hypnosis (Hilgard, 1975; Kirsch and Lynn, 1995; Wagstaff, 1998). The process is that in which cognition and its brain substrates culminate in the aforementioned mental state. And the behavioral procedure is that in which the hypnotist invokes the aforementioned process.

Individuals vary in their susceptibility to hypnosis (Weitzenhoffer and Hilgard, 1962; Stern et al., 1979; Lichtenberg et al., 2004). Most pertinent to the topic of the present study is the well-established observation that high-hypnotizable individuals can be induced during the hypnotic state into a situation in which, on termination of hypnosis, they are unable to recall information acquired either in the hypnotic session or before it, until presented with a prearranged reversibility cue. This

**A Study Session**



**B Test Session**



posthypnotic suggestion state is termed “posthypnotic amnesia” (PHA; Kihlstrom, 1997). PHA is hence a retrieval rather than storage deficit and resembles psychogenic or functional amnesia, for which it has been proposed to serve as a model (Kihlstrom, 1997; Barnier, 2002). PHA is believed to affect mostly information that is taxed in explicit memory tests (Kihlstrom, 1997).

That PHA can be induced and relieved under controlled conditions in a laboratory setting renders it an appealing model for investigating brain mechanisms of memory suppression, which are expected to control the transient retrieval block in functional amnesia. In this study, we subject high-hypnotic-susceptibility and low-hypnotic-susceptibility individuals to a controlled situation that permits them to encode real-life-like episodic memory. This is done by the presentation of a narrative documentary movie (Furman et al., 2007). A week later, we place the participants in the fMRI scanner, hypnotize them, and induce PHA. This is followed by testing the memory for details in the movie or details in the context in which the movie was shown, while brain fMRI signals are acquired (Figure 1). Memory performance is tested twice: once when the posthypnotic suggestion is active and once after it has been relieved by the reversibility cue. This allows acquisition of brain activity maps in and after memory suppression and comparison of brain activations in recall of target and context items in high-hypnotic-susceptibility individuals and in their low-susceptibility controls. Our study identifies large-scale neural circuits that are suppressed compared to baseline activity during suppression of memory performance. In addition, we show that left occipital and temporal cortices are suppressed preferentially, whereas the left rostralateral prefrontal cortex is activated preferentially when the memory performance is suppressed. We also demonstrate that in the high-susceptibility subjects, a network of brain regions shows recovery from suppression following the reversal of the posthypnotic suggestion. We propose that, whereas some of the regions identified in our study play a role in retrieval of long-term episodic memory, others are involved in inhibiting retrieval, possibly in a preretrieval monitoring stage.

**Figure 1. Experimental Design**

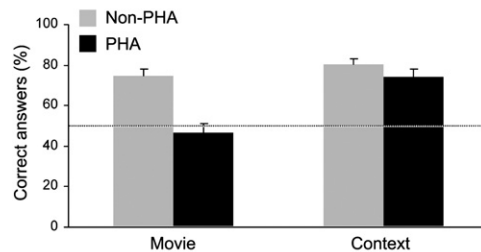
(A) Snapshots from the 45 min documentary movie presented in the *STUDY* session. (B) In the *TEST* session, performed a week later, all of the participants underwent hypnosis, during which they received a suggestion to forget upon termination of hypnosis the movie details seen in the *STUDY*, until they received a reversal cue that cancelled the suggestion. After termination of hypnosis, while under the posthypnotic suggestion (*Test 1*) and following cancellation of suggestion (*Test 2*), the participants were scanned while performing a computerized retrieval test that taxed memory for both movie details (*Movie*) and for the contextual details of the study session (*Context*). For further details, see *Experimental Procedures*.

**RESULTS**

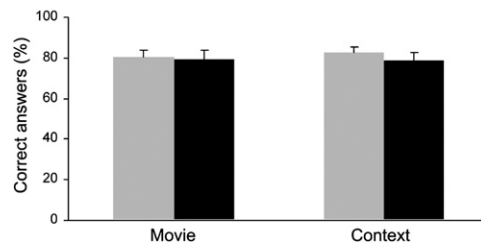
**Behavioral Performance  
Memory Performance**

Under the influence of the *FORGET* suggestion, the PHA group exhibited markedly reduced memory performance on *Movie* questions compared to the *Non-PHA* group (Figure 2A)

**A Memory performance: Test 1 - Suggestion**



**B Memory performance: Test 2 - No Suggestion**



**Figure 2. Memory Performance in the TEST Session**

(A) Performance of *PHA* (black) and *Non-PHA* (gray) groups on *Movie* (left bars) and *Context* (right bars) during *Test 1*. A mixed-model ANOVA analysis, using memory type as a within-subject factor and group as a between-subject factor revealed a significant interaction, with reduced performance for *PHA* subjects in *Movie* but not in *Context* ( $F_{1,22} = 20.38, p < 0.0005$ ). (B) Performance of *PHA* (black) and *Non-PHA* (gray) groups, on *Movie* (left bars) and *Context* (right bars) during *Test 2*. No effects were revealed in a mixed-model ANOVA. Dashed line indicates chance level performance. Error bars are SEM.

(46.6%  $\pm$  4.2% and 74.8%  $\pm$  3.3%, respectively,  $p < 0.00005$ ). No such difference was shown for *Context* (74.2%  $\pm$  4.2% and 82.9%  $\pm$  2.3%, respectively,  $p = 0.21$ ; interaction effect:  $F_{1,22} = 20.38$ ,  $p < 0.0005$ ). In contrast, after cancellation of *FORGET*, memory performance was similar in both groups and on both question types (*Movie*: *Non-PHA* = 80.42%  $\pm$  1.71%, *PHA* = 79.6%  $\pm$  2.44%; *Context*: *Non-PHA* = 82.9%  $\pm$  2.34%, *PHA* = 78.75%  $\pm$  3.9%; interaction effect:  $F_{1,22} = 0.66$ ,  $p = 0.42$ ). Thus, the memory block induced by *FORGET* was specific to movie details and reversible.

In order to examine whether the decreased memory performance in the *PHA* group was a result of demand characteristics (i.e., deliberately withholding the correct responses for movie details to comply with perceived test demands), the *SHAM* group replicated the experiment. Briefly, *SHAM* went through the study and test session in the same manner as did the other groups; however, prior to hypnosis, they received instructions to answer the questions during memory *Test 1* (i.e., under active posthypnotic suggestion) as if they were affected by the posthypnotic suggestion. They were not, however, instructed in any way what strategy to use in order to mimic the amnesic effect. Memory performance during *FORGET* for both *Movie* and *Context* in *SHAM* was lower than the *PHA* and *Non-PHA* (*Movie*: 33.06%  $\pm$  5.1%, *Context*: 59.4%  $\pm$  5.9%; between-subject main effect:  $F_{2,30} = 14.8$ ,  $p < 0.00005$ ). Complementary, Scheffe post hoc comparisons of the group factor across question types revealed significant differences among all groups, demonstrating a general reduced memory performance in the *SHAM* group compared to both *Non-PHA* ( $p < 0.00005$ ) and *PHA* groups ( $p < 0.05$ ). Upon cancellation of suggestion, memory performance was found to be similar to the other groups in both *Movie* and *Context* conditions (81.6%  $\pm$  2.1% and 76.1%  $\pm$  2.7%, respectively,  $F_{2,30} = 1.2$ ,  $p = 0.31$ ). Hence, *SHAM* showed significantly reduced memory performance in *Test 1* compared to the *PHA* group; whereas the *PHA* group performed at a chance level (46.6%  $\pm$  4.2%), memory performance in the *SHAM* group dropped well below the chance level (33.1%  $\pm$  5.1%), suggesting deliberate withholding of information.

### Reaction Times

In *Test 1*, the *PHA* group exhibited increased reaction times on *Movie* questions compared to the *Non-PHA* group (4473  $\pm$  257 versus 3879  $\pm$  152 ms, respectively). Increased reaction times in the *PHA* group were observed for *Context* as well (3768  $\pm$  212 versus 3260  $\pm$  131 ms), resulting in a main effect for group across question types ( $F_{1,22} = 4.7$ ,  $p = 0.04$ ). In contrast, after reversal of *FORGET* (*Test 2*), reaction times did not differ for both groups in *Movie* (*Non-PHA* = 2962  $\pm$  145 ms, *PHA* = 2803  $\pm$  183 ms) and *Context* (*Non-PHA* = 2567  $\pm$  122 ms, *PHA* = 2416  $\pm$  166 ms). In both *Test* phases, main effects were found for question type, exhibiting longer latencies for *Movie* questions than *Context* questions (question type main effects: *Test 1*:  $F_{1,22} = 40.4$ ,  $p = 0.000002$ ; *Test 2*:  $F_{1,22} = 26.9$ ,  $p = 0.00003$ ).

### Brain Activity

We set out to identify the neural correlates of suppressed memory performance that is postulated to be guided by the posthypnotic *FORGET* suggestion, by using whole-brain corre-

lation analysis across groups, as well as inter- and intragroup analysis of BOLD signal (for the flowchart of analysis, see Figure S1 available online).

### Overall Task-Related Brain Activity

Overall brain activity during *Test 1 Movie* compared to fixation baseline was obtained in each group separately in order to identify brain areas that participated in task processing. The *Non-PHA* group exhibited a vast network of activated regions correlated with answering the questionnaire for *Movie* questions (Figure 3A, top panel; Table S1). These included mainly visual processing regions, bilateral thalamus, basal ganglia, bilateral superior frontal gyrus (SFG), and cerebellum. In contrast, the *PHA* group exhibited activity only in a minor subset of these regions, namely bilateral occipital lobes, right SFG, cerebellum, and insula (Figure 3A, bottom panel; Table S1). The reduced overall activity in the *PHA* group suggests a general reduction in neural activity compared to *Non-PHA* while answering *Test 1 Movie* questions, i.e., under *FORGET* condition. To examine whether the reduced activity in the *PHA* group represented a generalized suppression phenomenon throughout the experiment, activity was also determined while answering *Context* questions versus baseline for each group. In contrast to *Movie* questions, the overall activity during *Context* questions versus baseline revealed in both groups several overlapping networks of activity, including visual sensory and perceptual regions, cerebellum, parietal lobes, SFG, and IFG (Figure 3B; Table S2). The fact that both groups showed activity in these regions indicates that the overall neural suppression in the *PHA* group was selective for the *Movie* information. We complemented this analysis by performing conjunction analyses between *PHA* and *Non-PHA* groups for *Movie* and for *Context* questions during *FORGET*. In line with the aforementioned results, smaller overlap of activation was found in *Movie* compared to that in *Context* (Figure S2).

### Whole-Brain Correlation between Brain Activity and Memory Performance

We correlated memory performance scores for *Movie* and beta values of the all-participant GLM during *Test 1*. Using a voxel-by-voxel whole-brain correlation analysis of memory performance and beta values of movie in *Test 1* in all subjects ( $r > 0.55$ ,  $p < 0.01$ , uncorrected), we revealed activity in several regions (Figure 4; Table S3). The highest correlations were found in left middle temporal gyrus ( $x, y, z$  peak activity location  $-55, -7, -16$ , BA 21,  $r = 0.64$ ,  $p = 0.001$ ), left superior temporal gyrus ( $-54, 14, -8$ , BA 38,  $r = 0.62$ ,  $p = 0.002$ ), and left middle occipital gyrus ( $-45, -76, -8$ , BA 19,  $r = 0.65$ ,  $p = 0.001$ ). Activity patterns exhibited a left occipito-temporal hemisphere network that was activated proportionally to the retrieval success of *Movie*. Direct correlation between the mean beta values of these regions and memory performance were plotted (Figure 4B). Thus, it seems that the ROIs delineated by this analysis specifically show an activity gradient that is proportionate to retrieval success.

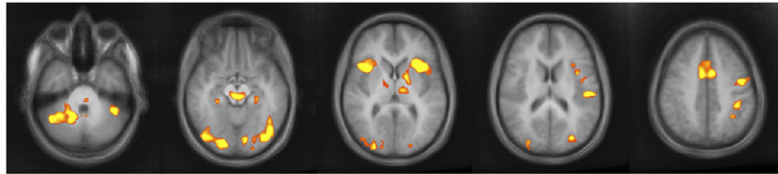
### Between-Group Comparison

We compared brain activity between *PHA* and *Non-PHA* subjects during retrieval of movie details in *Test 1* using a GLM consisting of all participants. As depicted in Figure 5A (see also Table 1), *Non-PHA* had higher activity compared to *PHA* in several regions, including right fusiform area (54,  $-22, -23$ ,

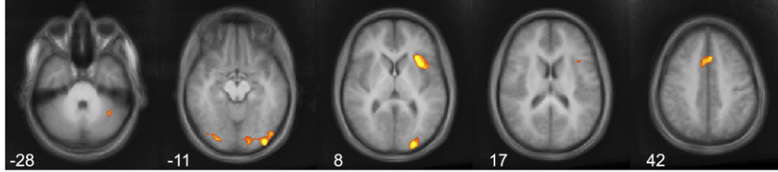


**A Movie questions**

Non-PHA

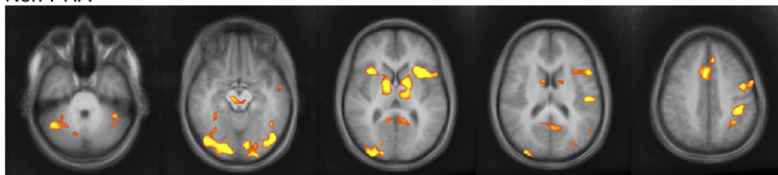


PHA

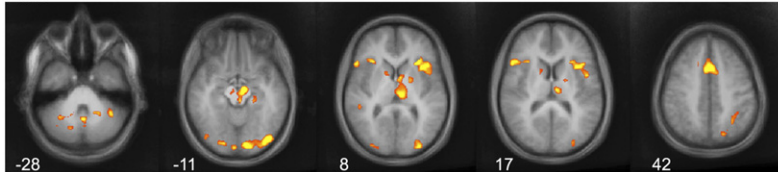


**B Context questions**

Non-PHA



PHA



BA 20), left middle occipital gyrus ( $-21, -85, -5$ , BA 18), and left anterior superior temporal gyrus ( $-48, 11, -5$ , BA 22). Higher activity in PHA was observed in one location only, the left rostrolateral PFC ( $30, 56, 6$ , middle frontal gyrus, BA 10). This is in line with the whole-brain correlation unveiling differential activation in the left occipito-temporal hemisphere (see above). ROI analysis of correlations between cluster-average beta values from *Movie, Test 1* and memory performance for all participants during *Movie, Test 1* was performed, revealing the following correlations (Figure 5C): right fusiform gyrus,  $r = 0.48$  ( $p = 0.02$ ); left middle occipital gyrus,  $r = 0.37$  ( $p = 0.09$ ); left inferior frontal gyrus,  $r = 0.53$  ( $p = 0.01$ ); left rostrolateral PFC,  $r = -0.39$  ( $p = 0.07$ ).

**Intra-Group Comparisons**

To examine the neural dynamics in BOLD signal between *Test 1* and *Test 2* in each group, we compared *Movie* in *Test 1* versus *Test 2*, and *Test 2* versus *Test 1* for each group separately. We hypothesized that suppression of memory observed for *Movie* questions during *Test 1* would be accompanied by reduced activity in the PHA group, as compared to the activity following alleviation of amnesic suggestion. Indeed, in the PHA group, higher activation patterns were observed only for *Test 2* compared to *Test 1*, while no activity was revealed for *Test 1* compared to *Test 2* (Table 2 and Figure 6). The clusters that showed the highest correlations with memory performance in a subsequent ROI analysis are delineated in Figure 6B and are found around the right fusiform area ( $27, -75, -11$ , BA 19), left middle occipital gyrus ( $33, -82, 4$ , BA 18), and left middle frontal gyrus

**Figure 3. Brain Activity on Movie Questions and Context Questions in Each Group**

(A) BOLD response during *Movie, Test 1* in Non-PHA (top panel) and PHA (bottom panel) groups. Statistical maps (radiological orientation) are shown for *Movie > baseline* and are overlaid on axial slices of the average anatomical scan of all subjects (z coordinates indicated for each image). Maps here and in (B) below were obtained with a threshold of  $t > 6$ ,  $p < 0.0001$ , cluster size  $> 150 \text{ mm}^3$ . Activity in the Non-PHA group is shown in multiple regions, including bilateral cerebellum, occipital lobes (BA 18), insula/inferior frontal gyrus (IFG) (BA 13/45), medial superior frontal gyrus (BA 6), and precentral gyrus (BA 4). The PHA group shows reduced activation; activity is in cerebellum, bilateral occipital lobes (BA 18), left insula/IFG (BA 13/45), and medial superior frontal gyrus (BA 6).

(B) BOLD response during *Test 1, Context > baseline* for Non-PHA (top panel) and PHA (bottom panel) groups.

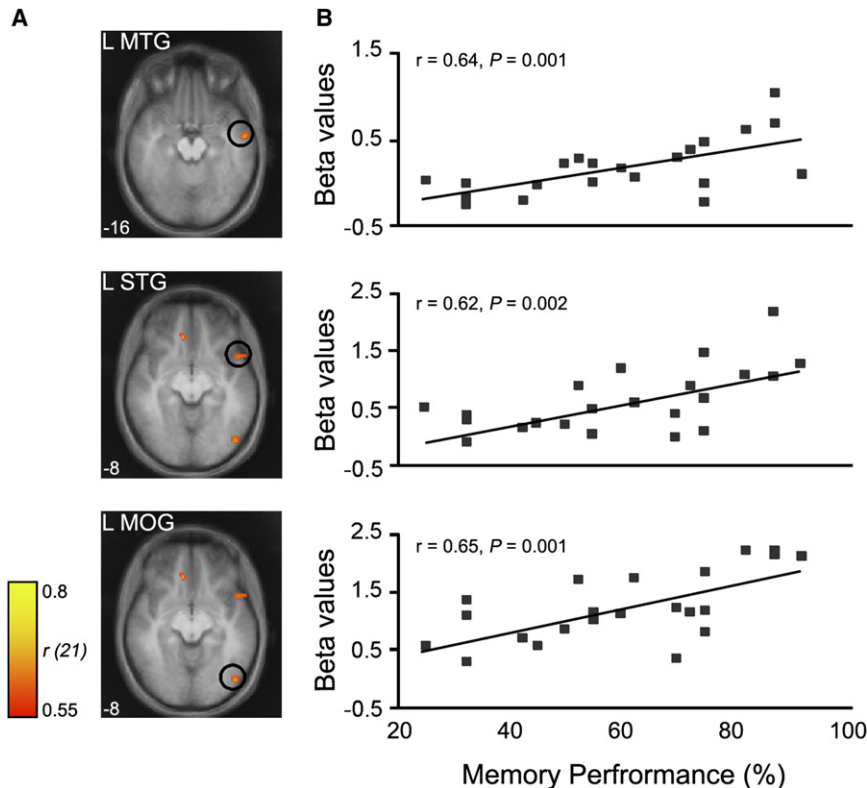
( $51, 32, 28$ , BA 46). For the aforementioned ROIs, beta values of *Movie* from both groups were analyzed in an ANOVA that included group (PHA, Non-PHA) and test (*Test 1, Test 2*) as factors. Interaction effects were found in all ROIs, stemming from elevated activation in the PHA group in *Test 2* compared to *Test 1*, whereas Non-PHA estimates were unchanged

between the scans (interaction effects of ROIs:  $F_{1,20}, p = 5.9, 0.025; 4.6, 0.04; 16.5, 0.0005$ , respectively; Figure 6B, right panels). It is noteworthy that with the threshold used, no clusters were found to show higher activity in *Test 1* compared to *Test 2*. Apparently, although PHA subjects were engaged in the same retrieval task for the second time, they showed exclusively higher activity patterns during the second retrieval, i.e., following alleviation of the amnesic suggestion.

In the Non-PHA group, the comparison between *Test 1* and *Test 2* revealed higher activity for *Test 1* in left parahippocampal gyrus ( $-24, -12, -14$ ), left superior frontal gyrus in two locations ( $-3, 26, 49$ , BA 8;  $-9, 8, 61$ , BA 6), and left medial frontal gyrus ( $-9, 50, 16$ , BA 10). Beta score ROI analysis of the delineated regions revealed interaction effects, resulting from decreased activity for the Non-PHA group during *Test 2* compared to *Test 1*, whereas no such decrease was revealed in the PHA group (interaction effects of ROIs:  $F_{1,20}, p = 7.8, 0.01; 8.8, 0.007; 5.8, 0.025$ , respectively; Figure 6A and Table 2). The opposite activity pattern (i.e., *Test 2 > Test 1*) was revealed as well in several regions (Table 2), although not in the same areas as in the PHA group.

**DISCUSSION**

We used posthypnotic amnesia (PHA) to investigate brain correlates of episodic memory suppression. In brief, our results show that (1) PHA of long-term, real-life-like memories is evident in



**Figure 4. Correlation of Memory Performance and BOLD Signal**

(A) Correlation maps overlaid on an average anatomical brain for all subject ( $n = 22$ ) between memory performance (percentage of correct answers) and beta values for *Movie* during *Test 1*. Clusters are shown in axial slices, circling regions of interest, from top to bottom: Left middle temporal gyrus, L MTG ( $x, y, z = -55, -7, -16$ ), left superior temporal gyrus, L STG ( $-54, 14, -8$ ), and middle occipital gyrus, L MOG ( $-45, -76, -8$ ). Effects are significant at  $r > 0.55$ ,  $p < 0.01$ , uncorrected, cluster size  $> 150 \text{ mm}^3$ .

(B) Correlation plots between memory performance and beta values of *Test 1, Movie*.

susceptible individuals in a controlled fMRI environment. The decrease in memory performance affects *FORGET*-targeted items while sparing contextual memory. (2) PHA is correlated with reduced activity in multiple brain areas, particularly in the left extrastriate occipital lobe and the left temporal pole. In contrast, increased activation is noticed in left rostrolateral prefrontal cortex. (3) Following reversal of the *FORGET* suggestion and recovery of normal memory performance, increased activity is observed in multiple areas, including occipital, parietal, and dorsolateral frontal regions.

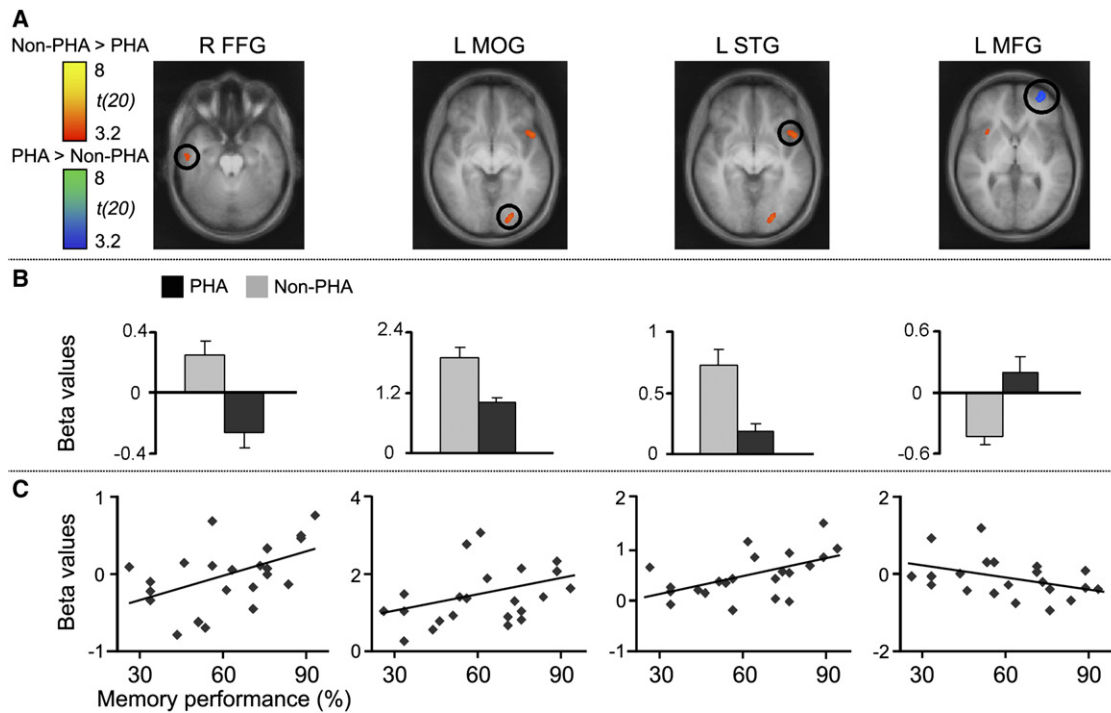
That the *PHA* group exhibited reversible reduction of memory performance under the control of the posthypnotic *FORGET* suggestion is in line with previous reports of reversible retrieval block in PHA. The memoranda targeted to be forgotten in previous studies were typically the hypnosis session itself (Evans, 1988; Kihlstrom, 1997), word lists (Barnier et al., 2001; Bryant et al., 1999; David et al., 2000), or autobiographical events (Barnier, 2002; Cox and Barnier, 2003). To the best of our knowledge, this is the first PHA study to use controlled, extended real-life-like memoranda, encoded well before the hypnosis session.

A potential drawback of hypnosis studies in general and PHA paradigms in particular is the risk of demand characteristics (Hilgard, 1975). It has been argued that the effect observed in PHA merely expresses subjects' wish to comply with the perceived task demands by intentionally withholding information (Coe et al., 1989). We approached this issue by examining a group of low-suggestibility participants, *SHAM*, who were instructed before the hypnosis to simulate PHA. The fact that *SHAM* displayed an exaggerated decrease in memory performance

suggests a strategy different from that used by the *PHA* group, who showed chance-level retrieval performance. Moreover, *SHAM* revealed a reduction in nontargeted memory items as well, implying a generalization of the simulated memory drop. These exaggerated and generalized effects are congruent with *PHA*-simulator results in previous studies (Williamsen et al., 1965; Kihlstrom, 1985), suggesting that the *PHA* cannot be attributed merely to demand characteristics (but see Wagstaff et al., 2001).

The brain regions that display above-baseline activity in the *Non-PHA* group in *Test 1* correspond to regions that were previously reported to subserve declarative retrieval and attention (Cabeza and Nyberg, 2000; Naghavi and Nyberg, 2005). In the same test, only a small subset of regions was activated in the *PHA* group on *Movie* questions. These regions might represent a minimal sensory, cognitive, and motor network required to perform the behavioral task in the scanner. The elevated activity in the brain of the *PHA* participants in comparison to baseline activity on the *Context* questions under the same conditions only highlights the specificity of suppression of performance on the *FORGET*-oriented memory items. It is noteworthy that hippocampus and certain related limbic structures, known to subserve declarative memory encoding and retrieval, did not display above-baseline activation in either of the groups in our analysis. We considered the possibility that this is because these circuits were more active during rest compared with task periods (Stark and Squire, 2001; Svoboda et al., 2006). However, we didn't observe higher hippocampal activation during baseline in comparing baseline to *Movie* (unpublished data). Further analyses using less stringent statistical thresholds and focusing on preselected anatomical ROIs might be required to further determine the role of hippocampus and related limbic circuits, as well as additional brain circuits, in our paradigm.

Correlation of brain activity with memory performance in all the participants, as well as the *PHA-NonPHA* groups comparison, revealed regions associated with the *FORGET* suggestion. Activity in the left middle occipital gyrus was significantly reduced during *FORGET* in the *PHA* group. Furthermore, activity in that



**Figure 5. Between-Group Comparisons on Movie Questions during Test 1**

(A) Between-group statistical maps for *Movie, Test 1* ( $t > 3.2$ ,  $p < 0.005$ , uncorrected, cluster size  $> 150 \text{ mm}^3$ ). BOLD activity is shown in axial slices. Encircled are the right fusiform gyrus, R FFG (54, -22, -23), left middle occipital gyrus, L MOG (-21, -85, -5), left superior temporal gyrus, L STG (-48, 11, -5), and left middle frontal gyrus, L MFG (-30, 56, 6; left rostralateral PFC).

(B) Plot of mean beta values for PHA (black) and Non-PHA (gray) for the ROIs depicted in (A). Values of  $t$  and  $p$ , from left to right, respectively: 3.6, 0.001; 3.8, 0.001; 3.9, 0.0007; -3.7, 0.001. Error bars are SEM.

(C) Beta values for *Test 1, Movie* for the respective ROIs correlated with memory performance for all subjects. Values of  $r$  and  $p$  are, from left to right, respectively: 0.48, 0.02; 0.37, 0.09; 0.53, 0.01; -0.39, 0.07.

area was significantly correlated with memory performance. Occipital activation is commonly detected in retrieval of nonverbal material (Cabeza and Nyberg, 2000). Theory and data both point to reactivation or reconstruction in retrieval of types of

**Table 1. Regions Showing Differences between Non-PHA and PHA in Test 1**

Non-PHA > PHA						
Region	x	y	z	$\text{mm}^3$	t Value	p Value
L middle occipital gyrus (BA 18)	-21	-85	-5	245	4.32	0.0003
R fusiform gyrus (BA 20)	54	-22	-23	382	5.48	0.00002
L superior temporal gyrus (BA 22)	-48	11	-5	719	4.42	0.0002
L postcentral gyrus (BA 3)	-39	-22	52	512	3.9	0.0008
R claustrum	33	14	4	342	4.02	0.0006
PHA > Non-PHA						
L middle frontal gyrus (BA 10) <sup>a</sup>	-30	56	6	678	3.43	0.002

<sup>a</sup> This area is referred to in the text as L rostralateral PFC.

representations that were active in encoding (e.g., Morris et al., 1977; Tulving, 1983; Polyn et al., 2005; Johnson and Rugg, 2007). For example, Johnson and Rugg (2007) report that recollection of scenes but not verbal information activates occipital regions that were activated in encoding of that specific stimuli type. Similarly, Vaidya et al. (2002) show that the middle occipital gyrus is activated in recognition of words that served as cues for encoded pictures but not for other words. It is therefore plausible to assume that reduced activity in middle occipital gyrus during *FORGET* represents suppressed reinstatement of memory scene traces.

The left temporal pole (BA 38 and anterior BA 22) showed similar activity patterns to those of the occipital lobe, both in correlations of brain activation with memory performance and in intergroup comparison of *Movie* questions during *FORGET*. The temporal pole is considered an association cortex based on its connectivity with multiple sensory systems and its activity in response to both visual and auditory stimuli (Olson et al., 2007). It was implicated in emotional and social processing, theory of mind, real-life memory, and formation of narratives from spoken sentences (Maguire et al., 1999; Maguire and Mummery, 1999; Graham et al., 2003; Gallagher and Frith, 2004; Olson et al., 2007). It fits hence to subservise retrieval of the socially and narrative-embedded audiovisual information

**Table 2. Regions Showing Intragroup Differences between Tests**

Non-PHA: Test 1 > Test 2						
Region	x	y	z	mm <sup>3</sup>	t Value	p Value
L parahippocampal gyrus	-24	-12	-14	1077	5.36	0.0003
L middle frontal gyrus (BA 10)	-9	50	16	365	4.55	0.001
L superior frontal gyrus (BA 8)	-3	26	49	346	4.74	0.0007
L superior frontal gyrus (BA 6)	-9	8	61	422	4.85	0.0006
Non-PHA: Test 2 > Test 1						
R inferior occipital gyrus (BA 18)	30	-91	-14	188	4.93	0.0005
R lingual gyrus (BA 18)	24	-91	-2	156	4.39	0.001
R precuneus (BA 7)	9	-70	37	349	6.44	0.00007
L precuneus (BA 7)	-9	-70	40	301	4.64	0.0009
R superior frontal gyrus (BA 9)	36	53	31	254	4.74	0.0007
L white matter	-30	-43	7	741	5.94	0.0001
PHA: Test 2 > Test 1						
R middle occipital gyrus (BA 18)	33	-82	4	861	6.05	0.0001
L middle occipital gyrus (BA 18)	-27	-82	7	316	4.95	0.0005
R fusiform gyrus (BA 19)	27	-75	-11	1848	3.67	0.004
L cuneus (BA 23)	-12	-70	10	184	4.57	0.001
R inferior parietal lobule (BA 39)	33	-58	40	877	5.95	0.0001
R precuneus (BA 7)	24	-76	46	499	5.22	0.0003
R middle frontal gyrus (BA 46)	51	32	28	432	5.12	0.0004
L middle frontal gyrus (BA 6)	-33	-1	46	263	5.45	0.0002
L superior frontal gyrus (BA 8)	-12	44	55	246	5.78	0.0001
R cerebellum	6	-67	-35	694	4.3	0.001
L brainstem	-3	-28	-5	316	5.79	0.0001

encoded during movie viewing. Indeed, in a recent study of subsequent memory for movie, activations were found in the right temporal pole during encoding of subsequently remembered items (Hasson et al., 2008).

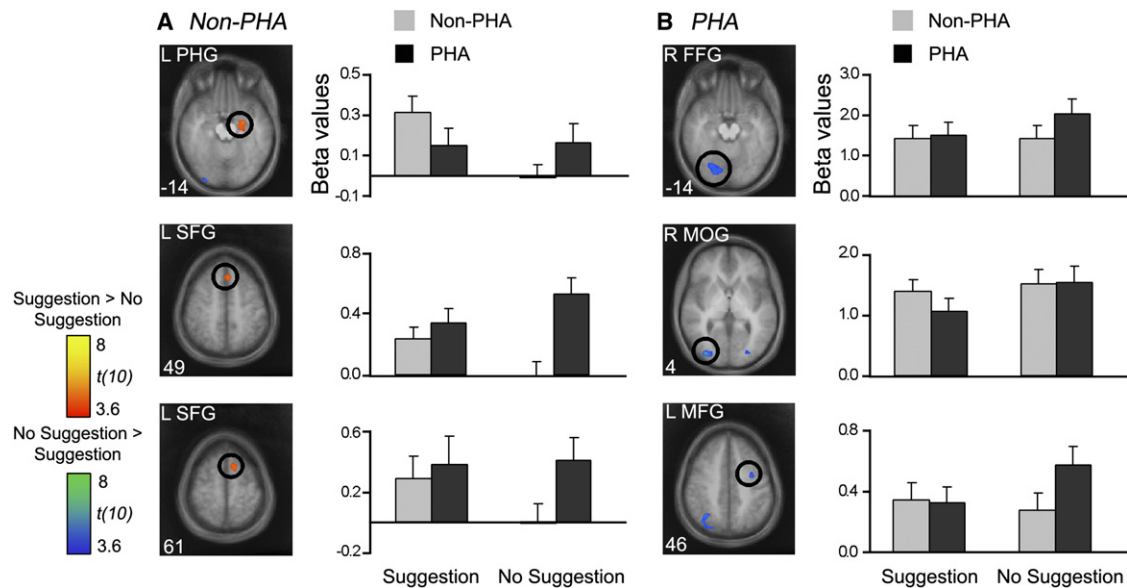
In contrast to the aforementioned regions, the left rostralateral prefrontal cortex (PFC), displayed preferential activity during suppression of memory performance. The engagement of PFC in retrieval of declarative long-term memory is proposed to be associated with content-invariant retrieval mode rather than with content-specific ephory (Lepage et al., 2000). The rostralateral PFC has been specifically implicated in meta-processes and executive functions engaged in retrieval of episodic memory (Nyberg et al., 2000; Gilbert et al., 2006; Moscovitch and Winocur, 2002). Burgess et al. (2007) propose that rostral PFC is a “gateway” linking the outside and inside world, switching

attention between environmental stimuli and self-generated representations. We suggest that the increased activation of rostralateral PFC in the PHA group during FORGET reflects an early implicit decision on whether or not to trigger further retrieval processes, taken on the basis of the correspondence of the external cue to the internal representation of the FORGET suggestion. We propose to dub the stage in which this early decision is taken as “preretrieval monitoring,” because the initiation of the retrieval cascade might be abated.

The possibility could be raised that activation of rostralateral PFC in memory suppression on *Movie* in PHA under FORGET reflects increased retrieval effort. The identity of brain substrates of retrieval effort has yet to be clarified (Rugg and Wilding, 2000), and though some studies did suggest BA 10 to be involved (Schacter et al., 1996), others specifically implicate other PFC regions (Buckner et al., 1998; Heckers et al., 1998; Sohn et al., 2003). We have attempted to tap into potential substrates of retrieval effort in our protocol by postulating that in the control subjects, the longer the RT on a task, the more effortful the retrieval (Buckner et al., 1998). We hence contrasted brain activity for incorrect (longer RT) and correct (shorter RT) answers in Non-PHA on *Movie* in Test 1, and identified activation in left superior frontal and right medial frontal gyri (BA 9), but not in rostralateral PFC (Figure S3). Taken together, we therefore deem less likely the possibility that rostralateral PFC activation in our study reflects increased retrieval effort rather than prereretrieval monitoring. Brain imaging methods with higher temporal resolution, i.e., EEG and MEG, might be useful in clarifying this issue further.

The differences in brain activity patterns between Test 1 (i.e., FORGET) and Test 2 (i.e., FORGET Reversed) were dissimilar for each of the groups. Whereas Non-PHA participants showed both reduction and enhancement of activity following FORGET cancellation, PHA showed practically only enhancement following FORGET cancellation. This enhancement in Test 2 contrasts with the widely reported phenomenon of repetition suppression in subsequent tests (e.g., Henson and Rugg, 2003; Schacter and Buckner, 1998). That repetition suppression effects were not observed for the PHA group in Test 2 is in line with the suppression observed in this group during Test 1. The brain regions that were activated preferentially upon reversal of the FORGET suggestion reveal a network of regions that has been documented in the literature in long-term memory retrieval (Svoboda et al., 2006; Yancey and Phelps, 2001; Cabeza and Nyberg, 2000). The areas in which recovery of activation was observed in Test 2 for PHA complement the areas in which activity was suppressed, in comparison with Non-PHA, in Test 1. The paralleled recovery of brain activity and memory performance strongly suggests that suppression was exerted at early stages of the retrieval process, thus preventing the activation of regions that are crucial for productive retrieval. This hence is congruent with our aforementioned proposal that PHA under FORGET affects an executive prereretrieval monitoring process, which produces an early decision on whether to proceed or not on retrieval, and in case of a *Movie* question, aborts the process. Such prereretrieval implicit pondering could be in line with, though clearly not proven by, the prolonged reaction times on both FORGET-targeted and untargeted items in the PHA group.





**Figure 6. Within Group Comparison on Movie questions in Test 1 versus Test 2**

(A) Statistical maps depicting voxels different between *Test 1, Movie* and *Test 2, Movie* in *Non-PHA*. Maps here and below were obtained with a threshold of  $t > 3.6$ ,  $p < 0.005$ , uncorrected, cluster size  $> 150 \text{ mm}^3$ . Encircled are the left parahippocampal gyrus, L PHG (-24, -12, -14), and left superior frontal gyrus, L SFG (BA 8, -3, 26, 49, and BA 6, -9, 8, 61). The corresponding beta values for *Test 1, Movie* (left pair of bars) and *Test 2* (right pair of bars) are plotted for *Non-PHA* (gray) and *PHA* (black).

(B) Maps of voxels different between *Test 1, Movie* and *Test 2, Movie* in *PHA*. Encircled are the right fusiform area, R FFG (BA 19, 27, -75, -11), right middle occipital gyrus, R MOG (BA 18, 33, -82, 4), and left middle frontal gyrus, L MFG (BA 6, -33, -1, 46). The corresponding beta values for *Test 1, Movie* (left pair of bars) and *Test 2* (right pair bars) are plotted for *Non-PHA* (gray) and *PHA* (black).

Error bars are SEM.

The postulated preretrieval monitoring is a top-down process. Top-down mechanisms, which enable the allocation of attention to relevant stimuli while ignoring irrelevant ones (Gazzaley et al., 2005), have been proposed to play a key role in behavioral manifestations of hypnosis that involve suppression or modulation of sensory input (Raz et al., 2006). In the present paradigm, bottom-up sensory input is held constant in both *Test 1* and 2 and only task demands are altered. Hence, even if only task constraints are taken as a guide, interpretation of the etiology of the memory suppression in terms of top-down modulation is indeed reasonable.

How do our findings correspond to previous data on memory suppression? It should be stated at the outset of this comparison that the term “suppression” is used in the literature in different connotations, ranging from suppression that is assumed to occur during ongoing normal retrieval, to suppression of unwanted memories as construed within the conceptual framework of psychiatry, to assumed suppression of proper retrieval in certain mnemonic pathologies. Sometimes it is equated or paralleled with the broad usage of “inhibition” in memory research (Roediger et al., 2007). Hence, one should note the conceptual framework that is explicitly or implicitly used in attempts to identify brain substrates of memory suppression. Furthermore, particularly pertinent to comparison among studies of different manifestations of suppression is the question at which time in the retrieval process memory is assumed to become suppressed. Retrieval is a multistage process (Rugg and Wilding, 2000; Sakai, 2003; Gardiner, 2007). As noted above, we

propose, on the bases of our data, that PHA abates a very early stage. This probably differs from some other paradigms of memory suppression.

Influential experimental paradigms have been developed to investigate memory inhibition and suppression. In *retrieval-induced forgetting*, retrieving exemplars from a set of learned items in a category was shown to inhibit retrieval of other, non-practiced exemplars (Anderson et al., 1994). In the *think/no think* paradigm, cueing to intentionally reject thinking about a paired associate was shown to ultimately suppress retrieval of that specific association (Anderson and Green, 2001, but see Bulevich et al., 2006). Neuroimaging studies using the *think/no think* paradigm implicate in memory suppression activation of regions in the dorsolateral prefrontal cortex (DLPFC) and attenuation of hippocampal activation (Anderson et al., 2004). Two procedural attributes of the *think/no think* paradigm should be particularly noted. First, participants are well trained, and second, suppression is exerted on memory immediately after the study phase. This should place high demands on working memory, hence the activation of PFC. In contrast, in our paradigm, complex memory items are taxed a week after their encoding. This is expected to tax working memory less.

Memory suppression has been also proposed to dominate certain pathologies in which the suppression mechanisms may not necessarily mimic or exacerbate suppression that occurs in normal retrieval. Such a pathology, by definition, is psychogenic or functional amnesia (Markowitsch, 1999). PHA has been specifically suggested as an experimental model for



functional amnesia (Barnier, 2002). Neuroimaging studies of functional amnesia are rare. PET studies have indicated both reduction (Markowitsch, 2003) and enhancement (Yasuno et al., 2000; Fink et al., 1996) in fronto-temporal regions when tested for recollection of apparently forgotten memory. In an fMRI study of a person suffering from functional amnesia for his native language and autobiographical memories, reduced frontal activity compared to controls was unveiled on working memory and lexical tasks involving the native language (Glisky et al., 2004). Although our data point to altered activity in fronto-temporal regions as well, additional combined neuropsychological and functional neuroimaging research is needed to delineate the role of identified brain circuits in functional amnesia that presents in the clinic. We postulate, however, that other forms of functional amnesia may also be a consequence of retrieval abortion at a preretrieval monitoring stage and, therefore, may indeed be modeled at least partially by PHA.

All in all, our data identify brain circuits that subserve suppression of retrieval of long-term memory of a real-life-like extended episode in the course of posthypnotic *FORGET* suggestion. Some of these regions are likely to play a role in normal retrieval. Others are likely to be engaged in dysfunctions that involve an executive decision to abort subsequent retrieval.

## EXPERIMENTAL PROCEDURES

### Participants

One hundred and thirty-seven volunteers were recruited from the Weizmann Institute of Science and the Faculty of Agriculture of the Hebrew University, Rehovot. The experimental protocol was approved by the Institutional Review Board (IRB) of the Sourasky Medical Center, Tel-Aviv, at which the fMRI scanning was carried out, and approval of the use of hypnosis was given by the Division of Medical Professions, Ministry of Health, Jerusalem. All the participants were native Hebrew speakers. They were given the hypnosis susceptibility test in groups (see below). Of these, 46 individuals who passed the predefined hypnotizability criterion were examined individually for their capacity to sustain posthypnotic amnesia (see below). On the basis of the posthypnotic test score, subjects were labeled as susceptible to posthypnotic amnesia (*PHA*) or not susceptible (*Non-PHA*). Ultimately, 25 individuals ( $25.8 \pm 2.3$  years, 17 female, 12 *PHA*) proceeded to participate in the experiment. Twenty-three performed the experiment in the MRI scanner (11 *PHA*) and two (1 *PHA*) were not tested in the scanner because of metal teeth braces and carried out the experiment outside the scanner. One subject from the *Non-PHA* group was later excluded from the analysis due to reading disabilities. In addition, nine subjects from the original volunteer pool who did not pass the hypnotizability criterion served as a *PHA SHAM* group and performed the experiment outside the scanner.

### Screening for PHA Susceptibility

Groups of 5 to 20 volunteers were presented with a 40 min lecture on the nature of hypnosis, given by a certified M.D., who later performed the hypnosis procedure (Y.C.). Following the lecture, subjects underwent a 15 min hypnotic assessment procedure, using standard relaxation techniques for hypnosis induction followed by five hypnotic suggestions adopted from the Stanford Hypnotic Susceptibility scale (Weitzenhoffer and Hilgard, 1962; Lichtenberg et al., 2004) and the Hypnosis Induction Profile (HIP; Spiegel and Spiegel, 2004). The hypnotic suggestions included arm levitation (item E, HIP), arm immobilization (item 8, Stanford scale), somatosensory mosquito hallucination, auditory mosquito hallucination, and visual mosquito hallucination (based on item 3, Stanford scale). Volunteers who exhibited successful performance on a minimum of three suggestions proceeded to undergo individual PHA screening.

In the individual PHA screening, each participant was instructed to read a short story thoroughly. Next, the participants were induced into a hypnotic state, using relaxation techniques, in the same manner as in the group session. Approaching the dehypnotization stage of the hypnotic procedure (i.e., termination of hypnotic state), approximately 20 min after reading the story, a suggestion to forget the story details was conveyed by the hypnotist, along with a reversibility cue, designed to cancel in due time the forgetting suggestion (see Supplemental Data). Following complete dehypnotization of the hypnotic state, a short memory pen-and-paper questionnaire was administered, containing 13 yes/no questions regarding the story. Upon completion of the questionnaire, the reversibility cue was provided, followed by administration of the same questionnaire again. The number of changed answers from the first to the second test was summed up for each participant, and the median score was then used to classify subjects as posthypnotic amnesia (PHA) subjects or Non-PHA subjects.

### Experimental Protocol

The protocol included a *STUDY* session and a *TEST* session. The *STUDY* was performed out of the magnet and the *TEST* in the magnet. The manipulation of memory by hypnosis was performed in the *TEST*.

### STUDY Session

The study material was a 45 min movie, produced and filmed in-house specifically to serve in real-life-like memory studies. The movie was a documentary depicting a routine day in the life of a young Israeli woman. It depicted both mundane activities such as preparing meals and talking on the phone, along with potentially more interesting events, such as rehearsing for a play, teaching a drama class, and riding rollerblades with friends (Figure 1A). The movie was viewed in a quiet room on a standard 17 inch computer monitor, with sound delivered through a headphone set. Participants were given written instructions that they were about to watch a 45 min movie and that their only task is to try to concentrate throughout. They were not specifically instructed to remember the movie details, and were not told they were going to be tested.

### TEST Session

Based on a prior study from our lab on long-term memory of cinematic material (Furman et al., 2007), showing high memory performance a week after learning, retrieval was assessed 1 week after viewing the movie. Prior to scanning, the participants signed informed consent and MRI safety forms.

After entering the scanner, participants lay passively in the absence of scanning and were induced into a hypnotic state through instructions conveyed by the hypnotist via the magnet's headset system. The induction into the hypnotic state lasted approximately 10 min and was performed by standard relaxation techniques. Toward the dehypnotization of the subject from the hypnotic state, the hypnotist presented the *FORGET* suggestion, which conveyed the instruction to forget the movie viewed during the study session, and a reversibility cue, intended to reverse *FORGET* at due time. Participants were then de-induced from the hypnotic state, followed by a memory test, administered while their brain was scanned (Figure 1B; *Test 1, FORGET*). Immediately following *Test 1*, the hypnotist cancelled *FORGET* by administering the reversibility cue, followed by a second scanning of the same memory test consisting of the same questions (*Test 2, FORGET Reversed*). The procedure was performed for participants in both PHA and Non-PHA groups.

The memory test was a computerized questionnaire (delivered on Presentation software, Neurobehavioral Systems, San Francisco, CA, version 10.3). It consisted of 40 questions about items from the movie (*Movie* questions) and 20 questions about contextual details from the *STUDY* session (*Context* questions). *Movie* questions targeted details from the movie itself, e.g., *The actress knocked on her neighbor's door on the way home (YES/NO)*. *Context* questions were designed to serve as a control for memory items that were not suggested to be forgotten posthypnotically, e.g., *During the movie, the door to the room was closed (YES/NO)*. Questions were constructed in the form of short sentences, of which half were true and half false. They were presented for 6 s each, showing simultaneously the question and the YES/NO options on the screen. Once an answer was given, the relevant label on screen (i.e., YES or NO) changed its color from orange to green, thus providing response feedback. After answering the questions, the text remained on screen for the remainder of the trial time (up to 6 s). The trial was completed by a 4–8 s blank event. The blank events included a fixating cross in the center of the screen. Answers and

reaction times were recorded onto a log file, enabling computation of correct response percentage and mean reaction time of each participant.

The experiments were presented on a PC in the magnet console room via an LCD projector, which projected onto a screen behind the subjects. The questions were viewed through a mirror mounted on the head coil, and answers were executed by pressing a four-button digital response box. Each retrieval test lasted 12.5 min. Head pads were placed around the head to reduce head movements, and ear plugs were given to subjects for noise protection.

#### **PHA SHAM Group**

The SHAM group performed the STUDY in the same manner as the other participants, while TEST was performed outside the scanner. In TEST, prior to the beginning of the hypnosis procedure, they were given written instructions (Supplemental Data) explaining that they were a control group in a PHA experiment. Specifically, they were told that they were about to receive a suggestion to forget certain information for a limited time period, until a reversibility cue is provided. In addition, they were instructed to act as if the suggestion affected them, even if that feeling was not genuine. Following the instructions, participants were induced into a hypnotic state and were given the FORGET suggestion as the other groups. Their task was to answer the memory questionnaire in Test 1 as if they were under suggestion, and in Test 2 as if the suggestion was reversed. The memory questionnaires were delivered via a standard PC on a 17 inch screen.

#### **fMRI Acquisition**

Imaging was performed on a 3T GE Signa Horizon echo speed scanner (Milwaukee, WI) with a resonant gradient echoplanar imaging system. All images were acquired using a standard quadrature head coil. The scanning session included anatomical and functional imaging. 3D sequence spoiled gradient (SPGR) echo sequence, with high-resolution 1 mm slice thickness (FOV = 24 × 24, matrix = 256 × 256, TR/TE = 40/9 ms) was acquired for each subject. This anatomical scan allowed for volume statistical analyses of signal changes during the experiment. In addition, T2 and FLAIR weighted scans were acquired as part of the clinical protocol of the imaging facility. For the BOLD scanning, T2\*-weighted images (TR/TE/Flip angle = 2000/40/80, FOV = 20 × 20 cm<sup>2</sup>, matrix size = 64 × 64) were acquired (32 oblique slices, 15° toward coronal plane from ACPG, thickness 4 mm, gap 0 mm, covering the whole cerebrum) in runs of 12,000 images (375 images per slice).

#### **Behavioral Analysis**

Memory performance was calculated separately for each condition type (i.e., *Movie* and *Context*) for each of the two memory tests in the TEST session (i.e., Test 1 and Test 2), by calculating the percentage of correct responses for each participant. Memory performance values were then transformed by using the arc-sine square-root transformation. The transformed scores were analyzed with mixed-model analyses of variance (ANOVAs) for each test separately, with question type (*Movie*, *Context*) as the within-subject factor and group (*PHA*, *Non-PHA*) as the between-subject factor. Reaction times (RT) of answer latency throughout the memory test sessions were analyzed by calculating the mean RT of individual subjects for each question type in each of the tests. Mean RTs were inserted into a mixed-model ANOVA for each test separately in the same manner as for the memory performance scores.

#### **fMRI Analysis**

Preprocessing and data analysis were performed using BrainVoyager QX 1.8 (Brain Innovation, Maastricht, Netherlands). Functional images were corrected for slice timing, head movements, and linear drifts. Low frequencies were filtered out from the data. Images were spatially smoothed using a 6 mm full-width at half-maximum (FWHM) Gaussian kernel. The first seven volumes (14 s) from the beginning of each scan were removed from the data set to allow for signal equilibrium. Functional and anatomical scans were spatially normalized by extrapolation into a 3D volume in Talairach space (Talairach and Tournoux, 1988). Functional scans were superimposed onto the 3D high-resolution SPGR volume set and were interpolated into the same resolution as the SPGR anatomical scans (voxel size: 1 × 1 × 1 mm).

Preprocessed time series data for each individual scan were analyzed with multiple regression. Three General Linear Models (GLM's) were specified to investigate the conditions of interest, generating separate regressors for

each question type (*Movie* questions and *Context* questions) in each scan (Test 1 and Test 2). GLM 1 included subjects from both groups and was used for correlation analysis and intergroup comparisons, while GLM 2 and 3 consisted of separate-group models for testing intragroup effects between Test 1 and Test 2 (Figure S1). Time periods between questions were considered as baseline. Trial lengths were considered as the time between text onset and subjects' response, while the remainder of the event (from answer until completion of 6 s) was defined as a separate condition. The condition time vectors were convolved with a canonical hemodynamic response function (HRF). Six head motion parameters were inserted in the GLM as covariate regressors (three translation and three rotation parameters).

#### **Overall Task-Related Activity**

Activity patterns for *Movie* and *Context* during Test 1 were determined by producing statistical maps for each group separately and for each of the two conditions against the fixation baseline throughout the scan. The statistical maps were thresholded at  $p < 0.0001$ , with a minimum cluster size of 150 mm<sup>3</sup>. The maps for each group were overlaid on the average anatomical brain of the 22 subjects, depicting activity on five axial slices for each group in each condition. The activation loci were collected for each group and were summarized in tables, providing the center of mass Talairach coordinates of each cluster.

#### **Memory-Related Activity**

In order to identify brain regions that are related to memory performance, a whole-brain voxel-by-voxel correlation between percentage of correct answers and BOLD measurements was computed for all the subjects combined. Memory performance score per subject in *Movie* questions in Test 1 was treated as a covariate and was correlated with beta values from GLM 1 (see above) for *Movie* > *Baseline*, Test 1. Thus, an activity map for all participants was obtained, revealing voxels that were significantly correlated with memory performance. The threshold used for obtaining the statistical map was set at  $r > 0.55$ ,  $p < 0.01$ , uncorrected, with cluster size of a minimum of 150 mm<sup>3</sup>. For extracting ROIs that were particularly correlated with behavior, for each cluster, the average beta value for each participant was extracted and correlated with memory performance for the whole group. The three clusters with the highest correlation values were plotted in a graph depicting the relation between memory performance and beta values in those regions (Figure 4B).

#### **Between-Group Comparison**

Statistical maps were generated by performing a random-effects two-sample t test contrast, comparing *Movie* questions in Test 1 between the two groups (using GLM 1, see above). Significance was tested at  $p < 0.005$ , uncorrected, and with cluster size of at least 150 mm<sup>3</sup>. Several of the resulting regions were selected for a region of interest analysis (see Results). For each cluster, the mean beta value across voxels for each subject was calculated for *PHA* and *Non-PHA* groups separately and plotted. Separate t tests were performed on the mean beta values of each ROI between the groups for specific estimation of effect. In addition, mean beta values of *Movie*, Test 1 from the selected ROIs were plotted against Memory performance in *Movie*, Test 1 for all subjects.  $r$  and  $p$  values of each correlation were reported.

#### **Test 1 versus Test 2**

Using the separate GLMs for each group (GLM 2 and 3) with the same conditions as described above, random-effects analysis was carried out for each group, comparing by a one-sample t test *Movie* questions between the two scans (Test 1 > Test 2 and vice versa). Statistical maps were obtained by this contrast, using a threshold of  $p < 0.005$ , uncorrected, with cluster size of at least 150 mm<sup>3</sup>. ROIs were chosen from these maps on the basis of highest correlations between beta value of memory Test 1 minus memory Test 2 (*Movie* condition) and memory performance of each participant. For those regions, mean beta values of *Movie* questions for each group (Test 1, Test 2), were analyzed with mixed-model ANOVAs with test (Test 1, Test 2) as the within-subject factor and group (*PHA*, *Non-PHA*) as the between-subject factor.

#### **Supplemental Data**

The Supplemental Data for this article can be found online at <http://www.neuron.org/cgi/content/full/57/1/159/DC1/>.

## ACKNOWLEDGMENTS

We are grateful to O. Furman, E. Furst, R. Ludmer, M. Moscovitch, U. Nili, S. Rosenbaum, T. Sharot, and G. Winocur for discussions and P. Lichtenberg for the Hebrew version of the Stanford Scale for Hypnotic Susceptibility. This work was supported by grants to Y.D. from The Minerva Foundation and The Nella and Leon Benozio Center for Neurological Diseases.

Received: August 24, 2007

Revised: October 26, 2007

Accepted: November 12, 2007

Published: January 9, 2008

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