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Intact Acquisition and Long-Term Retention of Mirror-Tracing Skill in Alzheimer's Disease and in Global Amnesia

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The ability of patients with Alzheimer's disease (AD) or global amnesia (AMN) to acquire skill for tracing a pattern seen in mirror-reversed view and to retain that skill over 24-hr intervals was examined. Both patient groups had poor recall and recognition of their mirror-tracing experience, but they acquired and retained mirror-tracing skill as well as normal control subjects. One AMN patient (H.M.) retained the skill over a year-long interval. Furthermore, the patients transferred their skill normally to an alternate pattern. These results indicate that the memory system underlying mirror-tracing skill learning is separable from medial-temporal structures compromised in AMN and AD and from neocortical areas compromised in AD. Brain regions relatively spared in early AD, such as the basal ganglia or cerebellum, may mediate critical aspects of the learning of novel sensorimotor associations that underlie skilled mirror tracing.

Alzheimer's disease (AD) is an age-related neurodegenerative disorder that impairs many domains of cognition, especially the learning of new information. AD patients have impaired recall and recognition of materials or experiences even after delays as short as a few seconds (e.g., Corkin, 1982). Experimental examinations of learning in AD patients, however, have revealed intact memory for certain kinds of experience in at least three domains. One domain is that of perceptual aftereffects such as the McCollough effect (Savoy & Gabrieli, 1991). A second domain consists of some kinds of repetition priming, in which learning is measured as a change in the processing of a stimulus because of prior exposure to that stimulus (e.g., Gabrieli et al., 1992, in press; Keane, Gabrieli, Fennema, Growdon, & Corkin, 1991).

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The third domain of preserved learning in AD is sensorimotor skill learning, which is measured as improved speed and accuracy in the execution of a sensorimotor task across repeated trials. AD patients have shown intact skill learning on two sensorimotor tasks: rotary pursuit (Eslinger & Damasio, 1986; Heindel, Butters, & Salmon, 1988; Heindel, Salmon, Shults, Walicke, & Butters, 1989) and serial reaction time (SRT; Knopman, 1991; Knopman & Nissen, 1987). In performing the rotary pursuit task, subjects try to maintain contact between a handheld stylus and a target metal disk the size of a nickel on a revolving turntable. With practice control subjects demonstrate skill learning by increasing the time per trial that they are able to maintain contact with the disk. AD patients showed normal rotary pursuit skill learning across trials and normal retention of that skill after intervals of 20 min (Eslinger & Damasio, 1986) and 30 min (Heindel et al., 1988, 1989).

Some AD patients have also shown intact skill learning on the SRT task. On each trial of the SRT task, a light appears at one of four possible locations on a computer monitor. Subjects respond by pressing one of four keys with each key placed directly below one of the four monitor locations. As soon as a light appears, subjects press the corresponding key. Subjects make few errors, and the measure of performance is the speed of response. In the first study examining SRT skill learning in AD, subjects were given five blocks of 100 trials each. Trials in the first four blocks were arranged in a repeating 10-trial sequence. The trials in the last block appeared randomly in the four locations (i.e., without any repeating pattern). Control subjects improved the speed of their reaction times across the four blocks of repeating trials. The increased speed of response was attributed to subjects' learning a sequence-specific skill because their reaction times slowed sharply in the final (random) block of trials. Although slower overall than control subjects, AD patients improved their speed of response at a normal rate across the repeating-sequence blocks and showed the typical slowing for the final block of random trials (Knopman & Nissen, 1987). The conclusion that SRT skill learning is intact in AD was weakened by the fact that 9 of the 28 AD patients failed to show evidence of sequence-specific learning because those patients had response times in the final (ran-

dom) block that were as fast or faster than those in the last block of the repeating-sequence trials. Another study reported intact SRT learning only in AD patients with very mild dementia; slightly more demented AD patients had impaired learning (Ferraro, Balota, & Connor, 1993). A third study examined SRT skill retention in AD patients and found that those who showed normal SRT learning in an initial test session retained the pattern-specific skill normally over a 1- to 2-week delay (Knopman, 1991). Although the preservation of SRT skill learning appears more variable in AD patients than that of rotary pursuit skill learning, both sorts of skill-learning studies indicate that AD patients can learn and retain some new skills.

Our study examined the ability of patients with AD or global amnesia (AMN) to acquire and retain over 24 hr a third kind of sensorimotor skill, mirror tracing. Mirror tracing was first used with a memory-impaired patient by Milner (1962) in her study of the AMN patient H.M. His severe and global anterograde AMN followed a radical bilateral medial temporal lobe resection of the anterior hippocampal complex, the amygdala, and some surrounding tissue (Scoville & Milner, 1957). H.M. traced a star reflected in a mirror on multiple trials on 3 consecutive days. This task requires subjects to inhibit and reverse powerful associations between vision and motor control of hand and arm movements. (In contrast, rotary pursuit and SRT learning do not appear to demand such direct reversal of overlearned sensorimotor mapping.) Initially, subjects perform the task slowly and make frequent errors by departing from the pattern, but with practice they gain a skill for mirror tracing. Subjects can then trace the star more quickly with fewer errors. Despite severe memory impairment, H.M. showed improved performance across trials each day. It is even more remarkable that he retained his skill from one day to the next and to an apparently normal extent.

Even as H.M. showed proficiency in mirror tracing, he failed to remember explicitly his previous experience with the task. The striking dissociation between spared sensorimotor skill learning and compromised recall and recognition launched the search for preserved learning in memory-disordered patients. It is these results that guide most modern theories of the neurological organization of memory (e.g., Cohen & Squire, 1980; Gabrieli, 1991; Schacter, 1990; Squire, 1992; Tulving, 1985). There has been, however, only one other case study of mirror tracing in a memory-impaired patient: A patient with AMN following bilateral thalamic infarction showed normal acquisition of mirror-tracing skill (Nichelli, Bahmanian-Behbahani, Gentilini, & Vecchi, 1988).

Our study resembled Milner's (1962) investigation in that subjects traced a star seen in mirror-reversed view on 3 consecutive days, but it expanded on her work in four ways. First, we examined mirror-tracing learning in groups of AD and AMN patients, including H.M. Second, we included formal measures of recall and recognition of prior mirror-tracing sessions. Milner's study of H.M. and the study of Nichelli et al. (1988) omitted formal testing of recall or recognition for the prior mirror-tracing sessions, largely because the severity of AMN in each case was well documented and more careful measurement seemed unnecessary. Although this assumption may hold for those case studies, it cannot be made for all AMN and AD patients because the nature and severity of memory dysfunction may vary. Third, we examined H.M.'s long-term retention of the mirror-tracing skill by testing him after delays of 1 week, 2 weeks, and about 1 year. Fourth, we included a second pattern at the beginning and end of the 3-day protocol to examine whether patients could transfer their skill between different patterns in a normal fashion. It has been suggested that at least some types of learning in memory-disordered patients are unusually inflexible or hyperspecific (Glisky, Schacter, & Tulving, 1986). A striking example of such hyperspecificity comes from another study of H.M., in which he was trained over many trials to learn a short path in a stepping-stone maze (Milner, Corkin, & Teuber, 1968). When attempting to learn a longer path that included the shorter path, he failed to exhibit any transfer to the part of the longer path identical to the previously learned shorter path. If such hyperspecificity characterizes skill learning in either AD or AMN patients, then transfer between patterns should be impaired.

The preservation of rotary pursuit and SRT learning in AD patients suggests that such patients may be able to acquire and retain mirror-tracing skill. AD patients, however, have shown a complex pattern of impaired and intact learning capacities. For example, AD patients have shown intact repetition priming on some, but not all, tasks that have revealed normal priming in AMN. AD patients, like AMN patients in previous studies, show intact magnitudes of priming on tasks requiring stimulus identification, such as perceptual identification of words and pseudowords, and the identification of complete or fragmented pictures (e.g., Gabrieli et al., 1992, in press; Keane et al., 1991). Unlike AMN patients, however, AD patients have impaired priming on tasks that require generation, such as word stem completion and word associate generation (e.g., Gabrieli et al., 1992, in press; Heindel et al., 1989; Huff, Mack, Mahlmann, & Greenberg, 1988; Keane et al., 1991; Salmon, Shimamura, Butters, & Smith, 1988; Shimamura, Salmon, Squire, & Butters, 1987). It is unknown whether AD selectively compromises some forms of skill learning preserved in AMN, as it does some forms of repetition priming, and whether mirror tracing elicits intact or impaired skill learning in AD.

Method

Subjects

The three groups of subjects were 9 patients with AD[1], 8 normal control (NC) subjects who did not differ significantly from the AD patients in age or educational level, and 3 nondemented AMN patients.

[1] About half of the AD patients who met our inclusion and exclusion criteria could not perform the mirror-tracing task. Those patients were unable to complete the first trial, and after about 10 min we ended the testing. Patients who could move more than a few inches in the first trial were able to complete all 21 trials. Failure was not associated with variables we examined (e.g., severity of dementia). Patients who could not perform the task may have had particular impairments in relevant domains of cognition, such as apraxia or spatial disorientation, or they may have been less tolerant of the frustration that often accompanies performance at the beginning of mirror tracing.

AD patients. The 4 men and 5 women in this group were referred from the Memory Disorders Unit of the Massachusetts General Hospital and met National Institute on Aging and National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria for the diagnosis of probable AD (Khachaturian, 1985; McKhann et al., 1984). These patients had clinical assessments demonstrating progressive worsening of memory and other cognitive functions and an absence of other brain diseases or systemic disorders that could account for the progressive deficits in memory and cognition. The assessment of patients included a neurological examination, cognitive tests, either magnetic resonance imaging or computerized tomography, and blood laboratory tests. Inclusion criteria required patients to obtain scores below 20 on the Blessed Dementia Scale (BDS; Blessed, Tomlinson, & Roth, 1968) and below 6 on the Hachinski Ischemic Scale (Hachinski et al., 1975). Consecutive patients who met the above inclusion–exclusion criteria and who were able to perform the cognitive tests were asked to participate in our study. The AD group had a mean age of 71.9 years (range 61–87) and a mean educational level of 12.9 years (range 8–18). The severity of dementia ranged from mild to moderate as indicated by BDS scores (range = 9–18.5; M = 14.1). Not one of the subjects was institutionalized.

NC subjects. The NC group consisted of spouses of the AD patients, spouses of patients participating in other studies at the Massachusetts Institute of Technology Clinical Research Center, and subjects recruited through newspaper notices. The NC group included 3 women and 5 men with a mean age of 66.0 years (range = 58–74) and a mean educational level of 13.4 years (range = 12–16).

AMN patients. We studied 3 AMN patients. One was H.M., age 60 at the time of testing. He had undergone bilateral medial temporal lobe resection in 1953 at age 27 in an attempt to alleviate otherwise intractable epilepsy (Scoville, Dunsmore, Liberson, Henry, & Pepe, 1953). The surgical removal was estimated to extend 8 cm back from the tips of the temporal lobes, including the prepyriform gyrus, uncus, amygdala, hippocampus, and parahippocampal gyrus. Temporal neocortex was reported to have been spared. Since the resection H.M. has had a severe and pervasive anterograde AMN (Corkin, 1984; Milner et al., 1968; Scoville & Milner, 1957). The 2nd AMN patient was a 61-year-old woman who became amnesic following a bilateral stroke of the posterior cerebral arteries. The 3rd AMN patient was a 50-year-old man whose amnesia followed a herpes simplex encephalitis infection. Both had bilateral lesions of medial temporal lobe regions. (See Corkin et al., 1985, for additional information about these 3 patients.)

Materials

The mirror-tracing apparatus consisted of an aluminum plate on which nonconducting tape was placed in one of two patterns: a six-pointed star (similar to Milner, 1962) or a double hexagon with the same number of sides and angles as the star. One pattern at a time was mounted on a wooden board hidden from the subjects' view by a near-vertical metal barrier. Subjects had to reach around the metal barrier, and they were able to see the pattern and their hand only in a mirror mounted on the far side of the wooden board. For each trial, a counter recorded the number of times subjects went off the pattern (errors). A timer recorded the total duration of time off the pattern, and a stopwatch recorded the time to complete tracing of the pattern.

Two questionnaires measured subjects' cued recall and recognition of their experience in doing the task. In the cued recall questionnaire, subjects answered eight questions read aloud by the examiner. Two questions called for a yes or no response: "Have you been in this room before?" and "Have you ever seen this apparatus?" The other six questions were open ended. They asked (a) when and for how long they had last performed with the apparatus, (b) which hand or hands had been tested, (c) what position they had been in when performing the task, and (d) what sounds had been heard during the test (because the counter made a clicking sound with each error). The recognition questionnaire consisted of 10 multiple-choice versions of the questions from the cued recall questionnaire as well as pictorial multiple-choice displays from which subjects had to select the apparatus they had used (among four photographs of different testing apparatuses) and the two patterns they had traced (among eight patterns). Subjects filled out the recognition questionnaire and received assistance as needed from the examiner. Chance performance on the recognition questionnaire was 24%. (It is impossible to estimate chance performance on the cued recall questionnaire.)

Table 1
Percentage Correct for Normal Control (NC), Alzheimer's Disease (AD), and Amnesic (AMN) Groups on Tests of Cued Recall and Recognition Memory for Mirror-Tracing Experience

	Cued recall		Recognition	
Group	Day 2	Day 3	Day 2	Day 3
NC (n = 8)				
M	97.3	100.0	90.0	91.8
SD	5.1	0.0	12.9	7.8
AD (n = 9)				
M	66.7	81.7	64.3	70.1
SD	33.0	15.6	21.9	11.9
AMN (n = 3)				
M	57.0	49.7	59.3	55.7
SD	24.5	15.3	17.2	11.5

Procedure

Subjects held the stylus in their preferred hand. They were told to trace around the pattern from a starting mark and to work as quickly and accurately as possible. Testing consisted of one session per day for 3 consecutive days with seven trials per session. Subjects traced the double hexagon on the first trial on Day 1 and the last trial on Day 3. They traced the star on all other trials. The recall and recognition questionnaires were administered in that order at the beginning of the Day 2 and Day 3 sessions. H.M., who was tested initially in 1962 (Milner, 1962), was retested in our study. He received the standard 3-day protocol and was retested after delays of 1 week (Day 10), 2 more weeks (Day 25), and almost a year (Days 358 and 359).

Results

The scores of the AD and NC groups were compared statistically. Because there were only 3 AMN patients, we examined the performance of that group descriptively.

Cued Recall and Recognition

The cued recall and recognition questionnaires were scored as percentage of correct answers (see Table 1). The results were analyzed in two repeated measures analyses of variance (ANOVAs) with factors of group (AD and NC) and day (Day 2 and Day 3). The NC subjects (mean of 98.7% correct) recalled significantly more about their mirror-tracing experience than did the AD patients (mean of 74.2% correct), $F(1, 15) = 11.85$, $p < .01$. The NC subjects (mean of 90.9% correct) also were significantly more accurate in recognizing correct information about their mirror-tracing experience than were the AD

patients (mean of 67.2% correct), $F(1, 15) = 16.78, p < .01$. Of the three groups, the AMN group had the worst memory for the mirror-tracing experience with an overall score (average of cued recall and recognition scores) of 55.4% in comparison with 70.7% for the AD patients and 94.8% for the NC subjects. The ceiling performance of the NC subjects indicates that the magnitude of the patients' deficits was underestimated.

Mirror Tracing: Skill Learning

The three skill-learning measures were completion time (number of seconds taken to trace a pattern), errors (number of contacts with the metal plate signifying departures from the pattern), and time off (number of seconds spent off the pattern). Preliminary analyses indicated that the raw data for all three measures had large variances, especially for the AD patients. Consequently, analyses were performed both on the raw data and on log-transformed data, in which variances decreased to statistically acceptable levels. We report the analyses of the log-transformed data only; analyses of the raw data yielded essentially identical outcomes.

The three sets of skill-learning scores were analyzed in separate repeated measures ANOVAs with factors of group (AD and NC), day (Day 1, Day 2, and Day 3), and trial (seven trials per day; see Figure 1). Subjects showed skill learning by tracing the patterns progressively faster across days, $F(2, 30) = 77.14$, $p < .001$, and trials, $F(6, 90) = 33.89$, $p < .001$, by making fewer errors across days, $F(2, 30) = 70.79$, $p < .001$, and trials, $F(6, 90) = 12.11$, $p < .001$, and by decreasing the time off pattern across days, $F(2, 30) = 52.84$, $p < .001$, and trials, $F(6, 90) = 15.92$, $p < .001$. For all three learning measures, there were Day × Trial interactions indicating that within-day improvement across trials decreased across days: for completion time, $F(12, 180) = 8.46$, $p < .001$; for errors, $F(12, 180) = 3.75$, $p < .001$; for time off, $F(12, 180) = 6.46$, $p < .001$. There was no main effect of group on any skill-learning measure and, most important, no interaction between group and either trial or day, or both, thus indicating that the AD and NC groups improved similarly on mirror tracing. The learning of the AMN group was similar to that of the AD and NC groups (see Figure 2).

We conducted a separate analysis focusing on the most sensitive measures of skill retention, the first trials on Days 2 and 3. Trials 8 and 15 occurred 24 hr after Trials 7 and 14 and thus reflected only long-term retention; in contrast, the remaining trials on Days 2 and 3 included across-day and within-day learning. We performed separate ANOVAs with repeated measures on the three learning measures (completion time, errors, and time off) with factors of group (AD and NC) and trial (Trial 7 and Trial 8 or Trial 14 and Trial 15). None of these analyses yielded a reliable difference between the AD and NC groups. The AMN group showed similarly good across-day retention on most measures, except that they showed a small increase in time off from Trial 7 to Trial 8, whereas the AD and NC groups had small decreases in time off from Trial 7 to Trial 8. The AMN patients, however, showed greater improvement than any other group in time off from Trial 14 to Trial 15. Thus, overall, the AMN patients showed across-day retention that was similar to that of the AD and NC groups.

Mirror Tracing: Transfer Between Patterns

We examined transfer of the mirror-tracing skill between patterns in several ways (see Table 2). First, we focused on transfer of the mirror-tracing skill between the two different patterns at the beginning (Trials 1 and 2 on Day 1) and end (Trials 20 and 21 on Day 3) of testing. Separate ANOVAs with repeated measures were performed on the three learning measures (completion, errors, and time off) with factors of group (AD and NC) and trial (Trial 1 and Trial 2 or Trial 20 and Trial 21). From Trial 1 (double hexagon) to Trial 2 (star), subjects improved their performance by tracing more quickly, $F(1, 15) = 23.33$, $p < .001$; reducing the number of errors, $F(1, 15) = 15.35$, $p < .01$; and reducing time spent off the pattern, $F(1, 15) = 15.17$, $p < .001$. In no analysis of Trials 1 and 2 was there an effect of group or an interaction between group and any skill-learning measure. These results suggest that AD patients transferred their early learning from the double hexagon to the star in a way comparable to NC subjects.

Subjects transferred their mirror-tracing skill from Trial 20 (star) to Trial 21 (double hexagon) without increasing significantly either the number of errors or the time spent off the pattern. Subjects, however, slowed their completion times by an average of 7.7 s, $F(1, 15) = 10.66$, $p < .01$, which suggests that there was some consequence of changing the patterns. There was a significant interaction between group and trial on time off, $F(1, 15) = 5.38$, $p < .05$, with the AD patients decreasing time off (from 2.6 s to 2.1 s) and NC subjects increasing time off (from 0.8 s to 1.7 s) across the two trials. There was also a marginal interaction between group and trial for number of errors, $F(1, 15) = 3.11$, $p < .10$, with the AD patients decreasing their errors (from 8.1 to 6.1) and NC subjects increasing their errors (from 2.9 to 5.4). There was no group effect in any analysis, and no other interaction was significant. Thus, it appears that the AD patients had normal, or slightly better than normal, transfer of mirror-tracing skill from Trial 20 to Trial 21.

A final analysis examined learning from Trial 1 to Trial 21, the two trials with the double hexagon. Both AD and NC subjects reduced their time around, $F(1, 15) = 132.86$, $p < .001$, reduced time spent off the pattern, $F(1, 15) = 102.51$, $p < .001$, and decreased their numbers of errors, $F(1, 15) = 98.20$, $p < .001$. In no analysis was there a main effect of group or an interaction between trial and group. The 3 AMN patients transferred their mirror-tracing skill across patterns similarly to the way the NC and AD groups did.

Lasting Skill Retention in H.M.

H.M. performed the mirror-tracing task according to the standard 3-day protocol and was retested after delays of 1 week (Day 10), 2 more weeks (Day 25), and almost a year (Days 358 and 359). By all measures of performance, he demonstrated nearly complete retention of the mirror-tracing skill that he had acquired in the initial 3 days of practice (see Figure 3).

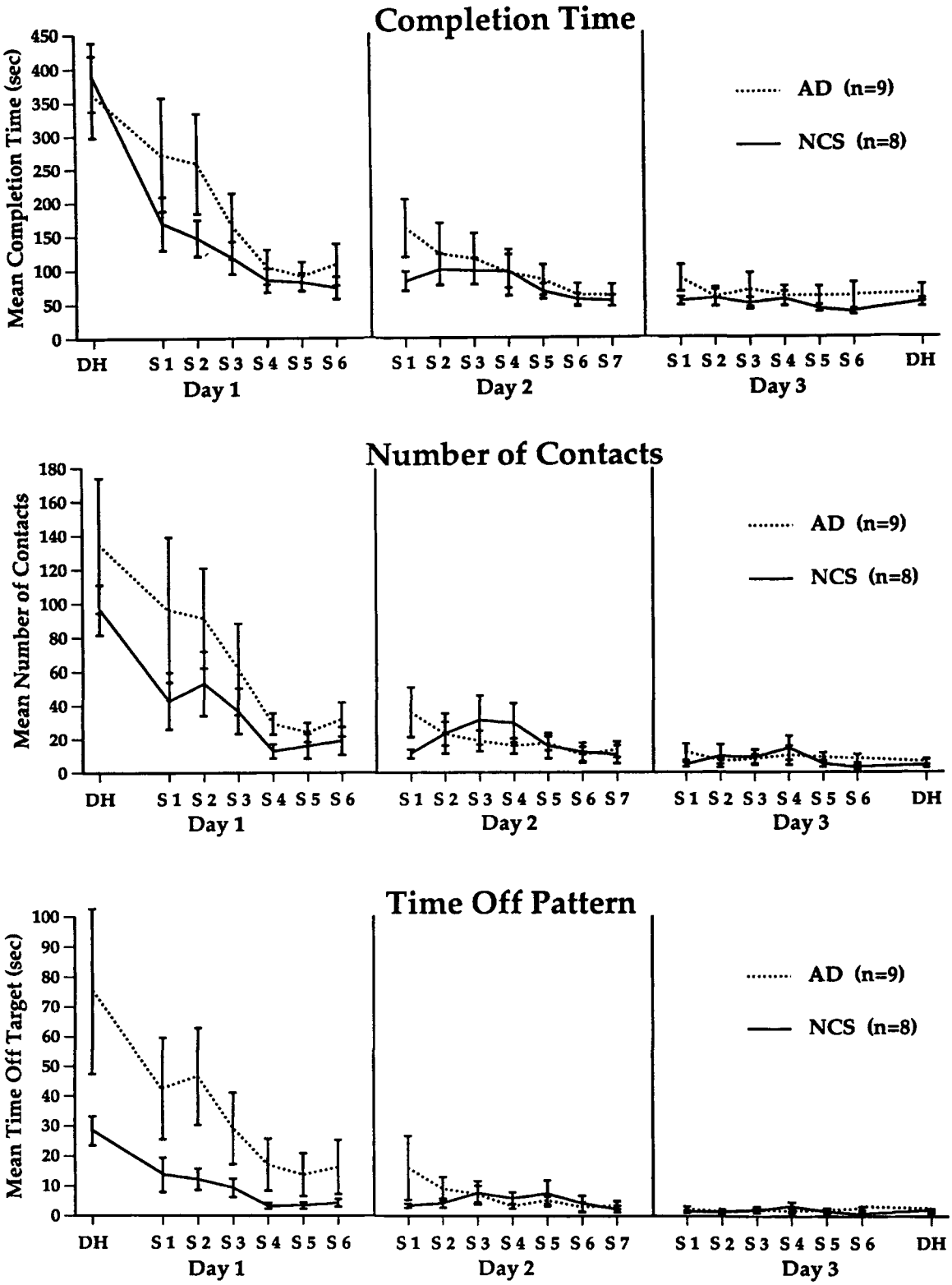

Figure 1. Mirror-tracing results for patients with Alzheimer's disease (AD) and normal control subjects (NCS). (Top: Mean time to trace double hexagon [DH] and star [S] patterns for seven consecutive trials on each of 3 consecutive days. Middle: Mean number of contacts for the same subjects on the same trials. Bottom: Mean time spent off pattern for the same subjects on the same trials. Brackets show standard errors of the mean.)

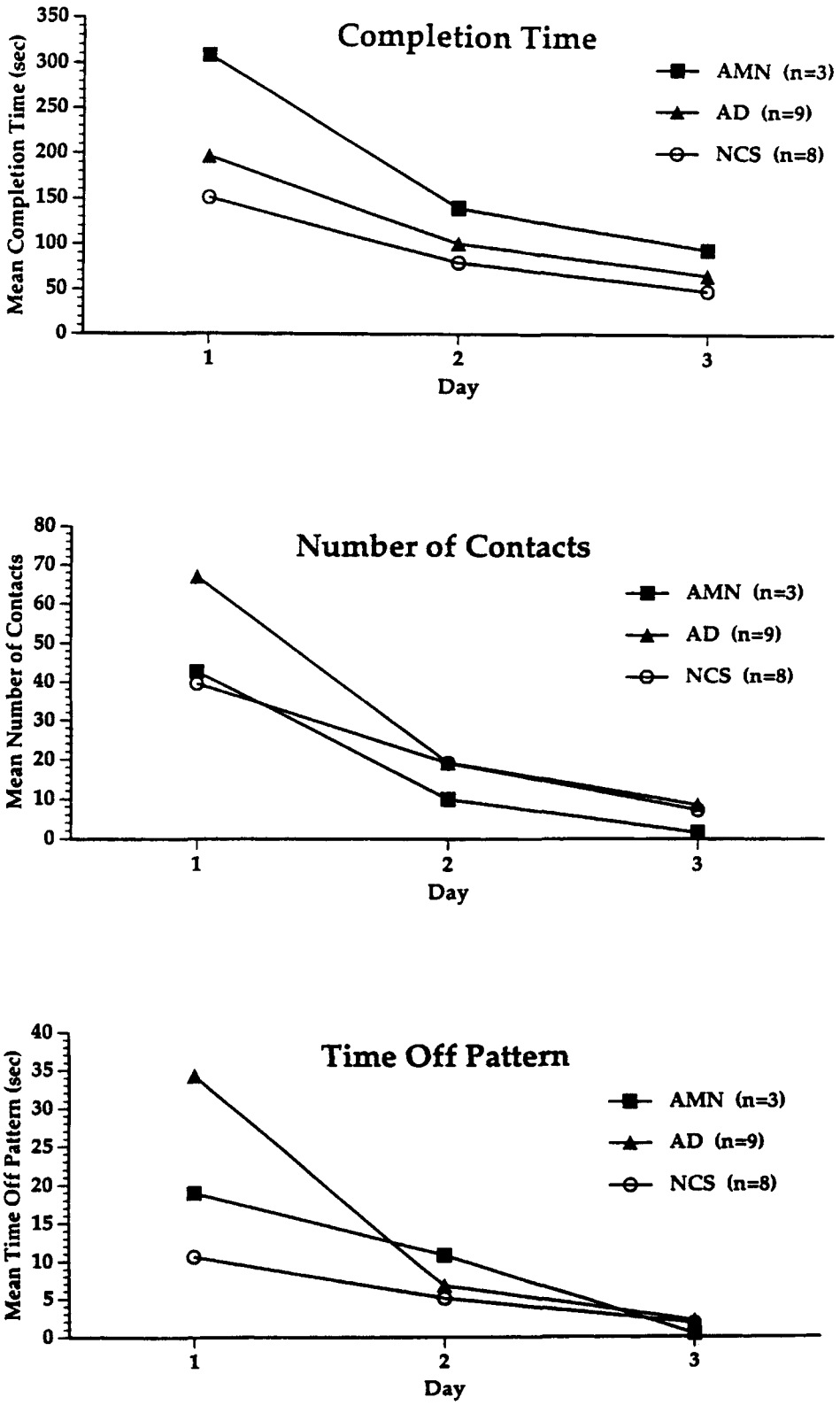

Figure 2. Mirror-tracing results for patients with circumscribed global amnesia (AMN), patients with Alzheimer's disease (AD), and normal control subjects (NCS). (Top: Mean time to trace patterns on each of 3 consecutive days. Middle: Mean number of contacts for the same subjects on the same trials. Bottom: Mean time spent off pattern for the same subjects on the same trials.)

Discussion

Our four main goals were to assess the status of mirror-tracing skill learning in AD and AMN, to dissociate empirically mirror-tracing skill learning from recall and recognition memory, to examine the long-term retention of mirror-tracing skill in memory-disordered patients, and to discover whether memory-disordered patients can transfer their newly acquired mirror-tracing skills between patterns. By all analyses the AD and AMN groups acquired and retained skilled mirror-tracing abilities normally. The patients did so despite greatly impaired recall and recognition of the materials with which, and the episodes in which, they had gained those skills. Both AD and AMN patients retained their newly acquired skills after 24-hr intervals, and H.M. retained his skill after an almost year-long interval. Patients transferred their skill from one pattern to another as well as did control subjects.

The finding of preserved mirror-tracing skill learning is in accord with prior studies of sensorimotor skill learning in AMN and AD. As in previous single case studies (Milner, 1962; Nichelli et al., 1988), the 3 AMN patients showed apparently normal skill learning. The sparing of mirror-tracing skill learning in early AD is consistent with the sparing of other sensorimotor learning abilities in AD (Eslinger & Damasio, 1986; Heindel et al., 1988, 1989; Knopman, 1991; Knopman & Nissen, 1987).

The long-term retention of newly learned skills in memory-disordered subjects is striking because of the pathologically poor retention of information that such patients show in daily life. One-week retention of SRT skill learning has been shown in AD patients (Knopman, 1991) and in AMN patients (Nissen, Willingham, & Hartman, 1989). H.M. retained the rotary pursuit skill completely after a 7-day interval (Corkin, 1968), and a group of AMN patients retained their skill for reading mirror-reversed text after a 93-day interval (Cohen & Squire, 1980). H.M.'s near total retention of his mirror-tracing skill after a 333-day interval underscores the long-lasting nature of such acquired skills. It is difficult to compare meaningfully H.M.'s mirror-tracing performance 30 years ago with his more recent performance in attempting to discern whether he had some savings over this long interval. What is clear in our study is that, although H.M. fails to learn what year it is even after a year's worth of exposure to that information, some intact memory system forgets nothing about mirror-tracing over that same interval.

AD and AMN patients showed the normal pattern of almost complete transfer of acquired mirror-tracing skill between two different patterns. This finding may appear to be at variance with examples of poor transfer shown by AMN patients. H.M. failed to transfer his knowledge of a short maze route, which he had acquired through many repetitions, to that same route when it was part of a longer maze route (Milner et al., 1968). Other AMN patients have shown abnormally poor transfer when completing sentences with computer terminology words that they had been trained to learn previously (Glisky et al., 1986). These two examples of impaired transfer may be said to indicate a hyperspecificity in AMN learning. Both examples, however, emerged from learning situations in which intensive drilling was used to compensate for otherwise impaired learning. H.M., for example, has shown greatly impaired maze learning under a variety of conditions (Corkin, 1968; Milner, 1962, 1965) and greatly impaired vocabulary learning under both laboratory and more natural conditions (Gabrieli, Cohen, & Corkin, 1988). Poor transfer of learning in those studies suggests that an unusual inflexibility of acquired information characterizes forms of learning that depend on impaired memory mechanisms. Impairment of those mechanisms was evident in the poor initial learning shown by AMN patients. Apparently, the intensive, compensatory drilling that raised AMN performance to a particular criterion did not produce a normal representation of the newly acquired knowledge. Rather, some abnormal, hyperspecific representation that satisfied the criterial measure of memory was created. The abnormality of that representation became manifest when H.M. and other amnesic patients could not transfer normally, or could not transfer at all, their newly acquired knowledge to satisfy a closely related but different mnemonic criterion.

Table 2
Measures of Transfer of Mirror-Tracing Skill Within and Between Patterns by Normal Control (NC), Alzheimer's Disease (AD), and Amnesic (AMN) Groups

Trials compared/ Measure of transfer	Group NC (n = 8)	AD (n = 9)	AMN (n = 3)
1[a] and 21[a] (same pattern)			
Time around (s)	329	305	592
Time off (s)	27	73	37
Errors (no. of contacts)	91	128	95
1[a] and 2[b] (different pattern)			
Time around (s)	209	96	336
Time off (s)	15	33	21
Errors (no. of contacts)	54	38	48
20[b] and 21[a] (different pattern)			
Time around (s)	−13	−3	−9
Time off (s)	−1	1	0
Errors (no. of contacts)	−3	2	2

Note. Scores are differences calculated by subtracting the mean of the second trial from the mean of the first trial in each comparison. The higher the score, the better the transfer. Negative scores indicate performance decrements between patterns.
[a]Star pattern. [b]Double-hexagon pattern.

In contrast, the normal flexibility exhibited by AMN patients in our study appears characteristic of preserved domains of learning in AMN patients, such as the transfer of reading inverted letters across different words (Cohen & Squire, 1980) or cross-modal transfer on a repetition priming task (e.g., Graf, Shimamura, & Squire, 1985). In those cases of normal transfer and flexibility, AMN patients showed normal rates of initial learning and did not require extra training to reach normal levels of performance. Thus, hyperspecificity may be a characteristic of learning that depends on residual recall and recognition abilities in AMN patients. This idea is similar to the hypothesis that AMN patients, especially those with hippocampal dysfunction, have a deficit in relational memory (Eichenbaum & Cohen, 1988). Our study shows that AD patients, who have many deficits beyond memory, can also show normal transfer in a preserved domain of learning.

In fact, AD and AMN patients appeared to show slightly

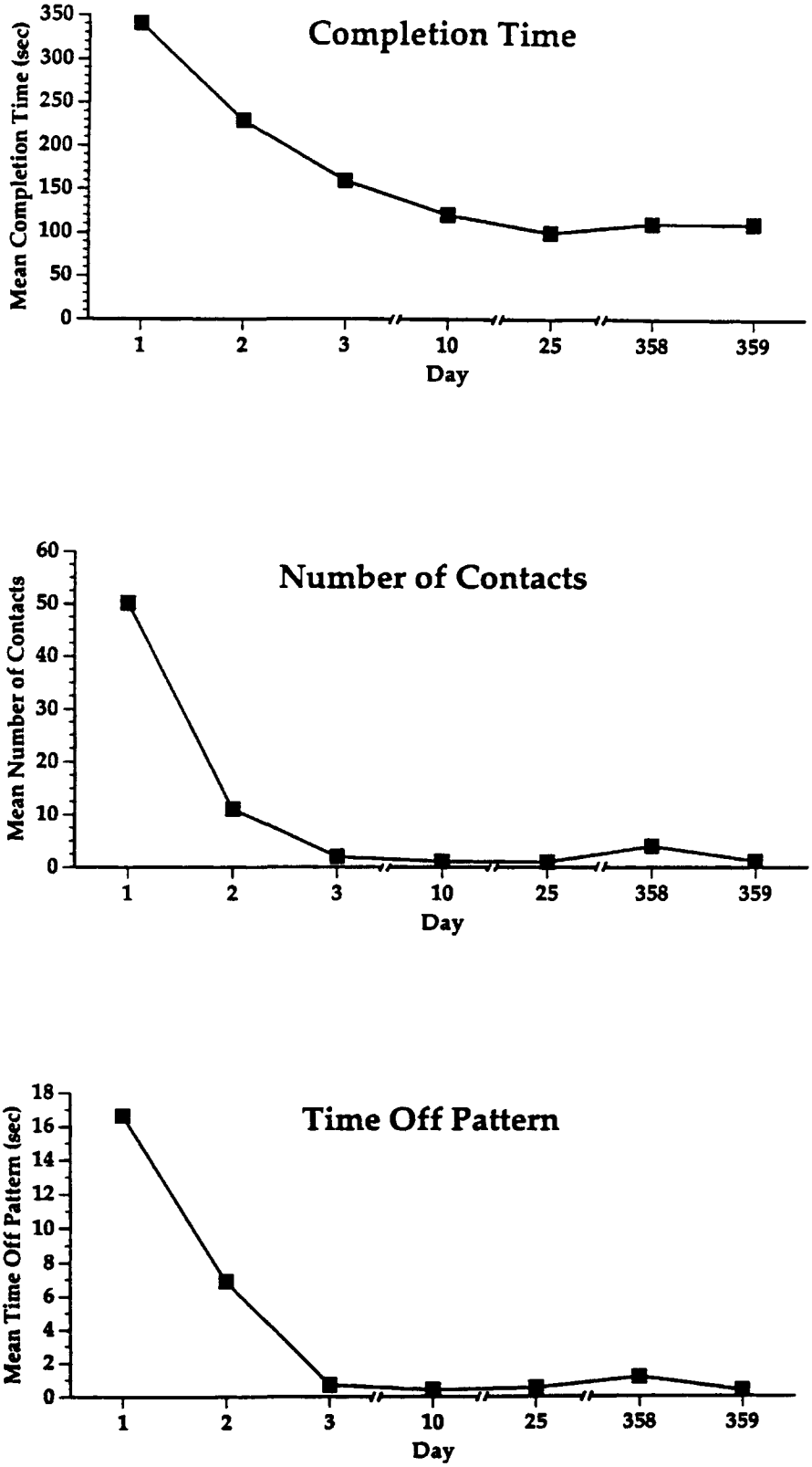

Figure 3.. Mirror-tracing results for H.M. (Top: Mean completion time per day for 3 consecutive days and after intervals of 1 week, 2 weeks, and nearly 1 year. Middle: Mean number of contacts for the same trials. Bottom: Mean time spent off pattern for the same trials.)

better transfer than NC subjects on the last two trials. This finding raises the possibility that intact recollection of 19 mirror-tracing trials with the star pattern hindered, to a small extent, NC subjects' transfer of mirror-tracing skill to the double hexagon. The hindrance could have resulted if NC subjects took advantage of, or believed incorrectly that they took advantage of, recollection of their mirror-tracing experience with the star pattern when tracing that pattern. NC subjects' recollection of tracing the star pattern, however, must have had little, if any, real effect on their star pattern mirror-tracing performance; otherwise, NC subjects would have shown better skill learning than AD and AMN patients, who had severely impaired recollection of their mirror-tracing experience with the star pattern.

All subjects appeared to transfer their mirror-tracing skill between patterns. Such transfer raises the question about the basis of mirror-tracing skill. One basis may be the learning of a general transformational rule that guides the reversal between the usual relation of visual input to motor output. Such a general rule would allow a subject to apply skill acquired from any pattern to any other pattern. An alternative basis could be the learning of specific visual-input-to-motor-output associations. In that case, subjects would learn different visual–motor associations for tracing lines of different orientations and perhaps different directions of movements. Although the basis of mirror-tracing skill has not been well characterized, one study examining mirror-tracing skill in normal subjects found evidence that mirror-tracing skill is orientation specific, that is, subjects who practiced mirror tracing a line at one orientation showed little transfer of skill when subsequently tracing another line at a different orientation (Willingham, Huber, Spear, & Gabrieli, 1991). Such evidence favors the idea that mirror-tracing skill is based on a set of specific associations rather than a general transformational rule (but see Cunningham, 1989, for evidence that newly learned visual–motor maps can develop general transformational rules). The patterns used in our study did not provide a test of the competing explanations of mirror-tracing skill because each pattern included line segments of a variety of orientations. The transfer we found, therefore, may have been not so much from one pattern to another as from specific line segments in one pattern to specific line segments in the other pattern; an analogous finding for specific learning underlying what appears to be generalized skill learning has been found by Masson (1986) for the reading of mirror-reversed text.

The dissociation between impaired recall and recognition (knowing that) and intact skill learning (knowing how) has been interpreted as reflecting distinctions between memory systems that acquire declarative or explicit knowledge versus those that acquire procedural or implicit knowledge (Cohen & Squire, 1980; Graf & Schacter, 1985). Our results are in accord with those dichotomies because the AMN and AD patients were impaired on the explicit tests of declarative knowledge (i.e., the cued recall and recognition tests) but unimpaired on the implicit tests of procedural knowledge (i.e., the skill learning measures of speed and accuracy). Limbic structures in the medial temporal lobe and related diencephalic and basal forebrain structures are thought to be essential for declarative or explicit memory. The 3 AMN patients in our study and AD patients characteristically have marked hippocampal lesions (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991; Brun & Englund, 1981; Hyman, Van Hoesen, Damasio, & Barnes, 1984), and AD patients have substantial damage to the basal forebrain (Whitehouse, Price, Struble, & Clark, 1982). Clearly these brain structures, whose integrity is vital for recall and recognition, are not important for learning mirror-tracing skill.

More recent experimental work has gone beyond the declarative–procedural and explicit–implicit dichotomies by revealing multiple dissociations among implicit or procedural forms of memory, with the different forms of memory preserved in AMN being variably affected by Alzheimer's, Parkinson's, and Huntington's diseases (e.g., Gabrieli et al., 1992, in press; Harrington, Haaland, Yeo, & Marder, 1991; Heindel et al., 1989; Keane et al., 1991). Consideration of the typical pathology in AD may provide some suggestion about the neural substrate of mirror-tracing skill. AD patients, unlike patients with circumscribed AMN, have substantial damage to frontal, temporal, and parietal neocortical regions (e.g., Arnold et al., 1991; Brun & Englund, 1981). Damage to these areas leads to widespread and substantial cognitive deficits in AD, but it appears to have little or no effect on the acquisition or retention of mirror-tracing skill. There are, however, some brain regions that are relatively unaffected in AD and that may mediate components of sensorimotor skill acquisition in mirror tracing. Such areas include primary motor, visual, and somatosensory neocortical regions, the basal ganglia, the thalamus, and the cerebellum.

Among these areas, there are theoretical and experimental sources of evidence indicating that the basal ganglia and the cerebellum may play important roles in some forms of skill learning. The theoretical evidence comes from Mishkin and his collaborators (Mishkin & Petri, 1984; Mishkin, Malamut, & Bachevalier, 1984), who, on the basis of animal research and anatomical connectivity, suggested that habits are learned and memories are retained by separable cortico-striatal and cortico-limbic systems. Mishkin and Petri also pointed to the cerebellum as a potential locus of habit learning. It now appears that multiple brain regions acquire and retain different kinds of habits in humans. For example, repetition priming appears to be a habit learned by neither cortico-striatal nor cortico-limbic systems but rather by cortico-cortical systems (e.g., Gabrieli et al., 1992, in press; Heindel et al., 1989; Keane et al., 1991; Shimamura et al., 1987). Mishkin's proposal, however, has received considerable support concerning striatal and cerebellar contributions to human skill learning.

Experimental evidence for the importance of the basal ganglia in human skill learning comes from studies of patients who have striatal abnormalities because of Huntington's disease (HD) or Parkinson's disease (PD). HD patients have shown selective impairments on several skill-learning tasks that had been learned well by AMN or AD patients, including reading mirror-reversed text (Martone, Butters, Payne, Becker, & Sax, 1984), rotary pursuit (Heindel et al., 1988, 1989), and SRT (Knopman & Nissen, 1991). PD patients have shown a more complex pattern of intact and impaired skill-learning capacities. Nondemented PD patients have shown intact rotary pursuit learning, but demented PD patients learned rotary pursuit poorly (Heindel et al., 1989). Another study

found impaired rotary pursuit learning in PD patients only on the 2nd and 3rd day of a 3-day protocol (Harrington et al., 1991). Nondemented PD patients have also shown impaired SRT learning (Ferraro et al., 1993). In addition to showing sensorimotor learning deficits, nondemented PD patients and some HD patients did poorly in learning a problem-solving skill relative to normal subjects and AMN patients (Saint-Cyr, Taylor, & Lang, 1988).

The exact relationship between the basal ganglia and skill learning remains unknown. It is likely that there are multiple forms of skill learning (e.g., Harrington et al., 1991), that different structures within the basal ganglia contribute differentially to specific aspects of skill learning, and that structures outside the basal ganglia also affected in HD and PD are also important for skill learning. In broad terms, nevertheless, the frequent link between basal ganglia injury and impaired skilled learning (and the characteristic sparing of that brain region in AMN and AD) nominates the basal ganglia as a potentially important region for learning the mirror-tracing skill.

Another brain structure that may be important for mirror-tracing skill learning is the cerebellum. Four patients with olivopontocerebellar atrophy syndrome (OPCA), who had lesions in the brain stem and cerebellum, showed poor learning on a mirror-tracing task (Sanes, Dimitrov, & Hallet, 1990). Patients with lesions limited to the cerebellar hemispheres, the vermis, or both did not have particular difficulties with mirror-tracing learning, which suggests important roles for the climbing fiber inputs from the inferior olive and mossy fiber inputs from the pontine nuclei to Purkinje cells in the cerebellar hemispheres (inputs that were likely damaged in the OPCA patients). Cerebellar patients have also been reported to show impaired motor adaptation in other altered visual environments (Gauthier, Hofferer, Hoyt, & Stark, 1979; Weiner, Hallett, & Funkenstein, 1983) and impaired visually guided tracking (Beppu, Nagaoka, & Tanaka, 1987; Beppu, Suda, & Tanaka, 1984). H.M.'s good performance on the mirror-tracing task is pertinent to consideration of the cerebellum because he has atrophy of the vermis and more marked atrophy of the cerebellar hemispheres (Corkin, 1984). His intact skill learning, therefore, supports the claim that the cerebellar hemispheres are not critical for learning mirror-tracing skill. OPCA is a complex and variable degenerative disorder; therefore, it is difficult to be certain which parts of or connections with the cerebellum are critical for mirror-tracing skill learning (also, other structures are often damaged in these patients, including the substantia nigra). Cerebellar brain regions are relatively spared in AD, and they could have contributed to intact mirror-tracing skill learning.

A recent positron emission tomography study is relevant because it examined which neural brain regions were activated, as measured by increased relative cerebral blood flow, when normal subjects performed rotary pursuit across a number of trials (Grafton, Mazziotta, Presty, Friston, Frackowiak, & Phelps, 1992). Motor execution (the difference between rotary pursuit performance and a baseline condition) was associated with cortical, nigrostriatal, and cerebellar activation. Activation in the latter two regions is consistent with evidence from the patient studies reviewed above. Skill learning, however, was linked with increasing activation in primary motor cortex, the supplementary motor area, and the pulvinar thalamus contralateral to the hand used to do the task. These results suggest that contributions from the cerebellum and basal ganglia may be important in the formation, and perhaps early expression, of newly acquired skills but that the long-term memory underlying skilled performance is located cortically. In that case, the cerebellum and basal ganglia may play roles in skill learning somewhat analogous to the role of the hippocampus in declarative memory. The hippocampus appears to be necessary for the acquisition and early expression of declarative memories, but the final locus of well-established declarative information appears to be neocortical (Squire & Zola-Morgan, 1991; Zola-Morgan & Squire, 1990).

Most of the neuropsychological studies reviewed above did not examine mirror tracing. Thus, one can only speculate at present in regards to their implications for identifying the distributed neural network that mediates the mirror-tracing skill, much less for characterizing the different roles played by specific components of that network in performance and in learning. The apparently normal ability of the AD patients suggests that structures relatively unaffected in AD may mediate a great deal of mirror-tracing skill learning. Our results show clearly that the integrity of brain regions critical for recall and recognition memory, language, attention, reasoning, and other cognitive faculties is not required for the robust acquisition of a mirror-tracing skill that is retained over long periods and that is flexible in transfer between patterns.

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1994 APA Convention "Call for Programs"

The "Call for Programs" for the 1994 APA annual convention appears in the September issue of the *APA Monitor*. The 1994 convention will be held in Los Angeles, California, from August 12 through August 16. The deadline for submission of program and presentation proposals is December 3, 1993. Additional copies of the "Call" are available from the APA Convention Office, effective in September. As a reminder, agreement to participate in the APA convention is now presumed to convey permission for the presentation to be audiotaped if selected for taping. Any speaker or participant who does not wish his or her presentation to be audiotaped must notify the person submitting the program either at the time the invitation is extended or before the December 3 deadline for proposal submission.