

Predicting Memory Training Response Patterns: Results From ACTIVE

Jessica B. S. Langbaum,^{1,2} George W. Rebok,¹ Karen Bandeen-Roche,³ and Michelle C. Carlson¹

¹Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland.

²Banner Alzheimer's Institute, Phoenix, Arizona.

³Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland.

Previous research suggests that there is a great deal of variability among older adults' response to memory training. Using latent class analysis, we examined data from the memory training arm of the Advanced Cognitive Training for Independent and Vital Elderly Trial (ACTIVE), a large randomized controlled cognitive training trial, to determine if there were distinct patterns of responsiveness to training. Additionally, we examined whether baseline demographic and cognitive factors were predictive of these response patterns. The results indicate that among memory-trained participants, there are 3 distinct response patterns, suggesting that participants gravitate toward specific mnemonic techniques. Furthermore, baseline memory and speed of processing abilities, age, and education are predictive of these distinct response patterns. Taken together, the findings suggest that we can characterize and predict older adults' response to memory training.

Key Words: Cognitive training—Aging—Memory.

COGNITIVE training has demonstrated the potential for improving or maintaining cognitive function in older adults. The majority of training studies aim to modify specific aspects of cognition, such as memory (Ball et al., 2002; Baltes & Kliegl, 1992; Caprio-Prevette & Fry, 1996; Rasmusson, Rebok, Bylsma, & Brandt, 1999; Singer, Lindenberger, & Baltes, 2003; Stigsdotter & Bäckman, 1989; Verhaeghen & Marcoen, 1996; Verhaeghen, Marcoen, & Goossens, 1992), speed of processing (Ball et al., 2002; Edwards et al., 2002), or reasoning (Ball et al., 2002; Baltes, Dittmann-Kohli, & Kliegl, 1986; Baltes, Sowarka, & Kliegl, 1989; Dittmann-Kohli, Lachman, Kliegl, & Blates, 1991; Willis & Nesselrode, 1990; Willis & Schaie, 1986), each of which often decline with age (Craik & Salthouse, 1992). Generally, findings from cognitive training studies have shown positive training effects specific to the domain of cognitive function that was the focus of the training intervention (Ball et al., 2002; Neely & Bäckman, 1993b; Rebok & Balcerak, 1989; Schmidt, Berg, & Deelman, 2001; Willis & Schaie, 1986). Studies designed to have follow-up measurement often report the maintenance of training effects lasting anywhere between three months and five years following the intervention (Ball et al., 2002; Neely & Bäckman, 1993a; O'Hara et al., 2007; Schmidt et al., 2001; Stigsdotter & Bäckman, 1989; Willis & Nesselrode, 1990; Willis et al., 2006).

Although memory training is an effective method for modifying cognitive abilities in older adults, there appears to be a great deal of variability in level of responsiveness among training participants. Evidence from cognitive studies suggests that not all adults respond to training or respond in the same manner, such that training may actually magnify baseline individual differences in cognitive functioning (Baltes

& Kliegl, 1992; Schaie, Willis, Hertzog, & Schulenberg, 1987; Willis & Nesselrode, 1990). Further support to this notion comes from neuroimaging studies, suggesting that only those individuals who benefit from training exhibit changes in neural activation and biochemistry (Nyberg et al., 2003; Valenzuela et al., 2003).

Although most, if not all, researchers would agree that there is heterogeneity among older adults' responsiveness to memory training, to date, previous studies have primarily focused on characterizing variability in terms of "responding" versus "not responding" as opposed to examining the actual patterns of variability (Baltes & Kliegl, 1992; Kliegl, Smith, & Baltes, 1989, 1990). Such findings would be useful in designing and allocating training platforms. For the former approach, researchers have focused on examining whether baseline demographic and cognitive factors influence a general response to memory training, that is, responding or not responding to training. Findings from this line of research suggest that factors such as increasing age (Brooks, Friedman, Pearman, Gray, & Yesavage, 1999; Sheikh, Hill, & Yesavage, 1986; Verhaeghen et al., 1992) and baseline cognitive status and performance on neurobehavioral measures (Hill, Yesavage, Sheikh, & Friedman, 1989; McKittrick et al., 1999; Singer et al., 2003; Yesavage, Sheikh, Friedman, & Tanke, 1990) may be the most influential in determining general response to memory training. However, this is not to say that other factors—including health status, baseline strategy use, and educational achievement—do not play a role, because the impact of these variables is not well understood.

One major difficulty in addressing the question of heterogeneity in response to training is that the vast majority of cognitive training studies report their findings by group or

Table 1. Demographic Characteristics at Baseline for Completers and Noncompleters of Memory Training

Baseline Characteristic	Completed Training (<i>N</i> = 619)	Did Not Complete Training (<i>N</i> = 84)*	<i>p</i> Value
Age	73.4 ± 5.9	74.2 ± 6.6	.27
Gender, female	76.9	72.6	.39
Race			.86
White	74.6	73.8	
African American	24.9	26.2	
Other/unknown	0.5	0.0	
Years of education	13.6 ± 2.7	13.4 ± 2.9	.41
MMSE score	27.4 ± 2.0	26.8 ± 2.2	.03
Memory composite	0.2 ± 2.5	-0.5 ± 2.6	.02
Reasoning composite	0.2 ± 2.7	-0.4 ± 2.8	.04
Speed composite	-0.1 ± 2.5	-0.02 ± 2.5	.75

Notes: Values are mean ± standard deviation or %. *Randomized to receive memory training.

MMSE = Mini-Mental State Examination. *p* values obtained using chi-square and *t* tests.

study condition, by using either mean level of performance or change scores, or report results by cognitive composite scores, rather than using other methods perhaps better suited for examining intraindividual change or interindividual differences associated with training (Willis, 1987). Until recently, most, if not all, memory training studies were conducted with relatively small sample sizes. Furthermore, participants in these studies tended to have relatively homogeneous demographic and cognitive characteristics, making these studies ill suited for examining training response variability (Rebok, Carlson, & Langbaum, 2007).

The memory training arm from the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial is an ideal source to examine variability in response to training. Initial findings from ACTIVE reported that 26% of the memory-trained participants demonstrated reliable improvement on a memory composite score immediately following training (Ball et al., 2002). The effect sizes were consistent with those reported by previous memory training studies (Verhaeghen et al., 1992), but the percentage improvements seem to indicate that there may be variability in responsiveness to the memory training provided in ACTIVE that can be better explored using individual memory test measures rather than a summary composite score. The present study attempts to identify patterns of responsiveness to memory training using multiple memory performance measures and to examine the demographic and cognitive predictors of training response variability.

METHODS

Participants

All participants who were correctly randomized in the ACTIVE trial to receive memory training (*N* = 703) were considered for the analyses. Recruitment procedures, sample characteristics, and study design have been described in detail elsewhere (Ball et al., 2002; Jobe et al., 2001). Briefly, the

randomized, single-blind trial examined the effectiveness of three cognitive training interventions—memory, inductive reasoning, and speed of processing—versus a no-contact control group, in improving mental abilities and daily functioning in independently living elderly adults older than 65 years. The present study will focus only on the participants randomized to the memory training arm of the study. To be enrolled in the study, participants were required to have a Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) score of 23 or better, not have a self-reported diagnosis of Alzheimer disease, and not have a self-reported substantial functional decline. Participants were included in the analyses if they completed 80% or more of the memory training, resulting in a sample size of 619 individuals (88%). The baseline characteristics for the 619 participants who completed training, compared with the 84 participants who did not complete at least 80% of the training sessions, are shown in Table 1. Participants who were randomized to receive memory training but did not complete at least 80% of the training sessions had significantly lower MMSE scores ($p < .03$) and lower baseline memory ($p < .05$) and reasoning ($p < .05$) composite scores.

Procedures

Demographic information was collected at enrollment. Neuropsychological testing to measure memory, reasoning, and perceptual speed was completed at baseline and immediately following the 10-week cognitive intervention (or no-contact control), and one, two, three, and five years postintervention. This study will report findings using data from the baseline and immediate posttraining sessions. In addition to the individual test scores at each time point, for each of the three cognitive abilities a composite score was also created (Ball et al., 2002).

In order to examine variability in response to memory training, data from the three memory tests used in ACTIVE were analyzed: Hopkins Verbal Learning Test (HVLT) (Brandt, 1991), Rey Auditory Verbal Learning Test (AVLT) (Rey, 1941), and the Rivermead Behavioral Memory Test paragraph recall (Wilson, Cockburn, & Baddeley, 1985). Overall total scores from each of these tests, HVLT and AVLT discrimination subscores (true positives *minus* false positives), AVLT postinterference free recall trial (Trial A6), and cognitive domain-specific composite scores were examined. Composite scores for each cognitive domain (memory, reasoning, and speed of processing) were calculated based on performance on all tests within that domain (Ball et al., 2002). All memory tests were modified in the following ways for group administration: audiotape administration, written responses by participants, and no delayed trials. Because the HVLT and AVLT were administered differently during the first replicate (wave) of ACTIVE baseline assessments compared with the remaining five replicates, data ($n = 67$; 11%) from these assessments were not included in the analyses; however, data from the Rivermead Behavioral Memory Test paragraph recall were included.

For each of the individual memory test measures administered (HVLt, AVLt, and Rivermead), participants were classified as having responded to memory training if their pre- to posttraining change score was 1 standard error of measurement (*SEM*) or greater than the control group's mean change score on that same measure. Specifically, for the control group, a pre- to posttraining change score and standard deviation were calculated for each measure. Using this standard deviation and the measure's test-retest reliability, the *SEM* was calculated for each memory test, based on the method outlined by Dudek (1979). The control group's mean change score was subtracted from the memory training group participant change score, creating a corrected change score. Memory training participants were classified as having positively responded to training if their corrected change score was 1 *SEM* or greater (i.e., "responder"). This approach is similar to that used by Moller and colleagues (1998). Memory training participants who improved substantially more than untrained controls would be considered "training improvers." One result of this classification algorithm is that now both "true improvers" and those who exhibited less pre-post drop compared with controls are considered to have positively responded to training. However, this approach was necessary given that ACTIVE used parallel but nonequivalent alternate forms of the assessments with no within-wave counterbalancing to overcome the differences in test difficulty.

Statistical Analyses

There are two statistical approaches to examine responsiveness to memory training. The first approach would be to keep all memory measures as continuous variables. This approach would be appropriate for selecting specific memory tests thought to indicate a latent construct. The second approach would be to transform the continuous variables into binary variables representing "response" on each particular measure. This later approach was chosen given that the primary interest of this study was to identify specific *patterns* of responsiveness. Additionally, this approach was consistent with the thought that the memory tests represent an index of response to memory training. Thus, the main objective of this study was to identify specific groupings of the memory measures (as binary variables), which would then represent different patterns of responsiveness to memory training.

In order to examine variability in response to memory training over all participants and summarize test performance, latent class analyses (LCAs) were performed using Mplus 3.11 Muthén, L., & Muthén, B. (1998–2006). Mplus user's guide. Los Angeles, CA. Briefly, LCA allows for the estimation of *M* classes of responsiveness to memory training, and the prevalences of responding to training on each particular measure vary between classes. The resulting parameters represent the probabilities of an individual in a given class of the

latent variable "memory training responsiveness" being a "responder" (i.e., their corrected change score was 1 *SEM* or greater) on that particular measure. This resulting conditional probability is an essential component of LCA, as is the assumption of conditional independence; in other words, given class membership, the memory measures are independent.

The latent class indicators consisted of six variables: HVLt total (Trials 1–3), HVLt discrimination (true positives minus false positives), AVLt total (Trials 1–5), AVLt postinterference free recall trial (Trial A6), AVLt discrimination (true positives minus false positives), and Rivermead Behavioral Memory Test paragraph recall total score (number of specified items immediately recalled). Maximum likelihood estimation procedures were used to accommodate missing data on the outcome variables. For each group of indicators, several models were fit to the data, increasing the number of classes in a stepwise manner from 1 to 4. Model fit was determined using the Akaike information criteria (AIC) and sample size-adjusted Bayesian information criteria (BIC).

Following the LCA model selection, the posterior probabilities were obtained and participants were assigned to the class with the highest modal probability in order to examine the predictors of responsiveness patterns. Demographic differences between the classes were explored using one-way analysis of variance, chi-square test, and Fisher's exact test. Univariate and multiple polytomous logistic regressions, also referred to as the multinomial logit model, were conducted to determine which, if any, baseline demographic and cognitive variables were predictive of class membership. This approach allows the effects of the independent variable to differ across categories of the outcome variable (Long & Freese, 2001). Additionally, it allows for the examination of relative risk ratios (RRRs), which can be interpreted as similar to the odds ratio. All demographic and regression analyses were conducted using Stata 8.2 (Stata Corp, College Station, TX).

RESULTS

Latent Class Analyses

Participants were classified as having improved on each memory measure (i.e., responded to training) if their pre- to posttraining change score was 1 *SEM* or greater than the control group's mean change score. These binary scores were then used as indicators in several LCAs in which the number of classes was increased in an iterative manner from 1 to 4 (Table 2). Based on model fit statistics (AIC, BIC), it was determined that a three-class model provided the best fit to the data. Class 1 ("HVLt class") is characterized by a high conditional probability of responding on the HVLt total and a moderate conditional probability of responding on the HVLt discrimination and the Rivermead test. Again, these conditional probabilities

Table 2. Latent Class Analysis Results for 1-, 2-, 3-, and 4-Class Models

Indicators	1-Class Model	2-Class Model		3-Class Model			4-Class Model			
	1	1	2	1	2	3	1	2	3	4
HVLT total	.541	.557	.529	1.00	.549	.306	.964	.334	.765	.453
HVLT discrimination	.276	.279	.274	.541	.268	.151	1.00	.000	.530	.156
AVLT total	.458	.739	.250	.292	.790	.267	.000	.631	.847	.277
AVLT A6	.313	.671	.046	.121	.712	.078	.142	.768	.608	.019
AVLT discrimination	.282	.456	.151	.119	.493	.187	.079	.485	.409	.171
Rivermead paragraph recall	.474	.543	.423	.543	.544	.382	.453	.481	.613	.409
Class size	1.00	.43	.57	.21	.36	.43	.08	.20	.23	.49
AIC	4,218.74	4,139.95		4,128.49			4,128.21			
BIC	4,226.12	4,155.92		4,153.07			4,161.39			

Note: AIC = Akaike information criteria; BIC = Bayesian information criteria; HVLT = Hopkins Verbal Learning Test; AVLT = Rey Auditory Verbal Learning Test.

represent the probability of a participant in Class 1 being classified as a responder (i.e., corrected change score was 1 SEM or greater) on that particular measure. In contrast, Class 2 (“AVLT class”) displays a high conditional probability of responding to AVLT measures and moderate-to-low conditional probabilities on the remaining measures. Class 3 (“low-level response class”) shows a low-to-moderate conditional probability of responding to the total score from each memory measure, with no distinct patterns of responsiveness emerging for this class. Based on the modal posterior probabilities, 123 participants were assigned to Class 1, 210 participants to Class 2, and 271 participants to Class 3. Mean changes in performance (e.g., gain scores) as a result of memory training for participants assigned to the three classes based on the posterior probabilities are displayed in Table 3.

Baseline demographic comparisons between participants assigned to the three classes based on the posterior probabilities are displayed in Table 4. The three classes differ in terms of race, mean years of education, highest educational level completed, mean MMSE score, and cognitive composite scores of memory, reasoning, and speed of processing. Compared with the other two classes, Class 1 (HVLT class) has a higher percentage of Caucasians; more years of education; higher baseline MMSE, memory, and reasoning composite scores; and better baseline speed of processing (lower score reflects faster performance). In contrast, Class 2 (AVLT class) has lower baseline memory and speed of processing performance, whereas Class 3 (low-level response class) has lower baseline reasoning composite scores.

Polytomous Logistic Regression Analyses

Univariate polytomous logistic regression analyses were used to examine which baseline variables are predictive of the odds of being assigned to Class 1 (HVLT class) or Class 2 (AVLT class) versus Class 3 (low-level response class). Predictors were selected in part based on findings from previous studies (e.g., Brooks et al., 1999; Hill et al., 1989; McKittrick et al., 1999; Verhaeghen et al., 1992; Yesavage et al., 1990). Results from the analyses are displayed in Table 5.

Comparing Class 1 to Class 3, several variables are found to be significant predictors of class membership. Baseline cognitive functioning is predictive of being in Class 1 compared with Class 3. Specifically, higher MMSE score (RRR 1.18, 95% confidence interval [CI] 1.06–1.32), better reasoning composite score (RRR 1.17, 95% CI 1.08–1.27), and speed of processing ability (RRR 0.89, 95% CI 0.82–0.97) are each associated with being in Class 1 compared with Class 3. Note that for the speed of processing composite, a lower score reflects better ability. In addition to these factors, Caucasian race (RRR 2.25, 95% CI 1.29–3.92) and having a college (RRR 4.20, 95% CI 1.69–10.39) or graduate level education (RRR 5.69, 95% CI 2.15–15.11) compared with not having a high school degree are each associated with being in Class 1 compared with Class 3. Examining results from the Class 2 versus Class 3 analyses, Class 2 participants are more likely to have a lower baseline memory composite score (RRR 0.88, 95% CI 0.81–0.96) and have a college degree compared with no high school diploma (RRR 1.84, 95% CI 1.01–3.34).

The results from the multiple polytomous logistic regression analysis are displayed in Table 6. Postregression comparisons were made between Classes 1 and 2 (Long & Freese, 2001). Model fit was assessed and there were no violations of multicollinearity or independence of irrelevant alternatives, nor were any of the dependent outcome categories (i.e., classes) able to be combined.

Table 3. Performance Gain for Memory Training Participants, by Class Membership

Measure	Class 1 (N=123)	Class 2 (N=210)	Class 3 (N=271)
HVLT total	2.2±2.9	-0.9±4.4	-3.2±4.4
HVLT discrimination	0.6±1.4	-0.3±1.9	-0.7±1.8
AVLT total	-3.1±5.8	3.6±5.8	-3.4±6.7
AVLT A6	-0.6±3.4	2.9±3.4	-1.0±2.9
AVLT discrimination	0.1±3.3	3.6±5.4	1.0±4.6
Rivermead paragraph recall	3.4±2.4	2.8±2.7	1.2±2.5

Notes: Gain scores calculated as posttraining performance minus baseline. Values are mean ± standard deviation. Class 1 is the HVLT class, Class 2 the AVLT class, and Class 3 the low-level response class.

HVLT = Hopkins Verbal Learning Test; AVLT = Rey Auditory Verbal Learning Test.

Table 4. Demographic Characteristics at Baseline for Memory Training Participants, by Class Membership

Baseline Characteristic	Class 1 (N=123)	Class 2 (N=210)	Class 3 (N=271)	p Value
Age (years)	73.2±5.4	73.7±6.1	73.2±5.9	.65
Age categories (years)				.43
65–74	53	57	60	
75–84	44	39	35	
85+	3	4	5	
Gender, female	79	74	78	.44
Race, Caucasian	85	74	71	.01
Years of education	14.5±2.6	13.6±2.6	13.2±2.7	.001 ^a
Highest education categories				.001
No high school degree	5	10	26	
High school degree	17	29	29	
College degree	53	45	41	
Graduate degree	25	16	14	
MMSE score	27.9±1.8	27.2±2.0	27.3±2.0	.01 ^a
Memory composite	0.7±2.5	−0.4±2.3	0.4±2.6	.001 ^b
Reasoning composite	1.1±2.5	0.04±2.6	−0.01±2.7	.001 ^a
Speed composite	−0.8±2.6	0.04±2.4	−0.01±2.5	.01 ^a

Notes: MMSE = Mini-Mental State Examination. *p* values obtained using chi-square test, one-way analysis of variance with Scheffé multiple comparison test, and Kruskal–Wallis test. Values are mean ± standard deviation or %. Class 1 is the “HVL” class, Class 2 the “AVLT” class, and Class 3 is the “low-level response” class.

^aClass 1 is significantly different from Class 2 and Class 3.

^bClass 2 is significantly different from Class 1 and Class 3.

Baseline cognitive domain abilities, as measured by the composite scores, remained significant predictors in the adjusted model, although the direction of the effect for the memory composite score changed from the unadjusted model. The results suggest that compared with Class 3, Classes 1 and 2 are each more likely to have lower baseline memory composite scores, holding all other variables constant. The odds of being in Class 1 relative to Class 3 decrease 0.87 times for every 1 unit increase in memory

composite score (95% CI 0.76–0.99), holding all other variables constant. This is in contrast to the findings in the unadjusted model, likely due to the inclusion of a suppressor variable exerting influence in the adjusted analysis. Baseline memory performance was also associated with the odds of being in Class 2 versus Class 3 (RRR 0.78, 95% CI 0.69–0.87). Although the reasoning composite was no longer a significant predictor of class membership in the adjusted model (RRR 1.08, 95% CI 0.95–1.25), speed of processing remained a significant predictor. These results indicate that relative to Class 3, Class 1 participants are more likely to have better speed of processing performance (RRR 0.98, 95% CI 0.78–0.98).

Age was found to be a significant predictor between Classes 1 and 3 but not for Class 2 versus Class 3. The odds of being in Class 1 relative to Class 3 were 1.83 times greater for 75- to 84-year-olds compared with being in the reference group (65- to 74-year-olds) (95% CI 1.07–3.15), holding all other variables constant. Caucasian race, a significant predictor between Classes 1 and 3 in the univariate analyses, was no longer significant once covariates were added to the model (RRR 1.42, 95% CI 0.74–2.72).

Education remained a significant predictor in the adjusted analyses. These results suggest that compared with Class 3, participants in both Classes 1 and 2 are more likely to have higher educational attainment, holding all other variables constant. The odds of being in Class 1 compared with Class 3 were 3.34 times greater for those having a graduate degree than for participants who did not graduate from high school (95% CI 1.06–10.46), holding all other variables constant. The odds of being in Class 2 relative to Class 3 were 2.36 times greater for participants who had a college degree compared with those who did not graduate from high school (95% CI 1.09–5.13) and 2.84 times greater for those who

Table 5. Unadjusted Polytomous Logistic Regression Models for Class Membership of Responsiveness to Memory Training

Baseline Variable	Unadjusted Models					
	Class 1 Versus Class 3			Class 2 Versus Class 3		
	RRR	95% CI	<i>p</i> Value	RRR	95% CI	<i>p</i> Value
Memory composite	1.05	0.96–1.15	.29	0.88	0.81–0.96	.002
Reasoning composite	1.17	1.08–1.27	.000	1.01	0.94–1.08	.82
Speed of processing composite	0.89	0.82–0.97	.01	1.01	0.94–1.08	.83
Age categories (years)						
65–74 (reference)	1.00	—	—	1.00	—	—
75–84	1.41	0.89–2.20	.14	1.17	0.79–1.72	.44
85+	0.53	0.15–1.89	.33	0.87	0.37–2.09	.76
Gender, female	1.03	0.62–1.75	.89	0.78	0.51–1.19	.26
Race, Caucasian	2.25	1.29–3.92	.004	1.16	0.77–1.74	.47
Educational attainment						
No high school degree (reference)	1.00	—	—	1.00	—	—
High school degree	1.92	0.72–5.14	.19	1.68	0.89–3.15	.11
College degree	4.20	1.69–10.39	.002	1.84	1.01–3.34	.05
Graduate degree	5.69	2.15–15.11	.000	1.87	0.93–3.78	.08
MMSE score	1.18	1.06–1.32	.004	0.98	0.89–1.07	.65

Notes: RRR = relative risk ratio; CI = confidence interval; MMSE = Mini-Mental State Examination. Class 1 is the “HVL” class, Class 2 the “AVLT” class, and Class 3 the “low-level response” class.

Table 6. Adjusted Polytomous Logistic Regression Models for Class Membership of Responsiveness to Memory Training

Baseline Variable	Adjusted Models					
	Class 1 Versus Class 3			Class 2 Versus Class 3		
	RRR	95% CI	<i>p</i> Value	RRR	95% CI	<i>p</i> Value
Memory composite	0.87	0.76–0.99	.03	0.78	0.69–0.87	.000
Reasoning composite	1.08	0.95–1.25	.23	1.09	0.96–1.24	.17
Speed of processing composite	0.87	0.78–0.98	.02	0.96	0.86–1.06	.39
Age categories (years)						
65–74 (reference)	1.00	—	—	1.00	—	—
75–84	1.83	1.07–3.15	.03	1.26	0.78–2.02	.35
85+	0.44	0.09–2.19	.31	0.47	0.15–1.46	.19
Educational attainment						
No high school degree (reference)	1.00	—	—	1.00	—	—
High school degree	1.34	0.47–3.95	.57	1.93	0.87–4.27	.11
College degree	2.70	0.98–7.44	.05	2.36	1.09–5.13	.03
Graduate degree	3.34	1.06–10.46	.04	2.84	1.12–7.24	.03

Notes: RRR = relative risk ratio; CI = confidence interval.

Class 1 is the “HVLTL” class, Class 2 the “AVLTL” class, and Class 3 the “low-level response” class. Models adjusted for all other variables in the table, plus gender, race, and baseline Mini-Mental State Examination score.

had a graduate degree than for those without a high school diploma (95% CI 1.12–7.24).

DISCUSSION

Results from the present study suggest that, in fact, there is variability in responsiveness to memory training in the ACTIVE trial. Our results indicate that there are distinct memory training response patterns and that the baseline predictors differ for each pattern. By grouping participants into two categories of “responded to training” and “not responded to training,” as is often done in training studies, there is a considerable loss of information that is critical for determining predictors of responsiveness and maintenance of training gains.

More than 90% of ACTIVE participants who completed memory training improved on at least one memory measure, supporting the idea of plasticity in cognitive functioning in older adults. With aging, there is a general trend of gradual cognitive decline, but with memory training, many older adults can improve their performance on memory tests. Given the variety of improvement patterns observed in the present study, it would suggest that the amount or degree of plasticity varies across individuals, as is suggested by the theory of cognitive reserve (Katzman et al., 1988; Stern et al., 1994). The implications of these results, such as whether initial improvement as well as responsiveness pattern affect long-term memory functioning, should be investigated in future studies.

Findings from the LCA revealed that in general, classes were created around the specific memory tests. That is to say, one class was formed in which the participants had a high conditional probability of responding to a particular HVLTL measure, whereas for participants in another class, their highest conditional probabilities of responding were for the AVLTL. This finding cannot be attributed to participants having little to no room to improve on the memory measures after training. Few, if any, participants were per-

forming at ceiling levels. However, in the present study, we cannot exclude the possibility that this finding is an artifact of test item difficulty. It is also unlikely that the latent class findings are a result of “teaching to the test.” ACTIVE ensured that the memory measures used at assessment were not equivalent to the materials used during training and should be considered indexes of whether training was effective. Rather, the gain scores suggest that perhaps classes were formed because some participants were improving on one specific measure, such as the HVLTL, whereas another group showed improvement on the AVLTL. It is possible that there are specific properties of the tests themselves, or even the strategies associated with better performance on these tests, that then enable some participants to improve on the measure, whereas others do not improve as much. Although the HVLTL and AVLTL are often considered to be analogous measures of episodic memory, they do differ in one notable respect—the HVLTL contains a list of *semantically* related words, whereas the AVLTL words are unrelated. For instance, the categorization strategy taught in ACTIVE may be best applied to the HVLTL. Overall, these results have implications for future memory training studies, which may use only one of the two measures or perhaps another “analogous” measure. By not including a variety of episodic memory measures, future studies would potentially underestimate the true level of responsiveness.

Although it is conceivable that the findings from the present study indicate that participants are improving on only a specific memory test and not responding to memory training per se, perhaps a more likely explanation for the HVLTL class and AVLTL class patterns is that the classes are arising due to differential strategy adherence or preference by the participants. There is a sizeable amount of research on strategy use in older adults and a growing body of literature on the impact of strategy use on training. Findings from behavioral studies suggest that the knowledge about

effective mnemonic strategies does not guarantee successful utilization (Camp, Markley, & Kramer, 1983; Dunlosky & Hertzog, 1998). It has been suggested that even when older adults are trained in a particular strategy, if they believe that it is less effective than their current system, they will rapidly revert to their own initial strategies (Camp et al., 1983). Strategy use has been thought to be largely an individual characteristic that is rather stable over time (Kliegel & Altgassen, 2006; Verhaeghen & Marcoen, 1994), although training can affect use and adherence (Saczynski, Margrett, & Willis, 2004; Saczynski, Willis, & Schaie, 2002). It is thought that the ability to self-generate strategies is associated with several demographic characteristics, including higher education, younger age, and Caucasian race (as compared with African American), and that the use of any strategy is associated with improved performance on the HVLTL, whereas no such relationship has been reported for the AVLTL (Saczynski, Rebok, Whitfield, & Plude, 2007). In ACTIVE, memory training participants were instructed on a variety of mnemonic devices, including categorization, visualization, organization, and method of loci strategies. Consequently, some participants may have preferred or adhered to one strategy over another, and this, coupled with the impact of baseline demographic and cognitive factors on strategy use and ability to benefit from training, may at least partially explain the present findings. Although it is doubtful that the present study's findings are the result of specific strategies being presented in such a way that they were more accessible to the highly educated participants, this idea cannot be entirely ruled out given the lack of data. However, given the fact that such a high percentage of participants exhibited some training benefit and there was a wide range of educational attainment among participants, this explanation is unlikely.

Examining the association between baseline demographic and cognitive features with responsiveness to memory training, we found that baseline memory and speed of processing composite scores, age, and higher educational attainment were all predictive of class membership after adjusting for other variables in the model. These results are notable given that previous research often grouped training participants into "improvers" or "non-improvers" and has had difficulty determining predictors of this binary responsiveness variable.

Taking other baseline factors into account, lower baseline memory ability, as measured by the memory composite score, was associated with being in Classes 1 and 2 compared with Class 3. Although no participants were performing at ceiling and thus had room for improvement, it is plausible that participants in Classes 1 and 2 simply had more room for improvement. Some support for this is seen in the mean gain scores for each class. However, for most measures, Class 3 had a negative mean gain in performance. It has been noted that there was an overall trend of decline on certain memory measures in ACTIVE between baseline

and posttraining assessments due to differences in test item difficulty, and as a result, most ACTIVE analyses utilize transformed scores to account for the discrepancies. Thus, it is difficult to say with certainty whether it is differential room for improvement or item difficulty that is driving the present results.

The differential role of speed of processing between Classes 1 and 3 is intriguing. Findings from previous studies have argued that age-related reductions in both episodic and working memory are at least partially mediated by a decline in speed of processing ability (Hertzog, Dixon, Hultsch, & MacDonald, 2003; Levitt, Fugelsang, & Crossley, 2006; Luszcz, Bryan, & Kent, 1997; Salthouse, 1991, 1996), potentially explaining why when both reasoning ability and speed of processing ability were included in the adjusted model, only speed remained a significant predictor. Specifically, better baseline speed of processing was associated with being in Class 1, a class predominantly characterized by improvement on the HVLTL, whereas lower baseline speed of processing ability was associated with being in Class 3, the low-level responsiveness class. Findings from Verhaeghen and Marcoen (1994) suggest that the speed of processing is associated with strategy use, which, as was previously discussed, is not only associated with the ability to benefit from cognitive training but also associated with test performance. The complex relationship between speed of processing ability and strategy use may aid in explaining the present results and is something that should be explored further in future studies.

Our results indicated that higher educational attainment was predictive of class membership. Previous research has suggested that higher education is associated with the ability to self-generate mnemonic strategies on memory tasks and is also associated with better performance on memory measures such as the ones used in ACTIVE (Saczynski et al., 2007; Van der Elst, van Boxtel, van Breukelen, & Jolles, 2005). For instance, higher educational attainment may allow participants to excel at the categorization in the HVLTL. However, it is also possible that education represents more than just years of schooling. It may also be a proxy variable for socioeconomic status, early life factors, occupational level, health practices, and perhaps even the willingness to engage in lifelong learning or new activities (Krieger, Williams, & Moss, 1997; Leigh & Fries, 1994), each of which may affect performance on memory tests and the ability to improve on them through memory training. Although it is possible that those with higher educational attainment may benefit most from memory training, longitudinal studies are needed to determine whether education affects the maintenance of training gains. Perhaps it is a combination of baseline demographic characteristics, including age and educational attainment, plus baseline cognitive functioning, particularly speed of processing ability, in addition to the ability and willingness to utilize the mnemonic strategies, that determines responsiveness to training. As previously mentioned,

we cannot rule out the unlikely possibility that strategy training was presented in such a manner that only specific strategies were accessible to highly educated participants.

There are potential limitations to this study. Although three distinct classes were identified using the objective memory measures in ACTIVE, it is conceivable that different patterns or number of patterns would be found if other memory measures, including a measure of delayed recall, were available in ACTIVE. Consequently, it is plausible that other predictors of responsiveness may have been identified if different measures were used to classify responsiveness. Therefore, caution should be exercised when interpreting the results in that these may not be the only predictors of responsiveness to memory training. Nevertheless, the three measures used in the present study are reflective of distinct aspects of episodic memory—the ability to learn and remember related words, unrelated words, and text. There were a few participants who did not demonstrate improvement on any of the memory measures; yet, in the LCA there was no “non responder” class. Most likely, this is because of the relatively small number of non responders (less than 10% of those who completed memory training), such that there was not enough power to detect a fourth pattern. However, we do acknowledge that Class 3, the low-level response class, may be closest to a non responder class. Along these lines, we cannot exclude the possibility that some participants had mild cognitive impairment, because ACTIVE was not designed to include diagnostic assessments, and any information would come from self-report. Lastly, although the exact composite of groupings may vary from study to study, the fact that such distinct patterns were found in the present study is in and of itself noteworthy. Although beyond the scope of this paper, future research may be warranted to further explore other patterns of responsiveness. Such approaches may include trichotomizing response into “no improvement,” “slight or some improvement,” and “marked improvement” or perhaps restricting analyses to the 26% of ACTIVE memory-trained participants who demonstrated reliable improvement on the memory composite score.

The present study has many notable strengths. ACTIVE is a large, randomized trial with a representative sample of older adults. Previous memory training studies had relatively small sample sizes, and the participants had relatively homogeneous baseline demographic and cognitive features. Because ACTIVE participants did not self-select into the memory training trial arm, we were able to address not only that there are distinct patterns of responsiveness but also which predictors are associated with type of responsiveness. The existence of distinct patterns of responsiveness to memory training provides evidence that not all older adults respond to training in the same manner. In fact, our results seem to indicate that participants did not acquire the various mnemonic strategies equally. Specific demographic and baseline cognitive measures are predictive of the patterns of responsiveness. These findings may be useful in determining

who prefers or benefits from each specific memory training strategy or techniques and design training platforms accordingly. Future work is needed to explore the long-term implications of class membership, especially in terms of maintenance of training gains.

FUNDING

ACTIVE is supported by grants from the National Institute on Aging and the National Institute of Nursing Research to the Hebrew Rehabilitation Center for the Aged (U01 NR04507), Indiana University School of Medicine (U01 NR04508), Johns Hopkins University (U01 AG14260), New England Research Institutes (U01 AG14282), Pennsylvania State University (U01 AG14263), University of Alabama at Birmingham (U01 AG14289), and University of Florida (U01 AG014276).

ACKNOWLEDGMENTS

This work was completed in partial fulfillment of J.B.S.L.'s PhD requirements. Portions of the data have been presented at the 59th Annual Meeting of the Gerontological Society of America (Dallas, TX, November 2006) and at the Cognitive Aging Conference Down Under (July 2007).

CORRESPONDENCE

Address correspondence to Jessica Langbaum, PhD, Banner Alzheimer's Institute, 901 East Willetta Street, Phoenix, AZ 85006. Email: jessica.langbaum@bannerhealth.com

REFERENCES

- Ball, K., Berch, D. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske, M., Morris, J. N., Rebok, G. W., Smith, D. M., Tennstedt, S. L., et al. (2002). Effects of cognitive training interventions with older adults: A randomized controlled trial. *Journal of the American Medical Association*, 288, 2271–2281.
- Baltes, P. B., Dittmann-Kohli, F., & Kliegl, R. (1986). Reserve capacity of the elderly in aging-sensitive tests of fluid intelligence: Replication and extension. *Psychology and Aging*, 1, 172–177.
- Baltes, P. B., & Kliegl, R. (1992). Further testing of limits of cognitive plasticity: Negative age-differences in a mnemonic skill are robust. *Developmental Psychology*, 28, 121–125.
- Baltes, P. B., Sowarka, D., & Kliegl, R. (1989). Cognitive training research on fluid intelligence in old age: What can older adults achieve by themselves? *Psychology and Aging*, 4, 217–221.
- Brandt, J. (1991). The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *Clinical Neuropsychologist*, 5, 125–142.
- Brooks, J. O., Friedman, L., Pearman, A. M., Gray, C., & Yesavage, J. A. (1999). Mnemonic training in older adults: Effects of age, length of training, and type of cognitive pretraining. *International Psychogeriatrics*, 11, 75–84.
- Camp, C. J., Markley, R. P., & Kramer, J. J. (1983). Spontaneous use of mnemonics by elderly individuals. *Educational Gerontology*, 9, 57–71.
- Caprio-Prevette, M. D., & Fry, P. S. (1996). Memory enhancement program for community-based older adults: Development and evaluation. *Experimental Aging Research*, 22, 281–303.
- Craik, F. I. M., & Salthouse, T. A. (1992). *The handbook of aging and cognition*. Hillsdale, NJ: Erlbaum.
- Dittmann-Kohli, F., Lachman, M. E., Kliegl, R., & Baltes, P. B. (1991). Effects of cognitive training and testing on intellectual efficacy beliefs in elderly adults. *Journal of Gerontology*, 46, 162–164.
- Dudek, F. J. (1979). The continuing misinterpretation of the standard error of measurement. *Psychological Bulletin*, 86, 335–337.
- Dunlosky, J., & Hertzog, C. (1998). Aging and deficits in associative memory: What is the role of strategy production? *Psychology and Aging*, 13, 597–607.

- Edwards, J. D., Wadley, V. G., Myers, R. S., Roenker, D. L., Cissell, G. M., & Ball, K. K. (2002). Transfer of a speed of processing intervention to near and far cognitive functions. *Gerontology, 48*, 329–340.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189–198.
- Hertzog, C., Dixon, R. A., Hulstsch, D. F., & MacDonald, S. W. S. (2003). Latent change models of adult cognition: Are changes in processing speed and working memory associated with changes in episodic memory? *Psychology and Aging, 18*, 755–769.
- Hill, R. D., Yesavage, J. A., Sheikh, J., & Friedman, L. (1989). Mental status as a predictor of response to memory training in older adults. *Educational Gerontology, 15*, 633–639.
- Jobe, J. B., Smith, D. M., Ball, K., Tennstedt, S. L., Marsiske, M., Willis, S. L., Rebok, G. W., Morris, J. N., Helmers, K. F., Leveck, M. D., et al. (2001). ACTIVE: A cognitive intervention trial to promote independence in older adults. *Controlled Clinical Trials, 22*, 453–479.
- Katzman, R., Terry, R., DeTeresa, R., Brown, T., Davies, P., Fuld, P., Renbing, X., Peck, A. (1988). Clinical, pathological, and neurochemical changes in dementia: A subgroup with preserved mental status and numerous neocortical plaques. *Annals of Neurology, 23*, 138–144.
- Kliegel, M., & Altgassen, M. (2006). Interindividual differences in learning performance: The effects of age, intelligence, and strategic task approach. *Educational Gerontology, 32*, 111–124.
- Kliegl, R., Smith, J., & Baltes, P. B. (1989). Testing-the-limits and the study of adult age differences in cognitive plasticity of a mnemonic skill. *Developmental Psychology, 25*, 247–256.
- Kliegl, R., Smith, J., & Baltes, P. B. (1990). On the locus and process of magnification of age differences during mnemonic training. *Developmental Psychology, 26*, 894–904.
- Krieger, N., Williams, D. R., & Moss, N. E. (1997). Measuring social class in US public health research: Concepts, methodologies, and guidelines. *Annual Review of Public Health, 18*, 341–378.
- Leigh, J. P., & Fries, J. F. (1994). Education, gender, and the compression of morbidity. *International Journal of Aging & Human Development, 39*, 233–246.
- Levitt, T., Fugelsang, J., & Crossley, M. (2006). Processing speed, attentional capacity, and age-related memory change. *Experimental Aging Research, 32*, 263–295.
- Long, J. S., & Freese, J. (2001). *Regression models for categorical dependent variables using Stata*. College Station, TX: Stata Press.
- Luszcz, M. A., Bryan, J., & Kent, P. (1997). Predicting episodic memory performance of very old men and women: Contributions from age, depression, activity, cognitive ability, and speed. *Psychology and Aging, 12*, 340–351.
- McKittrick, L. A., Friedman, L. F., Brooks, J. O., III, Pearman, A., Kraemer, H. C., & Yesavage, J. A. (1999). Predicting response of older adults to mnemonic training: Who will benefit? *International Psychogeriatrics, 11*, 289–300.
- Moller, J. T., Cluitmans, P., Rasmussen, L. S., Houx, P., Rasmussen, H., Canet, J., Rabbitt, P., Jolles, J., Larsen, K., Hanning, C. D., et al. (1998). Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. *Lancet, 351*, 857–861.
- Muthén, L., & Muthén, B. (1998–2006). Mplus user's guide, Los Angeles, CA.
- Neely, A. S., & Bäckman, L. (1993a). Long-term maintenance of gains from memory training in older adults: Two 3 1/2-year follow-up studies. *Journal of Gerontology, 48*, 233–237.
- Neely, A. S., & Bäckman, L. (1993b). Maintenance of gains following multifactorial and unifactorial memory training in late adulthood. *Educational Gerontology, 19*, 105–117.
- Nyberg, L., Sandblom, J., Jones, S., Neely, A. S., Petersson, K. M., Ingvar, M., Bäckman, L., (2003). Neural correlates of training-related memory improvement in adulthood and aging. *Proceedings of the National Academy of Sciences of the United States of America, 100*, 13728–13733.
- O'Hara, R., Brooks, J. O., III, Friedman, L., Schroder, C. M., Morgan, K. S., & Kraemer, H. C. (2007). Long-term effects of mnemonic training in community-dwelling older adults. *Journal of Psychiatric Research, 41*, 585–590.
- Rasmusson, D. X., Rebok, G. W., Bylsma, F. W., & Brandt, J. (1999). Effects of three types of memory training in normal elderly. *Aging Neuropsychology and Cognition, 6*, 56–66.
- Rebok, G. W., & Balcerak, L. J. (1989). Memory self-efficacy and performance differences in young and old adults: The effect of mnemonic training. *Developmental Psychology, 25*, 714–721.
- Rebok, G. W., Carlson, M. C., & Langbaum, J. B. S. (2007). Training and maintaining memory abilities in healthy older adults: Traditional and novel approaches. *Journals of Gerontology: Psychological Sciences and Social Sciences, 62*, 53–61.
- Rey, A. (1941). L'examen psychologique dans les cas d'encephalopathie traumatique. *Archives de Psychologie, 28*, 215–285.
- Saczynski, J. S., Margrett, J. A., & Willis, S. L. (2004). Older adults' strategic behavior: Effects of individual versus collaborative cognitive training. *Educational Gerontology, 30*, 587–610.
- Saczynski, J. S., Rebok, G. W., Whitfield, K. E., & Plude, D. L. (2007). Spontaneous production and use of mnemonic strategies in older adults. *Experimental Aging Research, 33*, 273–295.
- Saczynski, J. S., Willis, S. L., & Schaie, K. W. (2002). Strategy use in reasoning training with older adults. *Aging Neuropsychology and Cognition, 9*, 48–60.
- Salthouse, T. A. (1991). Mediation of adult age differences in cognition by reductions in working memory and speed of processing. *Psychological Science, 2*, 179–183.
- Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review, 103*, 403–428.
- Schaie, K. W., Willis, S. L., Hertzog, C., & Schulenberg, J. E. (1987). Effects of cognitive training on primary mental ability structure. *Psychology and Aging, 2*, 233–242.
- Schmidt, I. W., Berg, I. J., & Deelman, B. G. (2001). Prospective memory training in older adults. *Educational Gerontology, 27*, 455–478.
- Sheikh, J. I., Hill, R. D., & Yesavage, J. A. (1986). Long-term efficacy of cognitive training for age-associated memory impairment: A six-month follow-up study. *Developmental Neuropsychology, 2*, 413–421.
- Singer, T., Lindenberger, U., & Baltes, P. B. (2003). Plasticity of memory for new learning in very old age: A story of major loss? *Psychology and Aging, 18*, 306–317.
- Stern, Y., Gurland, B., Tatemichi, T. K., Tang, M. X., Wilder, D., & Mayeux, R. (1994). Influence of education and occupation on the incidence of Alzheimer's disease. *Journal of the American Medical Association, 271*, 1004–1010.
- Stigsdotter, A., & Bäckman, L. (1989). Multifactorial memory training with older adults: How to foster maintenance of improved performance. *Gerontology, 35*, 260–267.
- Valenzuela, M. J., Jones, M., Wen, W., Rae, C., Graham, S., Shnier, R., Sachdev, P. (2003). Memory training alters hippocampal neurochemistry in healthy elderly. *Neuroreport, 14*, 1333–1337.
- Van der Elst, W., van Boxtel, M. P., van Breukelen, G. J., & Jolles, J. (2005). Rey's verbal learning test: Normative data for 1855 healthy participants aged 24–81 years and the influence of age, sex, education, and mode of presentation. *Journal of the International Neuropsychological Society, 11*, 290–302.
- Verhaeghen, P., & Marcoen, A. (1994). Production deficiency hypothesis revisited: Adult age differences in strategy use as a function of processing resources. *Aging and Cognition, 1*, 323–338.
- Verhaeghen, P., & Marcoen, A. (1996). On the mechanisms of plasticity in young and older adults after instruction in the method of loci: Evidence for an amplification model. *Psychology and Aging, 11*, 164–178.

- Verhaeghen, P., Marcoen, A., & Goossens, L. (1992). Improving memory performance in the aged through mnemonic training: A meta-analytic study. *Psychology and Aging, 7*, 242–251.
- Willis, S. L. (1987). Cognitive training and everyday competence. *Annual Review of Gerontology & Geriatrics, 7*, 159–188.
- Willis, S. L., & Nesselroade, C. S. (1990). Long-term effects of fluid ability training in old-old age. *Developmental Psychology, 26*, 905–910.
- Willis, S. L., & Schaie, K. W. (1986). Training the elderly on the ability factors of spatial orientation and inductive reasoning. *Psychology and Aging, 1*, 239–247.
- Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Koepke, K. M., Morris, J. N., Rebok, G. W., Unverzagt, F.W., Stoddard, A. M., et al. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *Journal of the American Medical Association, 296*, 2805–2814.
- Wilson, B. A., Cockburn, J., & Baddeley, A. (1985). *The Rivermead Behavioral Memory Test*. Reading, UK: Thames Valley Test.
- Yesavage, J. A., Sheikh, J. I., Friedman, L., & Tanke, E. (1990). Learning mnemonics: Roles of aging and subtle cognitive impairment. *Psychology and Aging, 5*, 133–137.

Received January 11, 2008

Accepted June 9, 2008

Decision Editor: Elizabeth Stine-Morrow, PhD