Selectively Impaired Associative Learning in Older People with Cognitive Decline

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Abstract

■ Older people with declining cognitive function typically display deficits in declarative memory processes, often most evident on tests of associative learning (AL). The hippocampal formation (HF) is thought to be critically involved in the encoding and retrieval of such associations, consistent with neuroimaging findings that the HF is damaged in early stages of neurodegenerative disease and in older people with AL impairments. In the clinic, older people with cognitive decline commonly report difficulties associating names with faces. However, we have observed that such people are particularly impaired on tests requiring the association of novel stimuli. In Experiment 1, a series of AL tasks were administered to older people with cognitive decline to determine whether they were impaired at simply making associations, or at making associations between novel stimuli. In Experiment 2, we measured HF function in these subjects by administering an AL task designed to differentiate between HF-damaged and HF-intact individuals. Our experimental protocols were guided by a computational model of HF function in AL described by Gluck and Myers (1997). Older people with cognitive decline displayed impaired performance on tasks designed to be highly dependent upon intact HF function, including a task in which novel patterns and spatial locations were to be associated. These results suggest that the AL impairments observed in older people with cognitive decline may be due to HF dysfunction. ■

INTRODUCTION

Impairment in the ability to learn associations between stimuli is observed consistently in older people with mild cognitive impairment (MCI; Collie et al., in press; Petersen et al., 1999). Neurophysiological and neuroanatomical evidence from humans and nonhuman primates, as well as computational models of medial temporal lobe function, suggest that one role of the hippocampal formation (HF) is to facilitate such associative learning (AL; Eichenbaum, 2000; Henke, Weber, Kneifel, Wieser, & Buck, 1999; Wallenstein, Eichenbaum, & Hasselmo, 1998; Squire & Zola-Morgan, 1991). Further, these studies suggest that the HF is necessary for learning arbitrary relationships between stimuli. Therefore, one explanation for the AL deficits observed in older people with MCI is that they are a consequence of HF dysfunction. This is consistent with neuropsychological evidence that cognitive decline is restricted to episodic memory in individuals who later progress to Alzheimer's Disease (AD) and to neuroimaging findings of HF atrophy in both MCI and early AD (Collie & Maruff, 2000; Jack et al., 1999).

Models of AL in humans are derived partly from cognitive investigations of individuals with hippocampal region damage caused by insult (e.g., temporal lobe epilepsy, surgery) or neurodegenerative disease (e.g., AD). However, brain damage in these individuals is rarely limited to the HF. Disruptions to other brain regions may give rise to cognitive impairments that distort the magnitude or specificity of the AL deficit observed in such patients, and, thus, the interpretation of results from studies of brain damaged individuals may be problematic. Ideally, models of AL should be informed by results from studies in individuals with isolated HF damage, or, alternatively, by studies of patients who show specific impairments in AL.

Recently, we identified a group of older people with consistent and significant cognitive decline (Collie et al., in press). The majority of individuals with such impairments develop AD within a 4–5-year period (Petersen et al., 1999), and display reductions in hippocampal volume, in the absence of damage to other brain regions (Jack et al., 1999). In light of these findings, we have hypothesized that progressive cognitive decline in older people (in the absence of other medical or psychiatric conditions) may be indicative of a neurodegenerative process that is limited to the HF (Collie et al., in press). Consistent with this proposal, the predominant impairments in this group appear to involve learning and

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remembering events and episodes (episodic or explicit memory; Collie & Maruff, 2000). In our group, this episodic memory impairment is most reliable and robust on tasks that require AL (Collie et al., in press). Older individuals with cognitive decline may therefore be an ideal group in which to develop cognitive neuroscientific models of AL.

We sought to determine the conditions under which AL deficits occur in older individuals with cognitive decline. Recent findings strongly suggest that the HF is involved in novelty detection (Knight, 1996) and spatial navigation (Maguire, Burgess, & O'Keefe, 1999). It was therefore hypothesized that older people with cognitive decline, and proposed HF dysfunction, would display AL impairments most prominently on tasks containing novel stimuli, or stimuli presented in a spatial context.

EXPERIMENT 1

As stated, we recently observed AL impairments in older people with cognitive decline (Collie et al., in press). These impairments occurred on a task shown previously to be sensitive to the early stages of AD (Fowler, Saling, Conway, Semple, & Louis, 1997). This task requires the association of novel and unnameable stimuli (abstract patterns and spatial locations). In contrast, one of the difficulties reported earliest by older people with MCI and early AD is an inability to associate names and faces. Although this subjective complaint may also be considered an AL deficit, there are important differences between face–name and abstract pattern–location associations. For example, face–name associations are more practiced than pattern–location associations, as such associations are made many times each day. Experiment 1 aimed to determine the conditions under which older people with cognitive decline show impaired AL. Three AL tasks were administered: face–name, pattern–location, and pattern–word. It was hypothesized that impairments of greatest magnitude would be observed in the cognitive decline group when the stimuli to be associated were novel and unfamiliar (pattern–location task).

Results

No significant differences were observed between groups on demographic variables, or on neuropsychological tests of working memory, planning and problem solving, praxis, and verbal fluency and naming (Table 1). Consistent with the selection criteria, individuals with cognitive decline recorded poorer performance on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) word list delayed recall (WLDR) test than healthy matched control subjects, and a highly significant difference was observed between groups on the longitudinal slope of WLDR test performance.

Analysis of variance (ANOVA) revealed significant main effects of Group [F(1,31) = 5.51, p = .03; η^2 = 0.15] and Task [F(2,30) = 14.52, p < .001; η^2 = 0.36], as well as a significant Group×Task interaction [F(2,30) = 4.92, p = .04; η^2 = 0.12]. Post hoc t tests indicated that on the pattern–location AL task, subjects with cognitive decline made significantly more errors than controls. The effect sizes associated with these differences were small according to conventional statistical criteria (Table 2; Hinkle, Wiersma, & Jurs, 1994). In contrast, no group differences were observed on the face–name and pattern–word AL tasks. Post hoc t tests also revealed that the cognitive decline group made more errors on the pattern–location task than on the face–name [t(15) = 4.89, p < .001] and pattern–word tasks [t(15) = 2.31, p = .04], and more errors on the pattern–word than on the face–name task [t(15) = 2.80, p = .01]. In contrast, the matched control group made an equal number of errors on the pattern–location and pattern–word tasks [t(15) = .05, p = .96], but significantly more errors on these tasks than on the face–name task [pattern–location, t(15) = 3.77, p < .01; pattern–word, t(15) = 2.37, p = .03)]. The significant Group × Task interaction was investigated further by calculating difference scores

Table 1. Summary Demographic and Neuropsychological Data for Cognitive Decline and Matched Control Groups

	Matched Control	*Cognitive Decline*	*p Value*
n	16	16	
Age (years)	69.00 (5.15)	69.20 (7.28)	.98
Education (years)	11.66 (3.71)	12.50 (3.14)	.48
Sex (men/women)	6/10	7/9	
NART IQ	120.23 (7.21)	118.96 (9.32)	.36
CERAD subtests			
MMSE score	28.96 (1.14)	28.41 (1.62)	.19
WLDR score	9.00 (1.27)	6.77 (2.33)	.00
WLDR slope	0.21 (0.17)	−0.32 (0.27)	.00
Verbal fluency	22.42 (6.71)	20.17 (3.67)	.12
Naming	14.42 (0.79)	13.94 (1.02)	.14
Constructional praxis	9.47 (1.23)	9.59 (1.42)	.79
CANTAB subtests			
SWM search errors	24.54 (11.49)	24.93 (9.42)	.92
SWM strategy count	34.62 (3.71)	34.79 (3.45)	.90
TOL excess moves	11.85 (7.82)	13.43 (7.11)	.59

All data are reported as means (±*SD*). NART = National Adult Reading Test; MMSE = Mini-Mental State Examination; WLDR = Word List Delayed Recall Test; CERAD = Consortium to Establish a Registry for Alzheimer's disease test battery; CANTAB = Cambridge Neuropsychological Test Automated Battery; SWM = Spatial Working Memory test; TOL = Tower of London Test.

Table 2. Experiment 1: Performance of Cognitive Decline (n = 16) and Matched Control (n = 16) Groups on Pattern–Location, Face–Name, and Pattern–Word Associative Learning Tasks

AL Task	*Matched Control*	*Cognitive Decline*	*p Value*	*Effect Size*
Pattern–location errors	9.14 (6.16)	17.67 (10.51)	.01	0.24
Face–name errors	3.64 (3.08)	4.60 (3.81)	.46	0.02
Pattern–word errors	9.00 (7.61)	10.27 (7.99)	.66	0.01

All data are reported as means (±*SD*); AL = Associative Learning.

(errors on one task minus errors on another task) for each subject. Three difference scores were calculated for: (1) pattern–location errors minus face–name errors; (2) pattern–location errors minus pattern–word errors; and (3) pattern–word errors minus face–name errors. For each calculation, a positive value indicated more errors on the first named AL task, and a negative value more errors on the second named AL task. Independent samples t tests conducted on these data revealed that the cognitive decline group (mean = 13.07; *SD* = 10.35) had a significantly larger difference between their errors on the pattern–location and face–name AL tasks than the healthy control group [mean = 5.50; *SD* = 5.45; $t(30) = 2.45$, $p = .02$]. The cognitive decline group (mean = 7.40; *SD* = 12.41) also had a greater difference between their errors on the pattern–location and pattern–word AL tasks than the matched control group (mean = .14; *SD* = 9.65), however, this difference did not reach significance [$t(30) = 1.75$, $p = .09$]. No between group differences were observed for the face–name/pattern–word comparison [cognitive decline (mean = 5.67; *SD* = 7.84); matched control (mean = 5.36; *SD* = 8.54); $t(30) = .10$; p = 92].

Discussion

In Experiment 1, individuals with cognitive decline were observed to have poorer performance on a test of pattern–location AL than matched controls. However, no differences between these two groups were observed on tests of face–name and pattern–word AL (see Table 2). These results may be explained by the differences between the AL tasks administered in Experiment 1. The stimuli for the face–name task are encountered daily and may invoke cognitive processing other than that required to simply make an association (George et al., 1999). This task may therefore be less difficult than the pattern–location AL task, where the stimuli are abstract and unfamiliar. Similarly, the pattern–word task may also be considered a "practiced" task. In addition, the combination of spatial localization and abstract pattern recognition in the pattern–location task may have contributed to these results, given the role of the HF in spatial navigation (Maguire et al., 1999) and novelty detection (Knight, 1996), and the finding of HF atrophy in mildly impaired older people (Jack et al., 1999). This hypothesis is supported by the observation that both groups made more errors to pattern–location associations than to face–name associations, and that the magnitude of this difference was greater in the cognitive decline group. These results are consistent with the hypothesis that the HF is necessary for making arbitrary associations between abstract stimuli (Gluck & Myers, 1997).

An alternative explanation for these results is that the cognitive decline group performed poorly on the pattern–location task because it is more difficult than the other tasks. However, data from the control group suggest that the pattern–word and pattern–location tasks are equally difficult. Therefore, if the control data are taken as a de facto index of task difficulty, the dissociation observed in the cognitive decline group cannot be due to task difficulty. In addition, the performance of the cognitive decline group was equal to that of controls on difficult tasks of frontal lobe function.

EXPERIMENT 2

In Experiment 1, AL impairments were observed among individuals with cognitive decline only when the stimuli to be associated were novel and presented in dispersed spatial locations. The aim of Experiment 2 was to induce similar impairments using familiar, nonspatial stimuli in an AL task derived from anatomical and physiological observations of HF function, and designed to differentiate HF-intact from HF-damaged individuals.

Recently, Gluck and Myers (1997) developed a computational model of hippocampal function in AL. This cortico-hippocampal model has been shown to account for data from classical eyeblink conditioning studies in both animals and humans and, more recently, for cognitive data collected from normal humans and patients with medial temporal lobe amnesia (Myers, Gluck, & Granger, 1995; Myers et al., 2000). The specifics of this model have been described in detail elsewhere (Gluck & Myers, 1997) and will not be reiterated here. However, one of the predictions made by the cortico-hippocampal model is pertinent to the current study. The Gluck–Myers' model states that in order to learn that one stimulus (S1) predicts, or is associated with, another (S2), the individual must map the stimulus representation of S1 to an outcome (in this case S2). If two separate stimuli have similar representations, then the associations learned for one (S1a) are easily applied to the other (S1b). The cortico-hippocampal model predicts that if the two stimuli are to be associated with the same future stimuli (S2), then such stimulus compression (or generalization) is beneficial, and that learning associations can be facilitated if common underlying features

of the two similar stimuli (S1a and S1b) are identified. The Gluck–Myers model therefore predicts that the HF can selectively compress the representations of stimuli that are associated with the same future stimuli. A closely related function of the HF is to differentiate, or distinguish between, the representations of stimuli that are associated with different future stimuli. That is, if two similar stimuli (S1a and S1c) are to be associated with different future stimuli (S2 and S3, respectively), then compression of those two stimuli is not beneficial. In this case, the learning of associations is facilitated if the two stimulus representations S1a and S1c are differentiated.

In Experiment 2, we administered an AL task designed to assess the individual's ability to both compress stimulus representations that predict associations accurately and to differentiate stimulus representations that do not predict associations accurately. It was hypothesized that the cognitive decline group would perform poorly on this task relative to the healthy control group. According to the Gluck–Myers model, such a result would indicate that the cognitive decline group has impaired HF function.

Results

All subjects completed all phases of the task successfully. For the number of errors made in Phases 1–3, ANOVA revealed significant main effects of Group [$F(1,31) = 16.43$, $p < .001$; $\eta^2 = 0.35$] and Phase [$F(2,30) = 3.62$, $p = .04$; $\eta^2 = 0.20$], and a significant Group × Phase interaction [$F(2,30) = 3.83$, $p = .03$; $\eta^2 = 0.21$]. The same pattern of results was observed for the number of trials required to complete Stages 1–3 [Group: $F(1, 31) = 13.98$, $p = .001$, $\eta^2 = 0.32$; Phase: $F(2,30) = 10.94$, $p < .001$, $\eta^2 = 0.43$; Group × Phase: $F(2,30) = 3.47$, $p = .04$, $\eta^2 = 0.19$]. As significant interactions were observed, univariate tests of significance were conducted to determine the direction and magnitude of the main effects and interactions. Table 3 displays the data for these comparisons. There were no differences between cognitive decline and healthy control subjects on either the error score or the number of trials taken to complete Phase 1. Subjects with cognitive decline made significantly more errors and required significantly more trials to complete Phase 2 than healthy control subjects. For Phase 3, subjects with cognitive decline again made significantly more errors and required significantly more trials to complete the phase than control subjects. The effect sizes associated with these differences were greater than in Phase 2 but still small according to conventional statistical criteria (Hinkle et al., 1994). Although subjects with cognitive decline made more errors in total than the matched control subjects on Phase 4, this difference was not significant. However, a significant Phase 4 difference was observed when the number of errors to associations presented in Phases 1–3 were calculated for both groups, with the cognitive decline group making a greater number of errors than matched control groups (Table 3). No group differences were observed for the 12 newly presented associations in Phase 4. Interestingly, while the number of errors made by the cognitive decline subjects did not change between Phases 3 and 4 [$F(1,15) = 0.0$, $p = 1.0$], the matched control subjects made significantly more errors in Phase 4 than in Phase 3 [$F(1,15) = 9.95$, $p = .005$; $\eta^2 = 0.36$].

Table 3. Experiment 2: Performance of Cognitive Decline ($n = 16$) and Matched Control ($n = 16$) Groups on the Acquired Equivalence Task

	Matched Control	*Cognitive Decline*	*p Value*	*Effect Size*
Phase 1				
Errors	2.06 (2.51)	3.00 (2.68)	.31	0.03
Trials	12.42 (5.56)	14.69 (6.66)	.30	0.03
Phase 2				
Errors	2.00 (1.83)	6.85 (8.69)	.02	0.16
Trials	14.32 (5.82)	25.00 (19.77)	.03	0.14
Phase 3				
Errors	1.95 (2.32)	10.62 (12.20)	.005	0.24
Trials	21.32 (13.10)	44.61 (30.55)	.006	0.23
Phase 4				
Total errors (48 trials)	6.16 (5.16)	10.62 (7.69)	.06	0.11
"Old" errors (36 trials)	2.42 (3.63)	6.31 (5.23)	.02	0.17
"New" errors (12 trials)	3.74 (2.83)	4.31 (3.17)	.59	0.01

Group data are reported as means (±*SD*); for Phase 4, "Old" errors represents the number of errors made on associations learned in Phases 1–3, while "New" errors represents the number of errors made on associations presented for the first time in Phase 4.

For both cognitive decline and healthy control groups, correlations between the clinical (WLDR test and slope) and Experiment 1 outcome measures were generally negative and small to moderate in magnitude. However, with one exception these correlations were not significant, perhaps due to the small sample size. Correlations between clinical and Experiment 2 outcome measures were more variable.

Discussion

In Experiment 2, as the number of associations required for phase completion increased from two (Phase 1) to

four (Phase 2) to six (Phase 3), older people with cognitive decline made increasingly more errors and took longer to learn all associations. In contrast, control subjects were able to compress the associated stimuli into single stimulus representations, allowing a reduction in the number of associations required for completion of Phases 2 and 3. This facilitated performance on the task such that there was no increase in the number of errors made or the number of trials to completion in Phases 1–3 in control subjects. In Phase 4, cognitive decline subjects made more errors than controls on associations that they had learned to use as criteria in Phases 1–3, but not on newly presented associations, suggesting that cognitive decline subjects forgot the associations more quickly during the interphase interval. The pattern of AL deficits observed in the cognitive decline group in Experiment 2 is consistent with the type of impairments predicted by the Gluck–Myers cortico-hippocampal model to occur in individuals with HF damage.

When considered in conjunction with Experiment 1 results, the results of Experiment 2 provide further opposition to the hypothesis that the observed group differences are due to task difficulty. For example, the cognitive decline group performed more poorly than controls in Experiment 2 when only four associations were required, yet performed equally to controls in Experiment 1 when eight associations were required on the pattern–word and face–name tasks. Our proposal that the Experiment 1 tasks were more difficult than the Experiment 2 (Phases 2 and 3) tasks is supported by data from the control group, in which a greater number of errors were recorded on Experiment 1 tasks than in Phases 1–3 of the Experiment 2 task.

GENERAL DISCUSSION

Consistent with the findings of previous cognitive and neuroimaging research (Jack et al., 1999; Petersen et al., 1999), the results of this study suggest that AL impairments in older people with cognitive decline may be a consequence of HF dysfunction. Many previous neuroimaging and patient studies have demonstrated that the HF is important in AL (Henke et al., 1999; Dolan & Fletcher, 1997). As already stated, Gluck and Myers (1997) have proposed that one role of the HF in AL is to compress stimulus representations that overlap and predict a common outcome (in this case an associated stimulus). This stimulus compression aids AL when the individual is presented with more than one association. However, in Experiment 1, the stimuli presented in the pattern–location and pattern–word tasks do not overlap on any dimension and so are not able to be compressed. While the face stimuli presented in the face–name task may be compressed (hair color, sex), in no case do they predict a common outcome and therefore stimulus compression will not aid AL on this task. According to the Gluck–Myers model, individuals with cognitive decline (and hippocampal atrophy) should display impaired performance on all of these AL tasks relative to normal older people. This prediction proved accurate for the pattern–location task but failed to explain results from the face–name and pattern–word tasks. One potential reason for this discrepancy is that the ''practiced'' nature of the pattern–word and face–name tasks may have facilitated performance. Alternatively, performance on the face–name and pattern–word tasks may be mediated partly by cognitive processes other than those required to make an association (e.g., language, face recognition; George et al., 1999), whereas performance on the pattern–location task may only be mediated by cognitive processes dependent upon the HF. This interpretation of the results of Experiment 1 is supported by the results of Experiment 2, where the cognitive decline group displayed impairments predicted by Gluck and Myers (1997) to occur in individuals with HF damage. Further, in the cognitive decline group, performance on pattern–location (Experiment 1) and acquired equivalence (Experiment 2) tasks were correlated more strongly with decline than performance on pattern–word and face–name tasks. This suggests that the former tasks are more sensitive to the brain dysfunction underlying cognitive decline than the latter tasks. Considered together, this pattern of results is consistent with those expected to occur in HF-damaged individuals. These findings therefore support the proposal that the HF is critically involved in AL, and also that the HF is damaged in older people with declining cognitive function.

Implicit within the Gluck–Myers theory is that the compression of stimuli that predict similar future outcomes is nondeclarative and performed automatically by the intact hippocampus (Myers et al., 2000). However, such stimulus compression may also be performed as part of a strategy when task difficulty is low. An alternative explanation of the results of Experiment 2 is therefore that the healthy control group may have developed a strategy that facilitated their performance on the acquired equivalence task. The formation and execution of such strategies is dependent upon areas within the prefrontal cortex (Mesulam, 1998). Prefrontal damage and impairments on tasks of executive function have been observed in older people with MCI and early AD (Hanninen et al., 1997). The impaired performance in the cognitive decline group in Experiment 2 may therefore reflect disruption to prefrontal, rather than hippocampal, areas. However, the cognitive decline group displayed normal performance on tests of executive function (Table 1), suggesting that there was no disruption to prefrontal cortical areas in this group. Therefore, the AL impairments cannot be attributed to group differences in the formation and execution of a performance strategy.

Recent functional neuroimaging studies observe maximal hippocampal activation in normal individuals when

the stimuli to be learned are novel, but activation of other brain regions (e.g., dorsolateral prefrontal cortex) in response to the recombination of previously presented stimuli (Cohen et al., 1999; Strange, Fletcher, Henson, Friston, & Dolan, 1999; Dolan & Fletcher, 1997). Similarly, the hippocampus is purported to be involved in spatial learning and spatial localization (Maguire et al., 1999). Therefore, the findings in Experiment 1 that the cognitive decline group make disproportionately more errors on a task that requires multiple HF functions suggest that they have impaired HF function. These findings also suggest that tasks sensitive to hippocampal function may provide the best and earliest behavioral indication of cognitive decline in older people. Computational models of brain function may provide a useful theoretical framework in which to conduct behavioral and neuroimaging investigations of both normal and impaired individuals. In particular, functional neuroimaging studies may benefit from careful consideration of the predictions made by computational models prior to the design of tasks aimed at assessing the function of particular cortical and subcortical structures.

In conclusion, we have confirmed that older people with cognitive decline are impaired at tasks that require AL. However, this AL deficit appears to be specific to tasks that require the association of novel stimuli in a spatial context (Experiment 1), or to tasks designed to discriminate between HF-damaged and HF-intact individuals (Experiment 2). These findings are consistent with the proposal that the HF is involved in AL and suggest that the cognitive decline that occurs in some older people may be a consequence of impaired hippocampal function.

METHODS

Experiment 1

Subjects

Sixteen subjects with cognitive decline and 16 matched control subjects participated in this study. Cognitive decline subjects were selected using the method described by Collie et al. (in press) and outlined below. Control subjects were individually matched to the cognitive decline subjects on age, education, and gender. Table 1 displays summary demographic and cognitive data for both groups. All subjects were recruited from an ongoing study of aging conducted at independent research institute in Melbourne, Australia. All subjects spoke English as their first language. All subjects had been identified and screened for their involvement in a prior study (Collie et al., in press), however, a detailed medical history was taken from each subject prior to the administration of the experimental paradigms described here. Subjects were excluded from the study if they had a history of head injury, substance abuse, epilepsy, or any systemic medical condition that could cause cognitive impairment or brain dysfunction. Subjects were also excluded if they had a personal or family history of psychiatric or neurological illness including dementia, or were taking medication that may either enhance or be detrimental to cognitive function. Our recruitment protocol did not include brain imaging to rule out alternative etiologies (e.g., vascular) for the cognitive impairments observed in this study, however, individuals with a personal history of cardiovascular illness, as well as those at high risk for cardiovascular illness (i.e., high blood pressure, extensive family history) were excluded. Inclusion criteria for the aging study included age greater than 50 years, a Mini-Mental State Examination (MMSE) score >25, and a normal neurological examination. Informed consent was obtained from all participants prior to inclusion in the study.

Materials and Procedure

Subject selection. Prior to participation, all subjects were assessed semiannually for a period of 2–4 years. At each assessment, all subjects completed the CERAD neuropsychological test battery (Morris, Mohs, Rogers, Fillenbaum, & Heyman, 1988). The WLDR test of this battery was used to classify subjects. Each subject's performance on the five most recent administrations of the WLDR test was plotted as a function of time. A least-squares linear regression equation was fitted to these data and a line of best fit calculated. The slope of this line was used to classify subjects as declining (slope less than zero) or normal controls (slope equal to or greater than zero). Prior research indicates that the expected longitudinal pattern of performance on the WLDR test in normal older people assessed semiannually is one of improvement due to practice (McCaffrey, Duff, & Westervelt, 2000). Consistent with this, in a recent publication, we observed an average rate of improvement in normal older people of 0.55 words per year (of a maximum 10 words) over a 2-year period (Collie et al., in press).

Subject assessment. Prior to the administration of the experimental procedures, all subjects completed a screening battery consisting of the CERAD neuropsychological tests and the Spatial Working Memory and Tower of London tests from the Cambridge Neuropsychological Test Battery (CANTAB; Owen, Sahakian, Semple, Polkey, & Robbins, 1995). Three tests of AL were then administered to both cognitive decline and matched control subjects. The first test was a pattern–location AL task taken from the CANTAB. The second and third tests were face–name and pattern–word AL tasks developed independently in our laboratory using E-Prime software (Psychology Software Tools, 2000).

For the pattern–location task, eight filled white boxes were presented around the edge of the computer screen. At the beginning of a trial, each box opened for

2 sec, in random order, to reveal an abstract pattern. Each box was then closed so that its contents were no longer visible. A 2-sec delay was given between the closing of one box and the opening of the next. Subjects were instructed to remember which spatial location (box) contained which abstract pattern. After all of the patterns had been shown, a single pattern was presented in the center of the computer screen, identical to one of the patterns just shown. The subject was then required to touch the box that contained the identical pattern. Another pattern was then presented in the center, and the subject was required to touch the box that contained that pattern. This was repeated until all eight pattern–location associations had been remembered correctly. If the subject made an error, the trial was repeated. Subjects were allowed up to 10 trials to learn a single set of pattern–location associations. For the face–name task, eight unfamiliar faces were presented consecutively in the center of the computer screen for two seconds each. Each face was paired with a common Anglo-Australian name. These face–name pairs were presented in random order, and a 2-sec delay was given between the offset of one face–name pair and the onset of the next. After all pairs had been shown, a single face was presented in the center of the computer screen, and the subject was required to say the name associated with that face. Another face was then shown, and the subject was required to say the name associated with that face. This procedure was repeated until all eight associations had been made correctly. If the subject made an error, the trial was repeated. Subjects were allowed up to 10 trials to learn the face–name associations. The procedure for the pattern–word task was identical to that for the face–name task, except that the stimuli presented consisted of abstract patterns (in place of faces) and common words (in place of names). For all tasks, the number of errors was recorded.

Data Analysis. Prior to analysis, the distribution of data for all tasks was inspected for normality and heterogeneity of variance. A Group (2: cognitive decline; matched control) × Task (3: pattern–location; face–name; pattern–word) ANOVA was then conducted on the data to investigate the major hypotheses. In the event of a significant interaction, univariate tests of significance were used post hoc to investigate between group or between task differences.

Experiment 2

Subjects

The same subjects who participated in Experiment 1 also participated in Experiment 2 and were assessed within 6 months of completing those AL tasks. All subjects still met the inclusion and exclusion criteria.

Materials and Procedure

Subject assessment. In Experiment 2, all subjects were administered a computerized AL task developed by Schnirman et al. (1999). Subjects responded by pressing one of two labeled keys, with the remainder of the keyboard masked. Each trial consisted of the presentation of a person's face at the top of the screen with two colored fish side by side at the bottom. A text message below the fish asked the subject, "Which fish does this person have?" to which the subject responded by pressing either the right or left key. An outline appeared

Table 4. Correlations Between Clinical and Experimental Measures in Cognitive Decline and Matched Control Groups

	Matched Control		*Cognitive Decline*	
	WLDR Score	*WLDR Slope*	*WLDR Score*	*WLDR Slope*
Experiment 1				
Pattern–location errors	−0.47	−0.53*	−0.29	−0.39
Face–name errors	−0.19	0.31	−0.03	0.01
Pattern–word errors	−0.02	−0.30	−0.34	−0.17
Experiment 2				
Phase 1 errors	0.02	0.16	0.29	0.34
Phase 2 errors	0.40	0.14	−0.21	−0.46
Phase 3 errors	0.04	−0.07	0.04	−0.35
Phase 4 errors	0.10	0.29	−0.31	−0.16

WLDR score = most recent Word List Delayed Recall test score; WLDR slope = linear slope of WLDR test performance over 24 months.
*$p < .05$.

around the fish selected by the subject. For the first three stages of the test, if the response was correct, visual feedback was given in the form of a text message saying "correct." If the response was incorrect, a visual feedback was given (incorrect) and a warning tone sounded. For the final stage (Stage 4: recall), no feedback was given. Throughout the test, four different faces (dark-haired adult male, blonde adult female, blonde male child, dark-haired female child) and four different colored fish (red, green, blue, yellow) were presented.

In Phase 1, subjects were required to associate two faces with two different colored fish. When eight correct consecutive associations had been made, two further faces were introduced (Phase 2), and the subject was required to learn the associations between these new faces and the existing fish, while continuing to make the associations learned in Phase 1. The task progressed to Phase 3 once eight correct consecutive associations had been made. In Phase 3, the remaining two fish stimuli were introduced, and the subject was required to learn the associations between these new stimuli and two of the existing faces, while also making the associations learned in Phases 1 and 2. At Phases 2 and 3, the number of face–fish associations could be reduced (compressed) by identifying a common underlying component of the face stimuli (age, sex, or hair color) that defined the association with the fish stimuli. Phase 3 ended when eight correct consecutive associations had been made. An instruction screen then appeared informing the subject that they would now be required to remember the associations made in Phases 1–3 without receiving feedback about the accuracy of their responses. Phase 4 then began, and the remaining two face–fish associations were introduced. Phase 4 consisted of 48 trials, with six exemplars of each of the eight possible face–fish associations appearing on the screen. The number of errors made in Phases 1–4 was recorded, as was the number of trials taken to complete Phases 1–3.

Data analysis. A Group (2: matched control, cognitive decline) × Phase (3: Phase 1, Phase 2, Phase 3) ANOVA was conducted for both the number of errors made and the number of trials taken to complete each phase. In the event of a significant interaction, univariate tests were used post hoc to determine the significance and effect size associated with group differences. Data for Phase 4 were analyzed separately using independent samples t tests as the number of trials was held constant at 48, and also because there were qualitative differences between the feedback given in Phase 4 (none) compared to the three earlier phases (visual and auditory feedback).

In order to further clarify the relationship between clinical status and AL task performance, we calculated the correlations between the clinical (WLDR test score, WLDR slope) and experimental measures for both the cognitive decline and healthy control groups, for both Experiments 1 and 2. The results of this analysis are presented in Table 4.

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