Research Report

AROUSAL-MEDIATED MEMORY CONSOLIDATION: Role of the Medial Temporal Lobe in Humans

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Abstract—*Although the influence of emotional arousal on declarative memory has been documented behaviorally, the mechanisms underlying arousal-memory interactions and their representation in the human brain remain uncertain. One route through which arousal achieves its effects on memory performance is by regulating consolidation processes. Animal research has revealed that the amygdala strengthens hippocampal-dependent memory consolidation in a limited time window following participation in an arousing task. To examine whether this integrative function of amygdalo-hippocampal structures extends to the human brain, we tested unilateral-temporal-lobectomy patients on an adaptation of a classic paradigm in which levels of physiological arousal at encoding modulate retention over time. Subjects rated emotionally arousing (taboo) and neutral words on an arousal scale while their skin conductance responses (SCRs) were monitored. Recall for the words was assessed immediately and after a 1-hr delay. Both temporal-lobectomy patients and control subjects generated enhanced SCRs and arousal ratings for the arousing words at the time of encoding. However, only control subjects exhibited an increase in memory for the arousing words over time. This group difference in the effect of arousal on the rate of forgetting suggests that the role of medial temporal lobe structures in memory consolidation for arousing events is conserved across species.*

Emotional arousal has the capacity to modulate memory at several stages of information processing, including stimulus perception, encoding, and retrieval. Psychological studies in humans have demonstrated that arousal critically alters both attentional focus and consolidation of memories (Christianson & Loftus, 1991; Eysenck, 1976; Heuer & Reisberg, 1992; Revelle & Loftus, 1992). If arousal acts specifically on memory consolidation, its influence should magnify following a delay, as consolidation is a process that occurs over time. There is behavioral evidence to suggest that when arousal is manipulated at encoding and recall is probed at multiple retention intervals, material studied under high arousal is retained relatively better after a delay than immediately following encoding (Eysenck, 1976; Heuer & Reisberg, 1992). In a classic method used to unveil this type of mechanism, paired associates to words varying in their emotional content are recalled at several time delays after encoding. Paired associates to high-arousal words typically show greater resistance to forgetting than paired associates to low-arousal words, an interaction that emerges at retention intervals longer than 20 min in duration (Kleinsmith & Kaplan, 1963). The neural substrate mediating this behavioral phenomenon, however, is unknown.

Studies conducted in nonhuman animals implicate the amygdala as a key brain structure that enhances hippocampal-dependent memory formation for arousing events (McGaugh, Introini-Collison, Cahill, Kim, & Liang, 1992; Packard, Cahill, & McGaugh, 1994). The amygdala's mechanism of action involves both direct interconnections with the hippocampus and indirect feedback via the release of hormones in the periphery. To investigate whether this function of the medial temporal lobe extends to the human brain, we tested unilateral-temporal-lobectomy patients on an adaptation of Kleinsmith and Kaplan's (1963) classic arousal memory task. We developed a novel variant to the original task that expanded the number of items to be recalled and tested memory for the studied words themselves rather than single-digit paired associates. We hypothesized that the patients, whose locus of brain damage included the amygdala, hippocampus, and surrounding cortex, would not exhibit forgetting-resistant memory traces for the arousing words. Such a finding would suggest that the integrity of the medial temporal lobe is essential for consolidating declarative memories for arousing stimuli in the human brain.

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METHOD

The patients included in the study underwent a unilateral *en bloc* resection of the anteromedial temporal lobe, including the amygdala, hippocampus, and adjacent cortex, as a surgical treatment for medically intractable epilepsy (Spencer & Spencer, 1985; Spencer, Spencer, Mattson, Williamson, & Novelly, 1984). These patients provide a unique opportunity to examine dysfunction of the amygdalo-hippocampal system in a relatively large, homogeneous subject population without the severe amnesia that results from bilateral damage to the hippocampus (Novelly et al., 1984). Ten left-temporal-lobectomy patients (3 male, 7 female; mean age = 31.1 years, SD = 8.1) and 12 right-temporal-lobectomy patients (5 male, 7 female; mean age = 38.8 years, SD = 7.9) participated in the study. Neuropsychological profiles for these patients have been described previously (LaBar, LeDoux, Spencer, & Phelps, 1995). All the patients were tested between 2 and 8 years postoperatively. Their data were compared with the data from 23 healthy control subjects (9 male, 14 female; mean age = 39.6 years, SD = 8.0) matched for age and level of education. None of the control subjects had a history of brain damage or neurological impairment. All subjects provided informed consent and were paid for their participation.

During encoding, each subject was shown 40 words (20 arousing, 20 neutral) in a random sequence on a computer screen (stimulus duration = 4 s, intertrial interval = 14 ± 2 s). The stimulus words were buffered by 4 additional filler words—2 words presented at the beginning of the sequence and 2 at the end—to reduce serial position effects in free recall. Arousing words consisted of profanities, sexually explicit words, and words depicting social taboos. Neutral words were low- to moderate-frequency words derived from a master list of affective word norms (Bellezza, Greenwald, & Banaji, 1986). Although frequency distributions were not available for most of the arousing words, it is assumed that taboo words are of relatively low frequency of occurrence in language (e.g., Williams & Evans, 1980).

Skin conductance responses (SCRs) to each word were recorded from the third and fourth digits of the subject's nondominant hand and scored according to conventional criteria (for details on the

Table 1. *Arousal ratings, reaction times, and familiarity ratings by subject group*

Word category	Control	Left temporal lobectomy	Right temporal lobectomy
	Arousal rating		
Arousing	2.54 ± 0.14	2.40 ± 0.19	2.37 ± 0.21
Neutral	1.36 ± 0.10	1.35 ± 0.09	1.18 ± 0.05
	Reaction time (in ms)		
Arousing	1,595 ± 91.0	1,528 ± 114.9	1,589 ± 145.0
Neutral	1,422 ± 87.4	1,369 ± 116.7	1,431 ± 95.9
	Familiarity rating		
Arousing	3.19 ± 0.36	3.63 ± 0.34	3.67 ± 0.28
Neutral	3.68 ± 0.30	4.46 ± 0.18	3.61 ± 0.37

Note. Values represent means ± *SEM.*

psychophysiological recording and analysis, see LaBar et al., 1995; Phelps, LaBar, & Spencer, 1997). SCR is a phasic measure of eccrine sweat gland activity, a reliable autonomic indicator of sympathetic nervous system excitation (Venables & Christie, 1973). After each word disappeared from the screen, the subject rated it on an arousal scale ranging from 1 (*not at all arousing*) to 4 (*very arousing*). Reaction times were recorded for the arousal ratings. Following the encoding phase, free recall for the words was assessed both immediately and after 1 hr of nonverbal distractor tasks.[1] Finally, subjects were asked to rate each studied word on a familiarity scale ranging from 0 (*not at all familiar*) to 6 (*very familiar*).

RESULTS

Table 1 summarizes the arousal ratings, reaction times, and familiarity ratings for the subject groups. Subjects rated the arousing words as less familiar and more arousing than the neutral words, $F(1, 34) = 4.34$, $p = .045$, and $F(1, 37) = 136.99$, $p < .001$, respectively. Reaction times were significantly longer for the arousing words than for the neutral words, $F(1, 37) = 10.53$, $p = .002$. Furthermore, all subjects produced larger SCRs to the arousing words than to the neutral words, $F(1, 32) = 51.60$, $p < .001$ (see Fig. 1). The statistical analyses did not yield any significant group interactions. Collectively, these findings suggest that the arousal manipulation at encoding was equally effective across all subject groups.

Despite the equivalence of the arousal manipulation at encoding, group differences emerged in the interaction of arousal with retention interval during memory testing. Most important, the recall scores were characterized by a significant three-way interaction of experimental group, word category, and retention interval, $F(2, 42) = 7.99$, $p = .001$.[2] As illustrated in Figure 2, only control subjects displayed differential forgetting rates for arousing versus neutral words, $F(1, 22) = 9.10$, $p = .018$ (Bonferroni corrected). This effect was due to a significant increase in recall for the arousing words over time, $t(22) = 2.73$ $p = .036$ (Bonferroni corrected). Evidence for forgetting-resistant memory traces for the arousing words was not found in either temporal-lobectomy group. In fact, the right-temporal-lobectomy group showed a trend for an interaction in the opposite direction (i.e., a steeper forgetting slope for arousing words than neutral words), although this interaction was not significant when adjusted for multiple comparisons, $F(1, 11) = 4.88$, $p = .147$ (Bonferroni corrected). When the left- and right-temporal-lobectomy patients were compared directly, a main effect of hemisphere ($F[1, 20] = 6.83$, $p = .017$) and a Hemisphere × Word Category interaction ($F[1, 20] = 8.76$, $p = .008$) emerged, indicating lower recall levels in the left-temporal-lobectomy patients, especially for taboo words. However, the three-way Hemisphere × Word Category × Retention Interval interaction was not significant. Therefore, although the temporal-lobectomy patients and control groups had equivalent levels of physiological and reported arousal at encoding, the memory performance of temporal-lobectomy patients was characterized by impaired consolidation for emotionally arousing words, as revealed by the lack of an effect of arousal on the rate of forgetting over time.

To ensure that the interaction of word category with retention interval seen in control subjects was not attributable to differences in overall levels of recall, we conducted two additional analyses. First, to rule out floor effects in the patient groups, the three-way analysis of variance (Group × Word Category × Retention Interval) was recalculated excluding subjects with no recall for the neutral words at either retention interval. This criterion removed 4 left- and 2 right-temporal-lobectomy patients from the analysis, but the resulting three-way interaction remained highly significant, $F(2, 36) = 6.01$, $p = .006$.

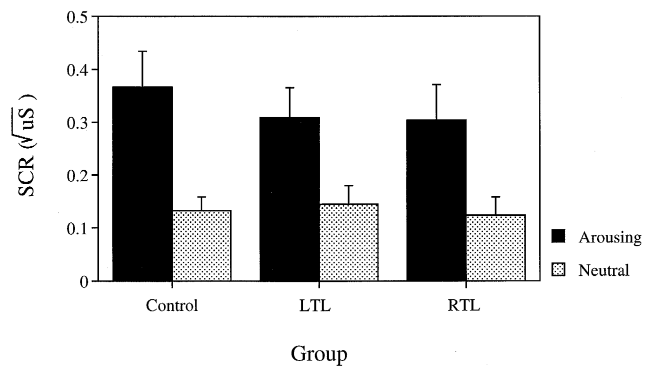

Fig. 1. Mean skin conductance responses (SCRs) to arousing and neutral words by subject group. Error bars represent 1 *SEM.* LTL = left temporal lobectomy; RTL = right temporal lobectomy; μS = microSiemens.

1. Subjects were also given a two-alternative forced-choice recognition test for the words immediately following the 1-hr delayed-recall test. The results from this test are not presented, as half of the subjects (14 control subjects, 7 right-temporal-lobectomy patients, and 2 left-temporal-lobectomy patients) performed at ceiling on at least one of the word categories (arousing, neutral).

2. We also found significant two-way interactions between experimental group and retention interval, $F(2, 42) = 6.91$, $p = .003$, and between experimental group and word category, $F(2, 42) = 6.85$, $p = .003$, as well as significant main effects for experimental group, $F(2, 42) = 30.50$, $p < .001$; retention interval, $F(1, 42) = 13.40$, $p = .001$; and word category, $F(1, 42) = 206.04$, $p < .001$.

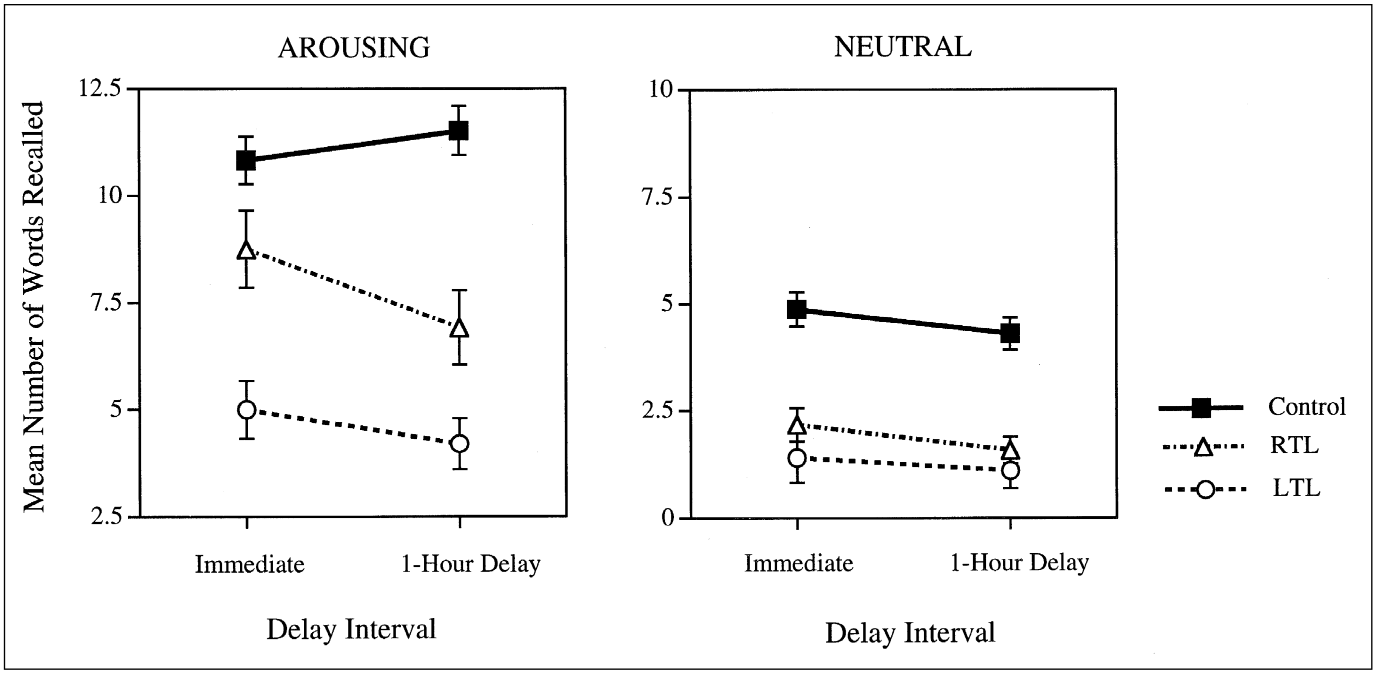

Fig. 2. Mean recall for arousing and neutral words at immediate and 1-hr retention intervals by subject group. Error bars represent 1 *SEM*. LTL = left temporal lobectomy; RTL = right temporal lobectomy.

Second, to show that the control subjects' performance was not related to initial levels of recall, we performed a median split within the control group to separate control subjects with high and low recall at the immediate test. A three-way analysis of variance conducted within the control group did not yield a significant Recall Level × Word Category × Retention Interval interaction, $F(1, 24) = 0.58$, $p = .453$. This finding demonstrates that the arousal-mediated consolidation effect did not interact with initial level of recall within the control group. Thus, the influence of arousal on forgetting rates is not related to differences in initial levels of recall within the control group nor to floor effects in the patient populations.

DISCUSSION

In nonhuman animals, the amygdala strengthens hippocampal-dependent memory formation for emotionally engaging tasks in a postencoding time window, revealing an integrative role of these brain structures in arousal-mediated memory consolidation (McGaugh et al., 1992; Packard et al., 1994). The results of the present study suggest that this function of the medial temporal lobe is conserved across species, contributing to knowledge of the faculties regulating arousal-memory interactions in the human brain. We found that temporal-lobectomy patients did not exhibit differential forgetting rates for words that differ in their arousal properties, despite the fact that the patients showed intact SCRs and arousal ratings to the words at the time of encoding. The mechanism underlying the impairment in the temporal-lobectomy patients is most likely related to consolidation processes, as the effects of arousal at encoding were augmented in delayed-recall performance in control subjects. Alternative explanations for the temporal influences of arousal on memory have been proposed, including differences in rehearsal strategies over time and sensitivity to serial position effects (Eysenck, 1976). In the present study, we minimized differences in rehearsal strategies between groups by testing memory incidentally and by filling the gap between the immediate and delayed retention intervals with nonverbal distractor tasks. Serial position effects were minimized by using filler items at the beginning and end of the list, and by randomizing items within the word list across subjects. For these reasons, we do not believe that these alternative mechanisms account for the failure to observe arousal-memory interactions in the temporal-lobectomy patients.

In addition to the significant arousal-memory interaction, main effects of subject group and arousal were observed. The main effect of subject group indicated that the left-temporal-lobectomy patients displayed the poorest levels of recall. These results are consistent with previous temporal-lobectomy studies revealing left-hemisphere dominance for verbal memory across emotional and nonemotional domains (Milner, 1975; Phelps et al., 1997). In the present study, when right- and left-temporal-lobectomy patients were compared, the Word Category × Retention Interval interaction did not vary with side of lesion, suggesting that the two patient groups were equally insensitive to the influence of arousal on memory consolidation. Except for the overall low levels of recall in the left-temporal-lobectomy group, we have consistently failed to find lateralized effects in this patient population across a variety of emotional memory tasks (LaBar et al., 1995; Phelps et al., 1997), although the right-temporal-lobectomy patients are significantly more impaired at processing facial expressions of emotion (Anderson, LaBar, & Phelps, 1996). In contrast, a positron emission tomography (PET) study (Cahill et al., 1996) reported correlations between right-lateralized amygdala activity during encoding of emotional film clips and subsequent recall in normal subjects. In the group-level subtraction analysis, however, Cahill et al. did not find right-amygdala activation in reaction to the emotional film clips, and another PET study showed activation in the left medial temporal lobe during encoding of emotionally unpleasant pictures (Lane et al., 1997). Therefore, lateralization of activity in the medial temporal lobe during emotional-processing tasks may be highly sensitive to the modality of the memoranda or other methodological variables. In addition, the lack of hemispheric specialization in temporal-lobectomy patients may be due to brain reorganization subsequent to seizure activity or epileptiform-induced damage in the contralateral hemisphere, which can be revealed using magnetic resonance spectroscopy (Incisa della Rocchetta et al., 1995).

The main effect of arousal indicates that, overall, arousing words were retained better than neutral words. In a previous study (Phelps et al., 1997), we found that temporal-lobectomy patients showed a retention advantage for nonarousing words that were positive or negative in emotional meaning (relative to emotionally neutral words) when memory was assessed immediately after encoding. A potential contributing factor to the memory retention of emotional words is that emotional words form a more cohesive semantic category than neutral words (Phelps & LaBar, 1997), and such categorical processing may not rely on temporal lobe mediation (Phelps et al., 1997). It is important to note that in the present study, the deficit in the temporal-lobectomy patients was not revealed until we examined forgetting rates for the emotionally arousing words over time. This points to the importance of measuring memory at multiple time points to unveil arousal-memory interactions dependent on the temporal lobe.

In a previous neuropsychological case report (Cahill, Babinsky, Markowitsch, & McGaugh, 1995), a patient with bilateral amygdala lesions due to Urbach-Wiethe disease exhibited deficits in recognition memory for an emotional story. Because memory was not assessed at more than one retention interval, however, it is unclear whether the deficit was related to memory consolidation or other factors. Additional research on the same task has shown that the emotional elements of the story serve to focus attention on central features during encoding (Heuer & Reisberg, 1992). This case study, then, may highlight an arousal-mediated attentional function of the amygdala, which may become apparent in more complex story tasks. Generalization to other patient populations remains to be tested, however (see Hamann et al., 1996).

The present study provides evidence for impaired arousal-mediated consolidation in a relatively large, homogeneous population of patients with damage to the medial temporal lobe, including the amygdala. The amygdala, therefore, may participate in multiple aspects of emotional memory formation in circumstances beyond those involving conditioned fear (Bechara et al., 1995; LaBar et al., 1995; see also Gallagher & Holland, 1994). One alternative hypothesis is that the deficit in the temporal-lobectomy patients is related to the damage sustained in the adjacent temporal lobe cortex. This potential confound cannot be ruled out until patients with more focal amygdalo-hippocampal lesions are tested on this paradigm. A second alternative hypothesis is that the deficit is attributable solely to the hippocampal damage sustained in these patients, with no discernable contribution of the amygdala. We do not believe this hypothesis is tenable because of the extensive animal literature implicating the amygdala and because of a recent study demonstrating intact memory enhancement for emotional pictures in amnesic patients with spared amygdala function (Hamann, Cahill, & Squire, 1997). The cooperative action of the amygdala and hippocampus in regulating declarative memory consolidation for arousing events represents one way in which brain regions specialized for emotional and cognitive functions normally interact to guide mental activity. Provided that the data reported here extend to nonverbal arousal domains, the results are important for understanding how emotionally salient events are encoded into long-term store, and have potential applications to studying dysfunctional consolidation mechanisms in affective memory disorders.

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REFERENCES

Anderson, A.K., LaBar, K.S., & Phelps, E.A. (1996). Facial affect processing abilities following unilateral temporal lobectomy. *Society for Neuroscience Abstracts, 22*, 1866.

Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., & Damasio, A.R. (1995, August 25). Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. *Science, 269*, 1115–1118.

Bellezza, F.S., Greenwald, A.G., & Banaji, M.R. (1986). Words high and low in pleasantness as rated by male and female college students. *Behavior Research Methods, Instruments, and Computers, 18*, 299–303.

Cahill, L., Babinsky, R., Markowitsch, H.J., & McGaugh, J.L. (1995, September 28). The amygdala and emotional memory. *Nature, 377*, 295–296.

Cahill, L., Haier, R.J., Fallon, J., Alkire, M.T., Tang, C., Keator, D., Wu, J., & McGaugh, J.L. (1996). Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proceedings of the National Academy of Sciences, USA, 93*, 8016–8021.

Christianson, S.-Å., & Loftus, E.F. (1991). Remembering emotional events: The fate of detailed information. *Cognition and Emotion, 5*, 81–108.

Eysenck, M.W. (1976). Arousal, learning, and memory. *Psychological Bulletin, 83*, 389-404.

Gallagher, M., & Holland, P.C. (1994). The amygdala complex: Multiple roles in associative learning and attention. *Proceedings of the National Academy of Sciences, USA, 91*, 11771–11776.

Hamann, S.B., Cahill, L., & Squire, L.R. (1997). Emotional perception and memory in amnesia. *Neuropsychology, 11*, 104–113.

Hamann, S.B., Stefanacci, L., Squire, L.R., Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1996, February 8). Recognizing facial emotion. *Nature, 379*, 497.

Heuer, F., & Reisberg, D. (1992). Emotion, arousal, and memory for detail. In S.-Å. Christianson (Ed.), *The handbook of emotion and memory: Research and theory* (pp. 151–180). Hillsdale, NJ: Erlbaum.

Incisa della Rocchetta, A., Gadian, D.G., Connelly, A., Polkey, C.E., Jackson, G.D., Watkins, K.E., Johnson, C.L., Mishkin, M., & Vargha-Khadem, F. (1995). Verbal memory impairment after right temporal lobectomy: Role of contralateral damage as revealed by ^{1}H magnetic resonance spectroscopy and T_2 relaxometry. *Neurology, 45*, 797–802.

Kleinsmith, L.J., & Kaplan, S. (1963). Paired-associate learning as a function of arousal and interpolated interval. *Journal of Experimental Psychology, 65*, 190–193.

LaBar, K.S., LeDoux, J.E., Spencer, D.D., & Phelps, E.A. (1995). Impaired fear conditioning following unilateral temporal lobectomy in humans. *Journal of Neuroscience, 15*, 6846–6855.

Lane, R.D., Reiman, E.M., Bradley, M.M., Lang, P.J., Ahern, G.L., Davidson, R.J., & Schwartz, G.E. (1997). Neuroanatomical correlates of pleasant and unpleasant emotion. *Neuropsychologia, 11*, 1437–1444.

McGaugh, J.L., Introini-Collison, I.B., Cahill, L., Kim, M., & Liang, K.C. (1992). Involvement of the amygdala in neuromodulatory influences on memory storage. In J.P. Aggleton (Ed.), *The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction* (pp. 431–452). New York: Wiley-Liss.

Milner, B. (1975). Psychological aspects of focal epilepsy and its neurosurgical management. *Advances in Neurology, 8*, 299–321.

Novelly, R.A., Augustine, E.A., Mattson, R.H., Glaser, G.H., Williamson, P.D., Spencer, D.D., & Spencer, S.S. (1984). Selective memory improvement and impairment in temporal lobectomy for epilepsy. *Annals of Neurology, 15*, 64–67.

Packard, M.G., Cahill, L., & McGaugh, J.L. (1994). Amygdala modulation of hippocampal-dependent and caudate nucleus-dependent memory processes. *Proceedings of the National Academy of Sciences, USA, 91*, 8477–8481.

Phelps, E.A., & LaBar, K.S. (1997). The role of organization in recall for affective words. *Abstracts of the Psychonomic Society, 2*, 4–5.

Phelps, E.A., LaBar, K.S., & Spencer, D.D. (1997). Memory for emotional words following unilateral temporal lobectomy. *Brain and Cognition, 34*, 512–521.

Revelle, W., & Loftus, D.A. (1992). The implications of arousal effects for the study of affect and memory. In S.-Å. Christianson (Ed.), *The handbook of emotion and memory: Research and theory* (pp. 113–149). Hillsdale, NJ: Erlbaum.

Spencer, D.D., & Spencer, S.S. (1985). Surgery for epilepsy. In L. Krantler (Ed.), *Neurological clinics: Vol. 3. Advances in neurosurgery* (pp. 313–330). Philadelphia: Saunders.

Spencer, D.D., Spencer, S.S., Mattson, R.H., Williamson, P.D., & Novelly, R.A. (1984). Access to the posterior medial temporal lobe structures in the surgical treatment of temporal lobe epilepsy. *Neurosurgery, 15*, 667–671.

Venables, P.H., & Christie, M.J. (1973). Mechanisms, instrumentation, recording techniques and quantification of responses. In W.F. Prokasy & D.C. Raskin (Eds.), *Electrodermal activity in psychological research* (pp. 1–124). New York: Academic Press.

Williams, L.J., & Evans, J.R. (1980). Evidence for perceptual defense using a lexical decision task. *Perceptual and Motor Skills, 50*, 195–198.

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