PERGAMON

Neuropsychologia 41 (2003) 1919–1928

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Dissociating medial temporal and basal ganglia memory systems with a latent learning task

Catherine E. Myers [a,*], Daphna Shohamy [b], Mark A. Gluck [b], Steven Grossman [b], Somporn Onlaor [c], Narinder Kapur [d]

[a] *Memory Disorders Project, Department of Psychology, Rutgers University-Newark, 101 Warren Street, Newark, NJ 07102, USA*
[b] *Center for Molecular and Behavioral Neuroscience, Rutgers University-Newark, 197 University Avenue, Newark, NJ 07102, USA*
[c] *Department of Physical Therapy, Faculty of Associated Medical Sciences, Chiang Mai University, Chiang Mai 50200, Thailand*
[d] *Department of Clinical Neuropsychology, Wessex Neurological Centre, Southampton General Hospital, Southampton SO16 6YD, UK*

Received 16 July 2002; received in revised form 12 December 2002; accepted 20 May 2003

Abstract

The medial temporal (MT) lobes and basal ganglia have both been implicated as brain substrates of associative learning. Here, we show a dissociation between medial temporal and basal ganglia damage using a latent learning task, in which prior exposure to cues, uncorrelated with each other, slows subsequent learning of an association between them. Consistent with prior work, we found a robust exposure effect in healthy controls, with exposed controls learning more slowly than non-exposed controls. This effect was abolished in medial temporal amnesia: both exposed and non-exposed amnesic patients learned at the same speed. A group of patients with basal ganglia damage due to Parkinson's disease showed a reversal of the effect: exposed subjects learned faster than non-exposed subjects. Our findings point to distinct and dissociable contributions of medial temporal lobe and basal ganglia structures to learning and memory.

Keywords: Hippocampus; Parkinson's disease; Memory; Learned irrelevance; Perceptual learning; Amnesia

1. Introduction

The medial temporal (MT) lobes, including the hippocampus and associated structures, have long been known to play an important role in learning and memory, but there is less agreement regarding the precise nature of this role. Currently, various theories implicate the hippocampal region in declarative memory (Squire, 1987), episodic memory (Tulving & Markowitsch, 1998), spatial learning (O'Keefe & Nadel, 1978; Nadel, 1992), contextual learning (Hirsh, 1974), configural learning (Sutherland & Rudy, 1989), temporal or sequence learning (Buzsáki, 1989; Levy, 1996), consolidation of new memories to long-term cortical storage (Nadel & Moscovitch, 1997; Teyler & DiScenna, 1986), learning of flexible relationships between stimuli (Eichenbaum, 1992), and so on. There is general agreement that some forms of learning are spared following hippocampal-region damage. For example, in classical conditioning, a previously neutral cue (the conditioned stimulus (CS)) is repeatedly paired with a response-evoking stimulus (the unconditioned stimulus (US)) until presentation of the CS alone evokes an anticipatory response. If the CS and US overlap and co-terminate (called the delay conditioning paradigm), learning of the CS–US association is not disrupted in MT amnesia (e.g. Weiskrantz & Warrington, 1979; Daum, Channon, & Canavan, 1989; Gabrieli et al., 1995) or in animal models of amnesia involving hippocampal-region damage (e.g. Schmaltz & Theios, 1972; Port, Mikhail, & Patterson, 1985). It is not enough, though, to conclude that classical conditioning is hippocampal-independent; if the conditioning paradigm involves more complex contextual, spatial, temporal, or configural relationships, then there may indeed be impairments after hippocampal-region damage (e.g. Hirsh, 1974; Nadel & Willner, 1980; Sutherland & Rudy, 1989; McGlinchey-Berroth, Carrillo, Gabrieli, Brawn, & Disterhoft, 1997; Clark & Squire, 1998).

One broad class of conditioning behavior affected by hippocampal-region damage is latent learning, in which prior unreinforced exposure to stimuli affects the speed of later learning about those stimuli. One example is learned irrelevance, in which prior exposure to CS and US, uncorrelated with each other, slows subsequent acquisition of

* Corresponding author. Tel.: +1-973-353-1080x3227; fax: +1-973-353-1272.
E-mail address: myers@pavlov.rutgers.edu (C.E. Myers).

0028-3932/$ – see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0028-3932(03)00127-1

the CS–US association, relative to non-exposed controls (Mackintosh, 1973). In rabbits, hippocampal-region damage abolishes the learned irrelevance effect, so that exposed and non-exposed animals learn at the same speed (Allen, Chelius, & Gluck, 2002). We have recently shown a similar latent learning effect in human amnesics with MT damage, using a computer-based task that embeds some of the features of the classically conditioned learned irrelevance paradigm. In this task, subjects have to learn that a neutral stimulus (a screen color change) predicts a salient event (a rabbit appearing under a magician's hat). Prior exposure to the color and rabbit, uncorrelated with each other, slows subsequent learning of the color–rabbit association in healthy control subjects (Myers, Oliver, Warren, & Gluck, 2000b). This latent learning effect is abolished in MT amnesia: exposed patients learn the association as quickly as non-exposed patients—and as fast as non-exposed healthy controls (Myers et al., 2000a).

Learned irrelevance is also related to the phenomenon of latent inhibition (Lubow, 1973), in which prior exposure to a CS alone (with no US exposure) slows later CS–US learning; latent inhibition is also abolished by hippocampal-region damage in animals (Kaye & Pearce, 1987; Solomon & Moore, 1975). It remains a matter of some debate whether learned irrelevance is just a special case of latent inhibition or whether it reflects explicit learning of a lack of correlation between CS and US (e.g. Baker & Mackintosh, 1979; Bennett, Maldonado, & Mackintosh, 1995; Bonardi & Hall, 1996; Matzel, Schachtman, & Miller, 1988). In either case, both learned irrelevance and latent inhibition are examples of latent learning phenomena that appear to require learning about neutral stimuli in the absence of direct pairing with a reinforcer.

There are a number of theories that address why such latent learning effects might depend on hippocampal-region mediation. One, based on a computational model of hippocampal-region function (Gluck & Myers, 1993, 2001), suggests that the hippocampal region is involved in forming new stimulus representations that include information about the context in which the stimulus has appeared in the past. If a stimulus is presented in a context where no reinforcer is present, representations form which compress together information about the stimulus and context; in effect, the stimulus is treated as just one more feature of the context. Later, when task demands change so that the subject must respond to the stimulus but not to the context alone, this representational compression must be explicitly undone, and learning is slowed relative to a condition with no stimulus exposure. Similar representational explanations of latent learning have been proposed by Mackintosh (1973), Hirsh (1974), Levy (1989) and Eichenbaum (1992). Because this explanation of latent learning depends on representational processes putatively mediated by the hippocampal region, it accounts for the fact that both latent inhibition and learned irrelevance are disrupted following hippocampal-region damage.

Other researchers have suggested that latent learning depends on the hippocampus for the ability to tune out attention to irrelevant stimuli (Moore & Stickney, 1980; Kaye & Pearce, 1987; Han, Gallagher, & Holland, 1995), or have implicated hippocampal afferents to the nucleus accumbens in the ability to recognize a novel or unexpected event and switch behavior accordingly (Weiner, 1990; Gray et al., 1995). These theories may not be mutually exclusive; latent learning may reflect several interacting processes which may each involve different brain circuits.

Whereas the hippocampal region may be required for latent learning, but not for learning simpler stimulus–response associations, the basal ganglia may play a somewhat complementary role. Many studies have implicated the basal ganglia in learning of incrementally acquired information, particularly where learning is based on error-correcting feedback (e.g. Divac, Rosvold, & Szwarcbart, 1967; Packard, Hirsh, & White, 1989; Kesner, Bolland, & Dakis, 1993; Mishkin, Malamut, & Bachevalier, 1984; Knowlton & Squire, 1993). For example, patients with basal ganglia dysfunction due to Parkinson's disease (PD) are often impaired on visuomotor sequence learning (Pascual Leone et al., 1995; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995), verbal serial reaction tasks (Westwater, McDowall, Siegert, Mossman, & Abernathy, 1998), and probabilistic classification (Knowlton, Mangels, & Squire, 1996). Animals with basal ganglia lesions are impaired on tasks that require gradual learning of cue–outcome relations or stimulus–response associations (Packard et al., 1989; Packard & McGaugh, 1992, 1996; Kesner et al., 1993; McDonald & White, 1993; Packard, 1999; Kim & Baxter, 2001). However, there is little evidence that basal ganglia damage disrupts the kind of learning believed to depend on the hippocampal region; for example, although PD patients are impaired on learning a probabilistic classification task, they are able to form declarative memories of the task session; conversely, amnesic patients can initially learn the task well but cannot later recall details of the task session (Knowlton et al., 1996).

These and related results have led a number of researchers to postulate that the hippocampal region and basal ganglia each play distinct and complementary roles in learning and memory, supporting two dissociable "memory systems" (Mishkin et al., 1984; Squire, 1994; Squire & Zola-Morgan, 1996; Knowlton et al., 1996; Packard & McGaugh, 1996; Robbins, 1996; Gabrieli, 1998; Poldrack et al., 2001; White & McDonald, 2002). Supporting this view are recent neuroimaging studies in healthy controls that demonstrate that the basal ganglia (specifically caudate) and medial temporal areas are differentially engaged during probabilistic category learning, with basal ganglia activation increasing, and medial temporal lobe activation decreasing, across trials (Poldrack et al., 2001); this finding suggests that these two brain areas may even compete with each other during learning. In animals, the interaction between these two systems can sometimes be seen in a single task domain. For example, rats with hippocampal system damage are impaired at learning

a win-shift protocol in an eight-arm radial maze, but not at a win-stay protocol; rats with dorsal striatal damage show the opposite pattern, and are impaired at win-stay but not win-shift (McDonald & White, 1993; see also McDonald & White, 1994).

Similarly, a recent study demonstrated a behavioral double dissociation between MT amnesics and medicated PD patients, with the MT amnesics learning an initial set of stimulus–response associations quickly, but failing to generalize when this information was presented in novel recombinations, while the medicated PD patients learned slowly but then generalized as well as controls (Myers et al., 2003).

Given our prior results with the computer-based latent learning task, in which MT amnesics were spared at simple stimulus–response learning but showed no effect of exposure (Myers et al., 2000a), one obvious question is whether we would again see a complementary pattern in PD patients. To the extent that latent learning in this task is hippocampal-dependent, PD patients should show spared latent learning, although they might learn stimulus–response associations more slowly overall.

The performance of PD patients on latent learning tasks is also of interest given findings implicating a strong dopaminergic component in latent learning phenomena, and given the dopaminergic disruption characteristic of PD. For example, latent inhibition is disrupted in rats by lesions to the mesolimbic dopamine pathway or by pharmacological manipulations of dopaminergic transmission (see Gray et al., 1997, for review). These findings might be taken to suggest that PD patients would therefore show disrupted latent learning. However, these and related studies highlight the ventral striatum as the critical site for latent inhibition (e.g. Solomon & Staton, 1982; see also Gray et al., 1995). In early-stage PD, however, dopamine loss is relatively limited to the dorsal striatum (Kish, Shannak, & Hornykiewicz, 1988), with relatively intact dopaminergic transmission in the ventral striatum. Therefore, one might predict that latent learning effects such as latent inhibition should be spared in early-stage PD. To date, one study that examined a form of latent inhibition in de novo Parkinson's patients demonstrated preserved latent inhibition in females, though not in males (Lubow, Dressler, & Kaplan, 1999).

There has been relatively less study of learned irrelevance, but an effect similar to learned irrelevance is preserved in PD: medicated PD patients are slower to learn about a previously irrelevant than a novel dimension in a two-choice task (Owen et al., 1993; Gauntlett-Gilbert, Roberts, & Brown, 1999). These findings suggest that this type of latent learning effect may indeed survive in PD patients.

Here, we examined performance on our latent learning task in medicated Parkinson's patients, MT amnesics, and healthy controls. We expected to replicate our prior findings that healthy controls learn the color–rabbit association more slowly if they had previously been exposed to these stimuli uncorrelated with each other, and that MT amnesics learn equally quickly regardless of exposure condition. We further expected that PD patients might show slow learning overall, but would show a preserved latent learning effect, with exposed PD patients learning even more slowly than non-exposed PD patients. If so, the two phases of this task (exposure and learning) may dissociate medial temporal from basal ganglia dysfunction.

2. Methods

2.1. Participants

Twenty individuals with mild to moderate Parkinson's disease participated in the study. PD patients were recruited from the movement disorder clinics at the University of Southern California (Los Angeles, CA) and St. Barnabus Hospital (Livingston, NJ), and from Parkinson's disease support groups in the Los Angeles and Sherman Oaks areas of California. Degree of parkinsonism averaged 2.55 (range 1–3.5) on the Hoehn–Yahr scale (Hoehn & Yahr, 1967). Time since onset of disease averaged 7.9 years (range 3–18). The PD group included 16 males and 4 females, with an average age of 62.55 years (range 50–79) and average education of 17.2 years (range 12–22). PD subjects were given medical and psychiatric screening to ensure absence of any other neurologic or psychiatric condition, including depression and dementia. All PD subjects were screened to exclude depression using the Beck Depression Inventory (BDI; Beck, 1987), cutoff = 12, or the Centers for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977), cutoff = 16, and were required to score 28 or greater on the Mini-Mental Status Exam (MMSE; Folstein, Folstein, & McHugh, 1975), consistent with absence of dementia. All PD subjects were on dopaminergic medication (Sinemet) at the time of testing. PD subjects volunteered for testing and were tested either in the clinical setting or at their homes.

Six individuals with anterograde amnesia following hippocampal or medial temporal damage served as the MT group. The group included three males and three females, with a mean age of 56.0 years (range 40–67), recruited through the Wessex Neurological Centre in Southampton. Etiology and neuroimaging information is given for these subjects in Table 1. Although hippocampal/MT damage was confirmed in all six subjects, there may be additional damage that is not detectable using structural imaging. Cerebellar and basal ganglia damage appear unlikely, as confirmed by radiological reports and neurological examinations. Recent data suggest that basal ganglia damage is less common than previously suspected following anoxia (Parkinson et al., 2002), while patients with amnesia following herpes simplex encephalitis may sustain only mild striatal damage (Kapur et al., 1994).

To assess degree of amnesia, all subjects in the MT group were given a series of neuropsychological tests of memory, cognition and attention. Key results are summarized in Table 2. MT subjects were given various tests of

Table 1
Demographic and etiology/imaging information for the MT subjects; age (in years) at time of testing

ID	Age	Gender	Etiology	Neuromaging (MRI)
EB	55	M	Limbic encephalitis	Bilateral hippocampal damage
NT	60	F	Paraneoplastic limbic encephalitis	Bilateral MT abnormality
MM	58	B	Carbon monoxide poisoning	Bilateral hippocampal damage
JK	67	F	Left hippocampal infarct	Left hippocampal damage
JN	56	F	Herpes simplex encephalitis	Bilateral MT damage (including hippocampus but extending laterally)
ML	40	M	Paraneoplastic limbic encephalitis	Bilateral hippocampal damage

Table 2
Summary of neuropsychological results for MT subjects

	EB	NT	MM	JK	JN	ML	Mean (S.D.)
WAIS-R VIQ	120	104	122	130	82	84	107.0 (20.4)
NART VIQ	110	106	117	105	80	82	100.0 (15.3)
Digit span	18	13	15	9	10	8	12.2 (3.9)
RMT words	39	28	42	26	31	23	31.5 (7.5)
AMIPB immediate story	NA	4	16	11	11	4	9.2 (5.2)
AMIPB delay story	NA	0	0	0	6	0	1.2 (2.7)
WMS-R LMI, immediate recall	22	NA	19	23	11	NA	18.8 (5.4)
WMS-R LMII, delayed recall	0	NA	0	0	2	NA	0.5 (1.0)

Wechsler Adult Information Scale-Revised (WAIS-R), verbal IQ (VIQ). National Adult Reading Test (NART). Recognition Memory Test, total words recognized (RMT). Adult Memory and Information Processing Battery, total items recalled (AMIPB). Wechsler Memory Scale-Revised (WMS-R); Logical Memory subtests, total items recalled (LMI, LMII).

immediate and delayed recall, such as the story recall portions of the Adult Memory and Information Processing Battery (Coughlan & Hollows, 1984) or the Logical Memory subtest of the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987). Most MT subjects scored well below the 50 percentile on immediate recall and all scored below the 10 percentile on delayed recall. MT subjects were also given the Wechsler Adult Information Scale-Revised (Wechsler, 1981) which generates various age-adjusted scores including a verbal intelligence quotient (VIQ) with an expected mean of 100 (S.D. 15). The MT group averaged a VIQ of 107.0 (S.D. 20.42, range 82–130). MT subjects were also given tests of attention and working memory, including the digit span subtest of the WMS-R; the average age-adjusted percentile score was 48 (S.D. 26.2, range 16–84 percentile). In summary, the MT group showed dense amnesia, as evidenced by significantly below normal performance on tests of memory, with little evidence of disruption on tests of cognition and attention.

Twenty healthy controls were also recruited through the Memory Disorders Project at Rutgers-Newark and the Motor Behavior Laboratory in Los Angeles. Control subjects were screened via self-report for absence of any existing neurologic or psychiatric condition and for absence of any medications that could affect cognition. This group included 11 males and 9 females, with a mean age of 61.2 years (range 44–73) and mean education of 16.8 years (range 12–20). Control subjects were also screened for absence of depression (BDI or CES-D), and averaged a score of 29.5 on the MMSE; they were also required to score within one standard deviation of age-appropriate norms on the WMS-R logical memory and digit span subtests. Control subjects volunteered or were reimbursed at the rate of US$ 10 h^{-1} for their participation.

Subjects in each group were randomly and evenly assigned to exposed and non-exposed condition. MT subjects were also run in a second session, at least 8 weeks after the first session, during which they received the alternate experimental condition (non-exposed or exposed). There were no significant differences in age between groups or among subjects assigned to each condition (ANOVA[1], group: $F(2, 46) = 2.22$, $P = 0.120$; condition: $F(1, 46) = 0.10$, $P > 0.500$; group × condition: $F(2, 46) = 0.21$, $P > 0.500$).

All subjects signed statements of informed consent prior to initiation of testing. The study was approved by the Institutional Review Board for Protection of Human Subjects at Rutgers University.

2.2. Apparatus

The experiment took place in a quiet testing room, with the task automated on a Macintosh i-book laptop or equivalent computer with a color screen programmed in the SuperCard language (Allegiant Technologies, San Diego, CA). The keyboard was masked except for two keys, labeled “yes” and “no”, used to input responses. The participant sat at a comfortable viewing distance from the computer screen (approximately 18 in.).

[1] Due to unequal sample size between groups, this and all subsequent ANOVAs reported here include correction for unbalanced design.

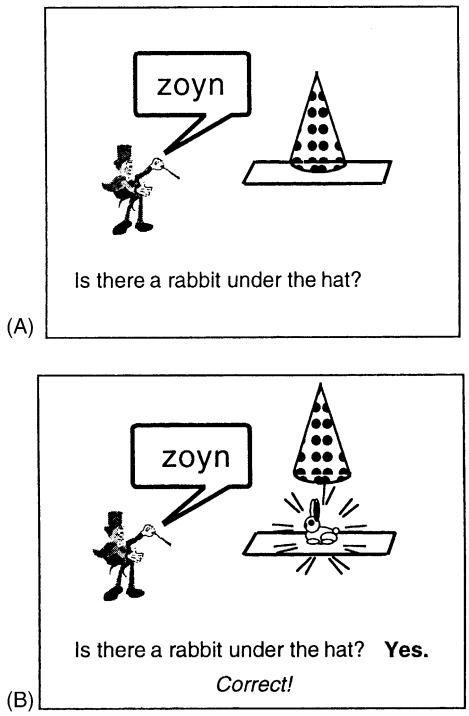

Fig. 1. Screen appearance at: (A) start of trial and (B) after subject responds correctly.

2.3. Stimuli

On each trial, the computer screen showed a cartoon magician waving a wand at a large hat (Fig. 1A). A large word balloon appeared over his head, with a "magic word" printed in black lowercase letters. These magic words were taken from a set of 30 monosyllabic nonwords; for each subject, 15 words were randomly selected and used in phase 1, and the remaining 15 words were used in phase 2. One of the phase 1 "magic words" was randomly selected to be the signal word *W* that would predict the rabbit in phase 1. The cartoon balloon above the magician could be colored red or green or uncolored (gray). One of the colors red and green was randomly selected to be the color C+ which would predict the rabbit in phase 2, while the other color was selected to be color C−.

2.4. Procedure

The procedure was as previously described in Myers et al. (2000b). At the start of phase 1, instructions appeared stating that a magician was trying to make a rabbit appear under his hat, and the participant's task was to predict whether or not the magician was successful. On each trial, the magician, hat, and magic word appeared, together with a prompt, "Is there a rabbit under the hat?"; the participant responded by pressing one of the two labeled keys ("yes" or "no"). The hat was then raised to reveal whether or not there was a rabbit underneath, and corrective feedback appeared along with a beep in the case of incorrect responding (Fig. 1B).

Phase 1 consisted of 30 trials. During 15 randomly selected trials, the signal word *W* was presented and the rabbit appeared. On the remaining trials, other words were presented and there was no rabbit. Thus, "magic word" *W* was perfectly predictive of, or correlated with, the rabbit in phase 1. In addition, for subjects in the exposed group, the cartoon balloon appeared in color C+ on 10 trials and in color C− on the remaining 20 trials, with the constraint that C+ and the rabbit were perfectly uncorrelated: that is, the probability of the rabbit's appearance was the same given color C+ or C−. For subjects in the non-exposed condition, the cartoon balloon was always uncolored (gray).

Phase 2 consisted of 60 trials, organized into four blocks of 15 trials. Each of the 15 phase 2 magic words occurred once in each block, in random order, with the constraint that no one word should co-occur with the rabbit more than twice in this phase. Instead, color C+ occurred randomly on five trials in each block, along with the rabbit. Color C− occurred on the remaining trials. Thus, color C+ was perfectly correlated with (or predictive of) the rabbit while color C− was negatively correlated with (or predictive of the absence of) the rabbit. Note that the magic words were now irrelevant with respect to predicting the rabbit, and that no magic word appeared both in phases 1 and 2.

In phase 2, subjects were defined as reaching criterion performance if they made 10 consecutive correct responses. Phase 2 was terminated early if the subject reached criterion performance.

3. Results

Fig. 2 shows the mean trials to criterion in phase 1 for each group. There was no significant effect of group or exposure condition (ANOVA; group: $F(2, 46) = 2.39$, $P = 0.103$; condition: $F(1, 46) < 0.01$, $P > 0.500$; group × condition: $F(2, 46) = 0.06$, $P > 0.500$).

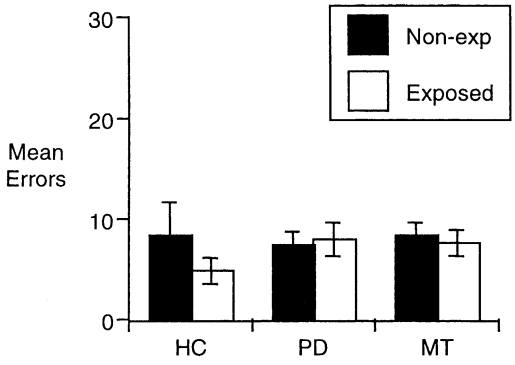

Fig. 2. Phase 1 performance in terms of total errors for healthy control (HC), Parkinson's disease (PD), and medial temporal amnesia (MT) subjects.

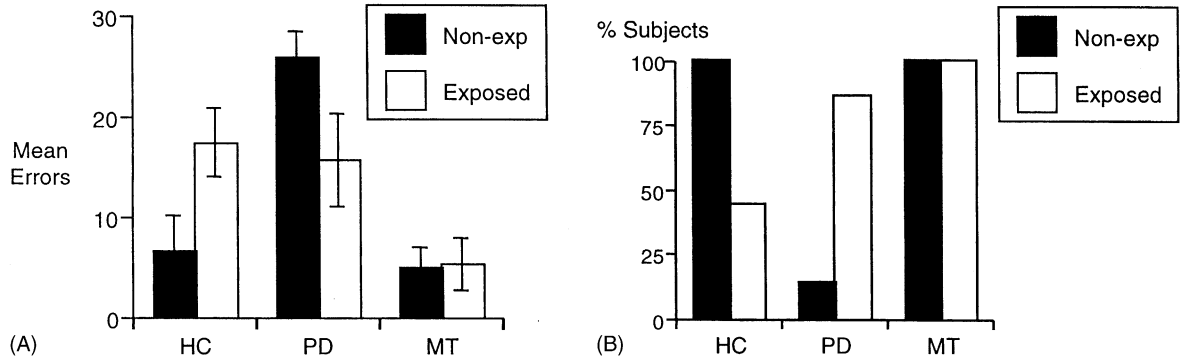

Fig. 3. Phase 2 performance, for subjects who previously solved phase 1: (A) total errors and (B) percentage of subjects reaching criterion.

Fig. 3A shows the mean trials to criterion in phase 2 for each group. There was a significant main effect of group (ANOVA, $F(2, 46) = 9.22$, $P < 0.001$), with no effect of exposure condition ($F(1, 46) = 0.02$, $P > 0.500$) and a group–condition interaction ($F(2, 46) = 6.51$, $P = 0.003$). Tukey HSD pairwise comparisons confirmed an exposure effect in the control group ($P < 0.001$) but not the MT group ($P > 0.500$). By contrast, in the PD group, exposed subjects actually outperformed non-exposed subjects ($P = 0.007$); this represented a reversal of the exposure effect seen in controls. The control non-exposed group and MT non-exposed group did not differ ($P > 0.500$), but both outperformed the PD non-exposed group (all $P < 0.01$). There were no significant differences among any of the exposed groups (all $P > 0.200$).

Fig. 3B shows the percentage of subjects who reached criterion in phase 2. Note that all MT subjects (exposed and non-exposed) reached phase 2 criterion. In the control group, significantly more non-exposed than exposed subjects reached criterion ($\chi^2(1) = 6.92$, $P = 0.009$). In the PD group, this relationship was reversed: significantly more exposed than non-exposed subjects reached criterion ($\chi^2(1) = 5.18$, $P = 0.023$).

In summary, the control group showed an exposure effect, which was eliminated in the MT group; the PD group showed a reversal of the expected exposure effect.

4. Discussion

Consistent with our prior study (Myers et al., 2000b), healthy controls showed an exposure effect, with exposed subjects learning more slowly than non-exposed subjects. This exposure effect is conceptually similar to learned irrelevance (LIRR), in that phase 1 exposure to two stimuli slows subsequent learning of an association between them in phase 2 (Baker & Mackintosh, 1979; Matzel et al., 1988). Clearly, this computer-based paradigm differs from "true" learned irrelevance in that the to-be-predicted event—the appearance of the rabbit—is not a true US in the sense of evoking an innate, species specific unconditioned response. Nevertheless, some of the same mechanisms for latent learning may apply in both domains.

Also consistent with our prior study (Myers et al., 2000a), MT amnesics showed abolition of the exposure effect. Not only did non-exposed amnesics learn phase 2 as quickly as controls, exposed amnesics learned phase 2 *faster* than exposed controls. Therefore, at least in the exposed condition, MT amnesics show a facilitation of learning; such facilitation has also been observed in other paradigms where brain-damaged patients may show reduced interference as a result of pathology (Kapur, 1996). This result is consistent with a large body of prior animal studies showing that hippocampal lesion can often facilitate simple stimulus–response learning in a variety of species and task domains (e.g. Isaacson, Douglas, & Moore, 1961; Schmaltz & Theios, 1972; Zola & Mahut, 1973; Eichenbaum, Fagan, Mathews, & Cohen, 1988).

We previously argued that the lack of exposure effect in amnesics was unlikely to be due to simple forgetting across the phases because amnesics are able to maintain information across a similar interval in other tasks (Myers et al., 2000a). Instead, we argued that the abolition of the exposure effect in MT amnesia reflected the fact that initial phase 1 learning in the amnesics—although fast—was qualitatively different from controls, and so did not support subsequent transfer when familiar stimuli from phase 1 were presented in a new context in phase 2 (Myers & Gluck, 1996; see also Myers et al., 2002). This is consistent with other studies suggesting that MT processing is important in early learning, and that MT lesions may change the nature of this early learning, leading to differences on subsequent transfer tests that require flexible use of this learning (Reber, Knowlton, & Squire, 1996; see also Eichenbaum et al., 1988; Eichenbaum, Otto, & Cohen, 1994).

In the current case, we cannot completely rule out the possibility that simple forgetting contributed to the lack of exposure effect in the MT group. Additionally, it is important to note that the amnesic group had broad MT damage; thus, it is possible that the transfer impairment reflects general disruption of the limbic–diencephalic circuit. However, at least in animals, the critical substrate for this type of latent

learning appears to be the hippocampal system, specifically entorhinal cortex (Allen et al., 2002; Shohamy, Allen, & Gluck, 2000), suggesting that hippocampal system damage may similarly underlie the deficit in MT amnesia.

In the PD group, phase 1 learning was not significantly impaired relative to controls. This contrasts our earlier study (Myers et al., 2003) in which PD patients were slower at stimulus–response learning than controls. One possible reason for this discrepancy is the relative difficulty of the two tasks. In the current study, phase 1 involved learning to associate a single stimulus (a particular "magic word") with a single outcome (the rabbit). In the earlier study, subjects were required to learn six concurrent associations in which individual stimuli were sometimes mapped to different responses on different trials. This could generate response conflict that, together with increased memory load, could cause the PD impairment. Phase 1 in the current experiment may have been simple enough to ameliorate the PD deficit.

In phase 2, subjects in the PD group showed a reversal of the expected exposure effect. That is, exposed PD subjects learned faster than non-exposed PD subjects. Again, PD subjects did not show an overall retardation of learning: the exposed PD patients learned as quickly as non-exposed controls.

This reversal of the exposure effect in PD subjects was not expected by our original hypothesis. One possible explanation for the reversal of the latent learning effect in PD patients may come from the idea of competition between the basal ganglia and the hippocampal memory systems (e.g. Packard et al., 1989; Poldrack et al., 2001). On this view, the basal ganglia and the hippocampus interact and compete during learning, such that damage to one system may facilitate performance by "freeing" the other system to exert behavioral control. This would be consistent with animal studies showing that caudate lesions may sometimes speed learning, presumably by removing striatal interference with hippocampal processing (e.g. Packard et al., 1989; Mitchell & Hall, 1988), as well as with recent imaging (fMRI) data, showing that increased basal ganglia activity during an incremental learning task is associated with decreased activity in the hippocampus (Poldrack et al., 2001). Based on this reasoning, removal (or disruption) of a potentially interfering striatal system might account for particularly fast hippocampal-based learning in the exposed condition among PD patients. However, it is less clear why this hippocampal benefit should not likewise be obtained in the non-exposed condition.

Another possible interpretation of the PD data could be a selective deficit at processing novel cues in the PD groups: perhaps subjects previously exposed to the color in phase 1 were better able to incorporate it into ongoing associations than subjects for whom the color was novel at the start of phase 2. This explanation would be generally consistent with prior findings that medicated PD patients are impaired at shifting attention during learning, particularly when the shift involves a different stimulus dimension than earlier learning (Downes et al., 1989). However, in other studies, PD patients have been shown to perform as well as controls on tasks that involve shifting attention to a novel stimulus dimension (Owen et al., 1993). Additionally, the fact that our PD patients were not impaired at phase 1 of the current task, when all stimuli were by definition "novel", argues against a selective novelty deficit in phase 2.

A third possible explanation is that the PD patients show generally slowed learning in phase 2 but that prior exposure to the stimulus actually facilitates this learning. In the non-exposed condition, phase 2 requires learning to inhibit responding to the previously relevant stimuli (word cues) in favor of new stimuli (color cues). The impaired performance by non-exposed PD patients could reflect a perseverative deficit. Several prior studies have documented such deficits in medicated PD patients performing extradimensional shifts (Downes et al., 1989; Gauntlett-Gilbert et al., 1999). PD patients likewise show enhanced negative priming, increased response time to a target stimulus that has served as a distractor on the previous trial (Wylie & Stout, 2002), as well as difficulty ignoring stimuli that served as targets on previous trials (Cools, Barker, Sahakian, & Robbins, 2001a,b).

However, our PD patients also showed faster learning in the exposed condition than in the non-exposed condition. Such a facilitatory effect of stimulus exposure has occasionally been observed, particularly in the animal literature, and is often termed "perceptual learning". To our knowledge, there are no prior data suggesting an increased tendency for perceptual learning in PD; in fact, two prior studies involving extradimensional shifts (Owen et al., 1993; Gauntlett-Gilbert et al., 1999) explicitly found that medicated PD patients were impaired on learning about a previously irrelevant dimension relative to a novel dimension—precisely the opposite of what we found in the current study. The reason for these conflicting results is not yet clear, although the prior studies differed from the current one on several levels; for example, the prior study by Owen and colleagues was more complicated (involving several successively trained discriminations), reported acquisition as well as reversal data, and used stimulus dimensions rather than unique stimuli. There are also differences among the patient populations; for example, our patients were somewhat more advanced in terms of motor symptoms (averaging 2.55 on the Hoehn–Yahr scale) than those of the Owen et al. study (who averaged 1.54). Future work will be required to determine which of these variables may be critical in determining whether PD subjects show impairment or facilitation in learning about previously exposed stimuli.

A final important factor that may have contributed to the current results is medication. Early-stage PD involves profound depletion of nigrostriatal dopamine, but has less effect on dopaminergic levels in other brain areas (for example, prefrontal cortex). All PD subjects in the current experiment were on dopaminergic medication at the time of testing. It might be the case that such medications remediate dopaminergic impairments in the depleted nigrostriatal circuitry but

actually have detrimental effects (through dopaminergic "overdosing") elsewhere (Cools et al., 2001a,b). This raises the possibility that heightened prefrontal dopamine levels could be responsible for the abolition of the latent learning effect in the medicated PD patients—just as healthy subjects on dopaminergic agonists show abolition of latent inhibition (Weiner, Lubow, & Feldon, 1988; Gray, Pickering, Hemsley, Dawling, & Gray, 1992). In this case, it might be that basal ganglia dysfunction alone might not suffice to disrupt latent learning, but that medication itself is responsible for the disruption. Consistent with this possibility are recent findings that suggest medicated, but not unmedicated, PD patients are impaired at computer-based associative learning (e.g. Shohamy, Myers, Onlaor, & Gluck, 2002). Only studies of controlled withdrawal of medication, or of never-medicated (de novo) PD patients, can help resolve these issues.

Nevertheless, the current results, like our prior study (Myers et al., 2003), demonstrate that a single associative learning task can provide a double dissociation between the effects of medial temporal damage versus basal ganglia dysfunction. In the current study, the effect of medial temporal amnesia was to abolish the effects of stimulus exposure, while the effect of basal ganglia dysfunction was to reverse the direction of this effect, so that exposed PD patients learned faster than non-exposed patients. Both amnesic and PD patients were significantly different from controls.

These findings are consistent with other results suggesting that medial temporal and basal ganglia structures may play complementary or even competitive roles during learning (e.g. Mishkin et al., 1984; Squire & Zola-Morgan, 1996; McDonald & White, 1993; Poldrack et al., 2001; Schroeder, Wingard, & Packard, 2002). Our findings suggest that, in healthy control subjects, both medial temporal and basal ganglia memory systems play distinct roles in mediating the effects of stimulus exposure, and that these roles are dissociable in a task where patients with damage to one memory system are forced to rely on the other system to drive learning.

Acknowledgements

The authors wish to thank Pat Abbot for her assistance.

References

Allen, M., Chelius, L., & Gluck, M. (2002). Selective entorhinal and nonselective cortical-hippocampal region lesions, but not selective hippocampal lesions, disrupt learned irrelevance in rabbit eyeblink conditioning. *Cognitive, Affective, and Behavioral Neuroscience*, *2*(3), 214–226.

Baker, A., & Mackintosh, N. (1979). Preexposure to the CS alone, US alone, or CS and US uncorrelated: Latent inhibition, blocking by context or learned irrelevance? *Learning and Motivation*, *10*, 278–294.

Beck, A. (1987). *Beck depression inventory*. San Antonio, TX: The Psychological Corporation.

Bennett, C., Maldonado, A., & Mackintosh, N. (1995). Learned irrelevance is not the sum of exposure to CS and US. *Quarterly Journal of Experimental Psychology*, *48B*, 117–128.

Bonardi, C., & Hall, G. (1996). Learned irrelevance: No more than the sum of CS and US preexposure effects? *Journal of Experimental Psychology: Animal Behavior Processes*, *22*, 183–191.

Buzsa'ki, G. (1989). Two-stage model of memory-trace formation: A role for "noisy" brain states. *Neuroscience*, *31*, 551–570.

Clark, R., & Squire, L. (1998). Classical conditioning and brain systems? The role of awareness. *Science*, *280*, 77–81.

Cools, R., Barker, R., Sahakian, B., & Robbins, T. (2001a). Enhanced or impaired cognitive function in Parkinson's disease as a function of dopaminergic medication and task demands. *Cerebral Cortex*, *11*, 1136–1143.

Cools, R., Barker, R., Sahakian, B., & Robbins, T. (2001b). Mechanisms of cognitive flexibility in Parkinson's disease. *Brain*, *124*, 2503–2512.

Coughlan, A., & Hollows, S. (1984). Use of memory tests in differentiating organic disorder from depression. *British Journal of Psychiatry*, *145*, 164–167.

Daum, I., Channon, S., & Canavan, A. (1989). Classical conditioning in patients with severe memory problems, Journal of Neurology. *Neurosurgery and Psychiatry*, *52*, 47–51.

Divac, I., Rosvold, H., & Szwarcbart, M. (1967). Behavioral effects of selective ablation of the caudate nucleus. *Journal of Comparative and Physiological Psychology*, *63*, 184–190.

Downes, J., Roberts, A., Sahakian, B., Evenden, J., Morris, R., & Robbins, T. (1989). Impaired extra-dimensional shift performance in medicated and unmedicated Parkinson's disease: Evidence for a specific attentional dysfunction. *Neuropsychologia*, *27*, 1329–1343.

Eichenbaum, H. (1992). The hippocampal system and declarative memory in animals. *Journal of Cognitive Neuroscience*, *4*, 217–231.

Eichenbaum, H., Fagan, A., Mathews, P., & Cohen, N. J. (1988). Hippocampal system dysfunction and odor discrimination learning in rats: Impairment or facilitation depending on representational demands. *Behavioral Neuroscience*, *102*, 331–339.

Eichenbaum, H., Otto, T., & Cohen, N. (1994). Two functional components of the hippocampal memory system. *Behavioural and Brain Sciences*, *17*, 449–518.

Folstein, M., Foistein, S., & McHugh, P. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189–198.

Gabrieli, J. (1998). Cognitive neuroscience of human memory. *Annual Review of Psychology*, *49*, 87–115.

Gabrieli, J., McGlinchey-Berroth, R., Carrillo, M., Gluck, M., Cermack, L., & Disterhoft, J. (1995). Intact delay-eyeblink classical conditioning in amnesia. *Behavioral Neuroscience*, *109*, 819–827.

Gauntlett-Gilbert, J., Roberts, R., & Brown, V. (1999). Mechanisms underlying attentional set-shifting in Parkinson's disease. *Neuropsychologia*, *37*, 605–616.

Gluck, M., & Myers, C. (1993). Hippocampal mediation of stimulus representation: A computational theory. *Hippocampus*, *3*, 491–516.

Gluck, M., & Myers, C. (2001). *Gateway to memory: An introduction to neural network modeling of the hippocampus in learning and memory*. Cambridge, MA: MIT Press.

Gray, J., Joseph, M., Hemsley, D., Young, A., Warburton, E., Boulenguez, P., Grigoryan, G., Peters, S., Rawlins, J., Taib, C. -T., Yee, B., Cassaday, H., Weiner, I., Gal, G., Gusak, O., Joel, D., Shadach, E., Shalev, U., Tarrasch, R., & Feldon, J. (1995). The role of mesolimbic dopaminergic and retrohippocampal afferents to the nucleus accumbens in latent inhibition: implications for schizophrenia. *Behavioral Brain Research*, *71*, 19–31.

Gray, J., Moran, P., Grigoryan, G., Peters, S., Young, A., & Joseph, M. (1997). Latent inhibition: The nucleus accumbens connection revisited. *Behavioural Brain Research*, *88*, 27–34.

Gray, N., Pickering, A., Hemsley, D., Dawling, S., & Gray, J. (1992). Abolition of latent inhibition by a single 5 mg dose of d-amphetamine in man. *Psychopharmacology*, *107*, 425–430.

Han, J. -S., Gallagher, M., & Holland, P. (1995). Hippocampal lesions disrupt decrements but not increments in conditioned stimulus processing. *Journal of Neuroscience*, *15*, 7323–7329.

Hirsh, R. (1974). The hippocampus and contextual retrieval of information from memory: A theory. *Behavioral Biology*, *12*, 421–444.

Hoehn, M., & Yahr, M. (1967). Parkinsonism: Onset, progression and mortality. *Neurology*, *17*, 427–442.

Isaacson, R., Douglas, R., & Moore, R. (1961). The effect of radical hippocampal ablation on acquisition of avoidance response. *Journal of Comparative and Physiological Psychology*, *54*, 625–628.

Jackson, S., Jackson, G., Harrison, J., Henderson, L., & Kennard, C. (1995). The internal control of action and Parkinson's disease: A kinematic analysis of visually-guided and memory-guided prehension movements. *Experimental Brain Research*, *105*, 147–162.

Kapur, N. (1996). Paradoxical functional facilitation in brain-behavior research. A critical review. *Brain*, *119*, 1775–1790.

Kapur, N., Barker, S., Burrows, E., Ellison, D., Brice, J., Illis, L., Scholey, K., Colbourn, C., Wilsson, B., & Loates, M. (1994). Herpes simplex encephalitis: Long term magnetic resonance imaging and neuropsychological profile. *Journal of Neurology Neurosurgery and Psychiatry*, *57*, 1334–1342.

Kaye, H., & Pearce, J. (1987). Hippocampal lesions attenuate latent inhibition and the decline of the orienting response in rats. *Quarterly Journal of Experimental Psychology*, *39B*, 107–125.

Kesner, R., Bolland, B., & Dakis, M. (1993). Memory for spatial locations, motor responses, and objects: Triple dissociation among the hippocampus, caudate nucleus, and extrastriate visual cortex. *Experimental Brain Research*, *93*, 462–470.

Kim, J., & Baxter, M. (2001). Multiple brain memory systems: The whole does not equal the sum of its parts. *Trends in Neuroscience*, *24*, 324–330.

Kish, S., Shannak, K., & Hornykiewicz, O. (1988). Uneven pattern of dopamine loss in the striatum of patients with idiopathic Parkinson's disease. Pathophysiologic and clinical implications. *New England Journal of Medicine*, *318*, 876–880.

Knowlton, B., Mangels, J., & Squire, L. (1996). A neostriatal habit learning system in humans. *Science*, *273*, 1399–1402.

Knowlton, B., & Squire, L. (1993). The learning of categories: Parallel brain systems for item memory and category knowledge. *Science*, *262*, 1747–1749.

Levy, W. B. (1989). A computational approach to hippocampal function. In R. Hawkins, G. Bower (Eds.), *Psychology of learning and motivation* (pp. 243–304). London: Academic Press.

Levy, W. (1996). A sequence predicting CA3 is a flexible associator that learns and uses context to solve hippocampal-like tasks. *Hippocampus*, *6*, 579–590.

Lubow, R. (1973). Latent Inhibition. *Psychological Bulletin*, *79*, 398–407.

Lubow, R., Dressler, R., & Kaplan, O. (1999). The effects of target and distractor familiarity on visual search in de novo Parkinson's disease patients: Latent inhibition and novel pop-out. *Neuropsychology*, *13*, 415–423.

Mackintosh, N. (1973). Stimulus selection: Learning to ignore stimuli that predict no change in reinforcement. In R. Hinde, J. Stevenson-Hinde (Eds.), *Constraints on learning: Limitations and predispositions* (pp. 75–96). New York: Academic Press.

Matzel, L., Schachtman, T., & Miller, R. (1988). Learned irrelevance exceeds the sum of CS-preexposure and US-preexposure deficits. *Journal of Experimental Psychology: Animal Behavior Processes*, *14*, 311–319.

McDonald, R., & White, N. (1993). A triple dissociation of memory systems: Hippocampus, amygdala and dorsal striatum. *Behavioral Neuroscience*, *107*, 3–22.

McDonald, R., & White, N. (1994). Parallel information processing in the water maze: Evidence for independent memory systems involving dorsal striatum and hippocampus. *Behavioral and Neural Biology*, *61*, 260–270.

McGlinchey-Berroth, R., Carrillo, M., Gabrieli, J., Brawn, C., & Disterhoft, J. (1997). Impaired trace eyeblink conditioning in bilateral medial-temporal lobe amnesia. *Behavioral Neuroscience*, *111*, 873–882.

Mishkin, M., Malamut, B., & Bachevalier, J. (1984). Memories and habits: Two neural systems. In J. McGaugh, G. Lynch, N. Weinberger (Eds.), *The neurobiology of learning and memory* (pp. 65–77). New York: Guilford Press.

Mitchell, J., & Hall, G. (1988). Caudate-putamen lesions in the rat may impair or potentiate maze learning depending upon availability of stimulus cues and relevance of response cues. *Quarterly Journal of Experimental Psychology B*, *40*, 243–258.

Moore, J., & Stickney, K. (1980). Formation of attentional-associative networks in real time: Role of the hippocampus and implications for conditioning. *Physiological Psychology*, *8*, 207–217.

Myers, C., & Gluck, M. (1996). Cortico-hippocampal representations in simultaneous odor discrimination learning: A computational interpretation of Eichenbaum, Mathews, & Cohen (1989). *Behavioral Neuroscience*, *110*, 685–706.

Myers, C., Kluger, A., Golomb, J., Ferris, S., de Leon, M., Schnirman, G., & Gluck, M. (2002). Hippocampal atrophy disrupts transfer generalization in non-demented elderly. *Journal of Geriatric Psychiatry and Neurology*, *15*(2), 82–90.

Myers, C., McGlinchey-Berroth, R., Warren, S., Monti, L., Brawn, C., & Gluck, M. (2000a). Latent learning in medial temporal amnesia: Evidence for disrupted representational but preserved attentional processes. *Neuropsychology*, *14*, 3–15.

Myers, C., Oliver, L., Warren, S., & Gluck, M. (2000b). Stimulus exposure effects in human associative learning. *Quarterly Journal of Experimental Psychology B*, *53*, 173–187.

Myers, C., Shohamy, D., Gluck, M., Grossman, S., Kluger, A., Ferris, S., Golomb, J., Schnirman, G., & Schwartz, R. (2003). Dissociating hippocampal vs. basal ganglia contributions to learning and transfer. *Journal of Cognitive Neuroscience*, *15*(2), 185–193.

Nadel, L. (1992). Multiple memory systems: What and why. *Journal of Cognitive Neuroscience*, *4*, 179–188.

Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. *Current Opinion in Neurobiology*, *7*, 217–227.

Nadel, L., & Willner, J. (1980). Context and conditioning: A place for space. *Physiological Psychology*, *8*, 218–228.

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon University Press.

Owen, A., Roberts, A., Hodges, J., Summers, B., Polkey, C., & Robbins, T. (1993). Contrasting mechanisms of impaired attentional set-shifting in patients with frontal lobe damage or Parkinson's disease. *Brain*, *116*, 1159–1175.

Packard, M. (1999). Glutamate infused posttraining into the hippocampus or caudate-putamen differentially strengthens place and response learning. *Proceedings of the National Academy of Sciences USA*, *96*, 12881–12886.

Packard, M., Hirsh, R., & White, N. (1989). Differential effects of fornix and caudate nucleus lesions on two radial maze tasks: Evidence for multiple memory systems. *Journal of Neuroscience*, *9*, 1465–1472.

Packard, M., & McGaugh, J. (1992). Double dissociation of fornix and caudate lesions on acquisition of two water maze tasks: Further evidence for multiple memory systems. *Behavioral Neuroscience*, *106*, 439–446.

Packard, M., & McGaugh, J. (1996). Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. *Neurobiology of Learning and Memory*, *65*, 65–72.

Parkinson, R., Hopkins, R., Cleavinger, B., Waver, L., Victoroff, J., Foley, J., & Bigler, E. (2002). White matter hyperintensities and neuropsychological outcome following carbon monoxide poisoning. *Neurology*, *58*, 1525–1532.

Pascual Leone, A., Grafman, J., Clark, K., Stewart, M., Massaquoi, S., Lou, J., & Hallett, M. (1995). Procedural learning in Parkinson's disease and cerebellar degeneration. *Annals of Neurology*, *34*, 594–602.

Poldrack, R., Clark, J., Pare-Blagoev, J., Shohamy, D., Creso Moyano, J., Myers, C., & Gluck, M. (2001). Interactive memory systems in the brain. *Nature*, *414*, 546–550.

Port, R., Mikhail, A., & Patterson, M. (1985). Differential effects of hippocampectomy on classically conditioned rabbit nictitating membrane response related to interstimulus interval. *Behavioral Neuroscience*, *99*, 200–208.

Radloff, L. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*, 385–401.

Reber, P., Knowlton, B., & Squire, L. (1996). Dissociable properties of memory systems: Differences in the flexibility of declarative and nondeclarative knowledge. *Behavioral Neuroscience*, *110*, 861–871.

Robbins, T. (1996). Refining the taxonomy of memory. *Science*, *273*, 1353–1354.

Schroeder, J., Wingard, J., & Packard, M. (2002). Post-training reversible inactivation of hippocampus reveals interference between memory systems. *Hippocampus*, *12*, 280–284.

Schmaltz, L., & Theios, J. (1972). Acquisition and extinction of a classically conditioned response in hippocampectomized rabbits (*Oryctolagus cuniculus*). *Journal of Comparative and Physiological Psychology*, *79*, 328–333.

Shohamy, D., Allen, M., & Gluck, M. (2000). Dissociating entorhinal and hippocampal involvement in latent inhibition. *Behavioral Neuroscience*, *114*, 867–874.

Shohamy, D., Myers, C., Onlaor, S., & Gluck, M. (2002). L-*Dopa impairs associative learning in Parkinson's disease*. Cognitive Neuroscience Society Abstracts. San Francisco.

Solomon, P., & Moore, J. (1975). Latent inhibition and stimulus generalization of the classically conditioned nictitating membrane response in rabbits (*Oryctolagus cuniculus*) following dorsal hippocampal ablation. *Journal of Comparative and Physiological Psychology*, *89*, 1192–1203.

Solomon, P., & Staton, D. (1982). Differential effects of microinjections of d-amphetamine into the nucleus accumbens or the caudate putamen on the rat's ability to ignore an irrelevant stimulus. *Biological Psychiatry*, *17*, 743–756.

Squire, L. (1987). *Memory and brain*. New York: Oxford University Press.

Squire, L. (1994). Declarative and nondeclarative memory: Multiple brain systems supporting learning and memory. In D. Schacter, E. Tulving (Eds.), *Memory systems* (pp. 203–231). Cambridge, MA: MIT Press.

Squire, L., & Zola-Morgan, S. (1996). Structure and function of declarative and non-declarative memory systems. *Proceedings of the National Academy of Sciences USA*, *93*, 13515–13522.

Sutherland, R., & Rudy, J. (1989). Configural association theory: The role of the hippocampal formation in learning, memory and amnesia. *Psychobiology*, *17*, 129–144.

Teyler, T., & DiScenna, P. (1986). The hippocampal memory indexing theory. *Behavioral Neuroscience*, *100*, 147–154.

Tulving, E., & Markowitsch, H. (1998). Episodic and declarative memory: Role of the hippocampus. *Hippocampus*, *8*, 198–204.

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale-Revised*. New York: The Psychological Corporation.

Wechsler, D. (1987). *Wechsler Memory Scale-Revised*. San Antonio, TX: The Psychological Corporation.

Weiner, I. (1990). Neural substrates of latent inhibition: The switching model. *Psychological Bulletin*, *108*, 442–461.

Weiner, I., Lubow, R., & Feldon, J. (1988). Disruption of latent inhibition by acute administration of low doses of amphetamine. *Pharmacology and Biochemistry of Behavior*, *30*, 871–878.

Weiskrantz, L., & Warrington, B. (1979). Conditioning in amnesic patients. *Neuropsychologia*, *17*, 187–194.

Westwater, H., McDowall, J., Siegert, R., Mossman, S., & Abernathy, D. (1998). Implicit learning in Parkinson's disease: Evidence from a verbal version of the serial reaction time task. *Journal of Clinical and Experimental Neuropsychology*, *20*, 413–418.

White, N., & McDonald, R. (2002). Multiple parallel memory Systems in the brain of the rat. *Neurobiology of Learning and Memory*, *77*, 125–184.

Wylie, S., & Stout, J. (2002). Enhanced negative priming in Parkinson's disease. *Neuropsychology*, *16*, 242–250.

Zola, S., & Mahut, H. (1973). Paradoxical facilitation of object reversal learning after transection of the fornix in monkeys. *Neuropsychologia*, *11*, 271–284.