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The Effects of the ACTIVE Cognitive Training Trial on Clinically Relevant Declines in Health-Related Quality of Life

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Objectives. The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study used three cognitive interventions (memory, reasoning, or speed of processing) in order to improve cognitive abilities. In this article, we evaluate ACTIVE's ability to avoid extensive decline in health-related quality of life (HRQoL).

Methods. ACTIVE enrolled 2,802 adults aged 65 or older and randomized them into one of three cognitive interventions or a no-contact control group. Researchers obtained data on 2,147 participants at the 24-month follow-up. We measured HRQoL by using the eight Short Form-36 scales, and we defined clinically relevant decline on each as a drop of 0.5 standard deviations from baseline. We defined extensive HRQoL decline as clinically relevant drops on four or more Short Form-36 scales, and we assessed this by using multiple logistic regression methods that adjusted for sociodemographic, cognitive, and health status covariates, and incorporated propensity score derived weights in order to adjust for potential attrition bias.

Results. We found that 25.0% of ACTIVE participants had extensive HRQoL decline. Participants in the speed-of-processing intervention arm were less likely to have extensive HRQoL decline (adjusted odds ratio = 0.643; $p = .004$) compared with controls, and participants in the memory and reasoning arms were equivalent to controls (adjusted odds ratios = 1.149 and 1.014, respectively; ps = .322 and .919, respectively).

Discussion. Although all three intervention arms improved cognitive ability, only the speed-of-processing arm protected against extensive clinically relevant decline in HRQoL.

ONE of the common issues facing older adults today is the fear of declining cognitive ability and the onset of difficulties with activities of daily living (ADLs) that is associated with this decline (Pathy, Morley, & Sinclair, 2006). Difficulties with basic, instrumental ADLs (IADLs), and cognitive ADLs are the primary risk factors for nursing home placement, which is perhaps the greatest concern facing older adults (Kane, Kane, & Ladd, 1998). These concerns are well founded. Research has shown that declines in cognitive abilities lead to increased risk of developing difficulties with IADLs, that the accumulation of IADL limitations leads to increased risk of developing difficulties with basic ADLs, and that, taken together, these functional declines are associated with increased likelihood of nursing home placement (Wolinsky, Callahan, Fitzgerald, & Johnson, 1992, 1993). Research has also shown that once older adults are placed in nursing homes, their risk of mortality is heightened, even after adjusting for a variety of functional status and comorbidity measures (Aneshensel, Pearlin, & Schuler, 1993; Wolinsky et al., 1992). Failure to thrive is thought to play an important role in this process (Braun, Wykle, & Cowling, 1988; Wolinsky, Stump, & Callahan, 1997). There is also evidence suggesting that after cognitive decline in elders has been documented, a triage process is often initiated, resulting in decreased proclivity for appropriate health services use, including both inpatient and outpatient services (Wolinsky, Culler, Callahan, & Johnson, 1994; Wolinsky, Stump, & Johnson, 1995).

It is not surprising, therefore, that there exists a multitude of interventions for older persons with cognitive impairment (Rowe & Kahn, 1998). Few interventions, however, have been targeted at delaying or preventing the onset of cognitive disabilities in cognitively intact older adults (Ball et al., 2002). This is unfortunate, given that many basic cognitive abilities and processes are related to measures of functional status, the need for care, and quality of life. Therefore, improving cognitive function might have short- and/or long-term effects on daily activities related to independent living and might also delay (or prevent the need for) nursing home placement, while ensuring the independence and dignity of the aging population.

In their recent, thorough, and compelling review of the accumulated longitudinal evidence supporting the cognitive reserve hypothesis, Fratiglioni, Paillard-Borg, and Winblad (2004, p. 343) concluded that there could be little doubt that "an active and socially integrated lifestyle in late life protects against dementia and [Alzheimer's disease]." However, investigators have not adequately studied the subsequent effects of maintained cognitive ability on the daily functioning of older adults and their quality of life (Ball et al., 2002). It was for that purpose that the National Institute on Aging and the National Institute of

Nursing Research sponsored the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study (Jobe et al., 2001). The primary objective of ACTIVE was to test the effectiveness and durability of three distinct cognitive interventions in improving the performance of older adults on basic measures of cognition and measures of cognitively demanding daily activities (e.g., food preparation, driving, medication use).

Previous reports from ACTIVE have strongly supported the effectiveness and durability of the three cognitive training interventions in improving the targeted cognitive ability (Ball et al., 2002). This article takes the next logical step by focusing on the ability of the three ACTIVE cognitive interventions to delay clinically relevant declines in health-related quality of life (HRQoL) during the first 24 months after their delivery. Consistent with standard conceptualizations of the disablement process (Wolinsky, 2006; Wolinsky & Miller, 2006), the presumed etiological mechanism is that the decline of cognitive abilities increases the likelihood of difficulty in performing ADLs and IADLs, which in turn leads to a deterioration in HRQoL (Ball et al.; Jobe et al., 2001). Evidence of the close association between cognitive function and HRQoL supports this conceptualization: (a) Higher cognitive function is related to higher HRQoL (Lloyd, Boyle, Bell, & Thompson, 2000); (b) decline in cognitive function is associated with lower HRQoL (Carmelli, Swan, LaRue, & Eslinger, 1997) and higher mortality (Wolinsky & Johnson, 1991); and (c) improvements in cognitive function are correlated with improvements in HRQoL (R. A. Cohen et al., 1999). Thus, preventing the loss of cognitive ability would likely also prevent decline in HRQoL.

Methods

Design

ACTIVE was a single-blind, randomized controlled trial with three treatment arms and a no-contact control group. Each treatment arm consisted of a 10-session intervention for one of three cognitive abilities (memory, reasoning, or speed of processing). Researchers provided a four-session booster training to a random subsample of trained participants approximately 11 months after training. Data collection personnel were blind to participant treatment assignment. Training exposure and social contact were standardized across interventions so that each intervention served as a contact control for the other two interventions. Therefore, the design allows for testing both social contact effects (via the contact control group) and retest effects (via the no-contact control group) on outcomes. Follow-up interviews occurred immediately following training and at 12 and 24 months after training. For further details, see Jobe and colleagues (2001).

Sample

Study organizers recruited from six field sites a large sample of adults aged 65 or older (including a substantial proportion of African Americans) who were living independent of formal care but at risk for loss of functional independence. From March 1998 through October 1999, organizers enrolled participants across these sites by using a variety of sampling frames and recruitment strategies described elsewhere (Jobe et al., 2001). These recruitment strategies yielded 4,970 potential participants. In addition to age, exclusion criteria were (a) cognitive impairment (a Mini-Mental State Examination [MMSE] score less than 23; Folstein, Folstein, & McHugh, 1975); (b) poor vision (less than 20/50); (c) dependence in hygiene, bathing, or dressing; (d) diagnosed Alzheimer's disease; (e) history of stroke in the previous 12 months; (f) cancer with limited life expectancy; (g) current chemotherapy or radiation treatment; (h) communication problems; (i) a planned move from the study site area; (j) scheduling conflicts that would preclude participation in study activities; and (k) prior involvement in similar cognitive training studies. In all, 905 participants (18.1%) were ineligible and 1,263 (25.3%) refused to complete screening or enroll in the study. Common reasons for ineligibility included MMSE scores less than 23 (29.8% of 905), vision impairments (21.2%), and scheduling conflicts (22.3%). Study organizers properly randomized 2,802 participants into the trial. At 24 months, researchers obtained complete data on 2,147 participants (76.6%). Common reasons for attrition were death (12.2% of 655), refusal to continue participating in the study at some point after baseline data collection (37.9%), and investigators' inability to locate participants (33.0%) at the 24-month follow-up. Attrition (and the reasons for it) was not associated with intervention or control group status (overall retention rates were 80.1%, 79.4%, 81.8%, and 79.1% in the memory, reasoning, speed, and control groups, respectively).

Interventions

Each of three interventions was directed at a specific cognitive ability: memory, inductive reasoning, or speed of processing. For each intervention, Sessions 1–5 focused on strategy instruction and exercises to practice the strategy. Sessions 6–10 provided additional practice exercises but introduced no new strategies. A trainer's manual contained scripted content for each of the 10 sessions. Reasoning training focused on inductive reasoning (the ability to solve problems that follow a serial pattern and that manifest in executive functioning). Researchers taught participants strategies for identifying the pattern or sequence required to solve a problem. Training exercises involved identifying patterns in both laboratory-type reasoning tasks and in everyday activities (e.g., understanding the pattern in a bus schedule). Memory training focused on verbal episodic memory, which deals with acquisition and retrieval of information acquired in a particular place at a particular time. Investigators taught participants mnemonic strategies for remembering lists and sequences of items, text material, and main ideas and details of stories and other text-based information. Training exercises involved recalling laboratory-like episodic memory tasks as well as tasks related to everyday activities (such as recalling a shopping list). Speed training focused on visual search and the ability to identify and locate visual information quickly in a divided attention format, with and without distraction. Participants practiced speeded tasks on a computer and were allowed to proceed to more complex tasks and faster and faster presentation speeds at their own pace. For further details, see Jobe and colleagues (2001).

HRQoL

The Short Form-36 (SF-36) is the most widely used HRQoL instrument in the world (Brazier, Harper, & Jones, 1992;

McHorney, Ware, & Raczek, 1993; Stewart, Hays, & Ware, 1988; Tarlov, Ware, & Greenfield, 1989; Ware & Kosinski, 1999; Ware, Kosinki, & Dewey, 2000; Ware & Sherbourne, 1992). It was developed through iterative data reduction experiences with a variety of precursor measures used in the Medical Outcomes Study. A detailed description of the development procedures is available elsewhere (Ware, 1996), as is the exact wording of the items (Ware & Kosinski; Ware et al.). Of the 36 items, 35 make up eight scales: physical functioning (10 items), role limitations due to physical functioning (4 items), bodily pain (2 items), general health perceptions (5 items), vitality (4 items), social functioning (2 items), role limitations due to emotional problems (3 items), and mental health (5 items).

Within scales, we imputed missing data by using a prorated method as long as the participant answers at least half of the items within a scale. Simply put, we imputed the average of those items for any unanswered items in that scale. Consistent with national norms, imputation occurred for less than 5% of the cases, and this did not vary by scale. Because of the different numbers of items and response options in each scale, we transformed raw scores to range from 0 (worst health) to 100 (best health). These could also be rescaled (normed) to national data having a mean of 50 and a standard deviation of 10 by applying the appropriate algorithm (Ware et al., 2000).

This study assessed whether the cognitive interventions resulted in clinically relevant changes in HRQoL. It was, therefore, necessary to establish criteria for such change. It is well known that J. Cohen (1969) suggested that effect sizes of 0.20 to 0.50 standard deviations are small, effect sizes of 0.50 to 0.80 standard deviations are medium, and effect sizes of 0.80 standard deviations or greater are large. Although others have argued for different categorical cut-offs, the most widely cited of these alternative categorical cut-offs for meaningful change are very close to Cohen's 0.50 standard deviation (or medium) level (Feinstein, 1999; Sloan, Loprinzi, & Kuross, 1998; Testa, 1987). Moreover, a recent meta-analysis of 38 studies found that the mean estimated meaningfully important difference was 0.495 standard deviations (Norman, Sloan, & Wyrwich, 2003). Furthermore, if there are seven response options for each question in the scale, an effect size of 0.50 standard deviations is remarkably close to estimates of human abilities to discriminate between two feeling states (Miller, 1956). Thus, we used the 0.50 standard deviation effect size in this study in order to define clinically relevant change in a single SF-36 scale; we defined extensive HRQoL decline as clinically relevant change in four or more of the eight SF-36 scales.

Attrition Bias

Loss to follow-up may introduce attrition bias, even in well-designed trials. One method of adjusting for potential attrition bias is to weight the data based on participation rates within propensity score quintiles. This method was developed by Rubin (1979) in order to adjust for the absence of random assignment in *observational studies*, subsequently popularized by Rosenbaum and Rubin (1983), and illustrated by D'Agostino (1998). We obtained the propensity scores from a multiple logistic regression model of attrition at 24 months by using the set of cognitive intervention dummy variables and the covariates (see below). Attriters were more likely to be older (adjusted odds ratio [AOR] = 1.025, $p < .001$) and to be men (AOR = 1.412, $p < .01$), but less likely to be Caucasian (AOR = 0.562, $p < .001$) or to have high MMSE scores (AOR = 0.871, $p < .001$). None of the cognitive interventions were associated with attrition. Overall, the propensity model for attrition fit the data reasonably well (Hosmer–Lemeshow statistic p value = .418; C statistic = .632), and, following standard methods, we weighted the data for the multivariable logistic regression by the inverse of the participation rate within propensity score quintiles. For comparative purposes, we also present here equivalent models that we did not weight to adjust for the potential attrition bias.

Covariates

In addition to adjusting for potential attrition bias in the multiple logistic regression analyses, we included 10 covariates in order to ensure that the estimated effects of the cognitive interventions on extensive decline in HRQoL were fully independent from the effects of other background factors. The covariates included age, gender, race, education, cognitive function, basic ADLs, IADLs, cognitive ADLs, comorbid medical conditions, and depressive symptoms. We measured age in years. We measured gender as a binary contrast of men (coded 1) versus women (coded 0). We measured race as a binary contrast of Caucasian (coded 1) versus African American (coded 0). We measured education in years. We measured cognitive function by using the MMSE (Folstein et al., 1975). We assessed ADLs based on self-reports of difficulty in task performance related to bathing, dressing, and hygiene consistent with the Minimum Data Set (J. Morris & Morris, 1997; J. N. Morris et al., 1997). Similarly, we measured IADLs consistent with the Minimum Data Set by using self-reports of difficulty in task performance for preparing meals, doing housework, managing finances, managing health care, using the phone, shopping, and traveling (J. Morris & Morris; J. N. Morris et al.). We measured cognitive ADLs by using the number of items correct on the Everyday Problems Test, which is based on 14 common problem-solving scenarios (e.g., medication labels, transportation schedules; Willis, 1994), each of which has two test items. We measured comorbid medical conditions by using the Older American Resources and Services protocol (Fillenbaum, 1988), which counts the number of self-reported chronic diseases. Finally, we measured depressive symptoms by using the 12-item version of the Center for Epidemiological Studies–Depression scale (Radloff, 1977).

Analysis

We drew the data used in this analysis from ACTIVE's baseline and 24-month follow-up assessments. The analytic sample consisted of the 2,147 participants who completed the 24-month assessment, and we weighted the data by the inverse of the participation rate within propensity score quintiles for the multiple logistic regression models of extensive decline in HRQoL at the 24-month follow-up (Hosmer & Lemeshow, 1989). In these models, we initially regressed extensive decline in HRQoL on a set of dummy variables representing the three cognitive intervention groups in order to obtain the crude effect estimates. We then added the covariates into the model in order to obtain the independent effects of the three cognitive interventions. We evaluated model fit by using the Hosmer-Lemeshow

Table 1. Means (or Percentages) of the Covariates and SF-36 Scale Scores at Baseline

Variable	Memory Intervention (n = 542)	Reasoning Intervention (n = 531)	Speed Intervention (n = 543)	Control Group (n = 531)	p
Covariate					
Age (years)	73.2	73.5	73.1	73.9	.121
Women (%)	77.7	77.0	78.1	75.3	.721
White (%)	76.4	75.7	75.3	75.7	.982
Education (years)	13.7	13.5	13.7	13.4	.230
MMSE	27.5	27.4	27.6	27.4	.354
ADLs	0.3	0.3	0.3	0.3	.562
IADLs	4.3	4.3	4.1	4.2	.878
EPT	19.5	19.1	19.4	18.9	.179
CES-D	4.8	5.4	5.1	4.9	.169
Chronic conditions	2.3	2.3	2.2	2.1	.135
SF-36 scale scores					
Physical functioning	70.4	68.9	69.9	69.7	.768
Role limitations (physical)	62.5	56.8	63.7	61.4	.021
Bodily pain	66.7	64.8	67.0	65.7	.329
Social functioning	88.0	85.4	86.5	88.0	.084
Mental health	81.5	79.3	79.5	80.5	.067
Role limitations (emotional)	76.6	73.0	75.9	76.7	.275
Vitality	62.8	61.0	62.3	61.7	.471
General health perceptions	70.2	68.6	70.7	69.1	.247

Note: SF-36 = Short Form-36; MMSE = Mini-Mental State Examination; ADL = activity of daily living; IADL = instrumental ADL; EPT = Everyday Problems Test; CES-D = Center for Epidemiological Studies–Depression scale.

statistic (desired homoscedasticity exists when the p value is *not* significant; Hosmer & Lemeshow), and the C statistic (values greater than 0.50 indicate meaningful improvement over chance, and values approaching 0.70 are considered good; Hanley & McNeil, 1982).

Results

Descriptive

Table 1 contains the means (or percentages) of the covariates and SF-36 scale scores at baseline for the participants in each of the ACTIVE treatment arms. Overall, the 2,147 ACTIVE participants who were successfully interviewed 24 months after intervention were 73.4 years old, 77.0% were women, 76.0% were Caucasian, and mean educational attainment was 13.6 years. The mean MMSE score was 27.5, the average number of ADLs with difficulty was 0.3, the average number of IADLs with difficulty was 4.3, the mean number of successful answers on the Everyday Problems Test was 19.2, the average number of depressive symptoms was 5.0, and the mean number of chronic conditions was 2.2. We observed no significant differences in the distribution of any of these covariates across the four treatment arms. The overall mean scores on the SF-36 scales were 69.8 on physical functioning, 61.1 on role limitations (physical), 66.1 on bodily pain, 87.0 on social functioning, 80.2 on mental health, 75.5 on role limitations (emotional), 62.0 on vitality, and 69.6 on general health perceptions. The only significant difference on the distribution of the SF-36 scale scores across the four treatment arms involved the role limitations (physical) scale, on which participants in the reasoning intervention averaged 4.3 points fewer than the grand mean. The relatively high mean scores on the SF-36 scales, especially in terms of social functioning, mental health, and role limitations (emotional), indicate that these ACTIVE participants were well adapted to their life situations, which was likely a function of their high average educational attainment, excellent MMSE scores, and limited levels of difficulty with basic, instrumental, or cognitive ADLs.

Table 2. Mean Changes From Baseline to 24-Month Follow-Up in SF-36 Scale Scores

SF-36 Scale	Memory Intervention (n = 542)	Reasoning Intervention (n = 531)	Speed Intervention (n = 543)	Control Group (n = 531)	p
Physical functioning	−5.4	−4.5	−3.9[a]	−5.3	.433
Role limitations (physical)	−6.6	−4.9	−3.9[a]	−4.8	.717
Bodily pain	−3.9	−1.7	−1.4[a]	−2.3	.195
Social functioning	−2.5	−2.6	−1.4[a]	−3.8	.337
Mental health	−0.9	−0.0	1.1[a]	−0.5	.096
Role limitations (emotional)	−0.2	−0.8	0.2[a]	−0.9	.961
Vitality	−2.2	−3.3	−1.9	−0.8[a]	.107
General health perceptions	−2.2	−2.4	−1.6[a]	−2.2	.855

Note: SF-36 = Short Form-36.
[a]Lowest row decline magnitude.

Table 2 shows the mean changes from baseline to the 24-month follow-up interview for each of the SF-36 scale scores for the participants in each of the ACTIVE treatment arms. These are crude (unadjusted) differences. In terms of the simple change (i.e., gain/loss) scores, there were no significant differences for any of the eight SF-36 scales across the treatment arms. This reflects on the insensitivity of any of the individual SF-36 scale scores in detecting changes over time (Wyrwich, Tierney, Babu, Kroenke, & Wolinsky, 2005). Table 3 shows the percentage of participants by treatment arm with clinically important declines (i.e., 0.50 standard deviations) on each of the SF-36 scales. Although the participants in the speed treatment arm always had the lowest percentages, only the differences for bodily pain were statistically significant.

Table 3. Percentage of Participants With Clinically Important Declines on the Eight SF-36 Scales at 24-Month Follow-Up

SF-36 Scale	Memory Intervention (n = 542)	Reasoning Intervention (n = 531)	Speed Intervention (n = 543)	Control Group (n = 531)	p
Physical functioning	27.9	26.4	22.6[a]	26.5	.220
Role limitations (physical)	33.0	34.8	29.8[a]	31.4	.343
Bodily pain	32.0	27.3	23.8[a]	27.8	.029
Social functioning	29.1	31.6	27.9[a]	31.3	.502
Mental health	28.9	27.3	23.5[a]	26.0	.218
Role limitations (emotional)	20.4	22.5	19.6[a]	20.2	.654
Vitality	34.1	37.1	31.7[a]	31.7[a]	.201
General health perceptions	31.2	32.9	29.8[a]	30.8	.737

Notes: SF-36 = Short Form-36. We defined a clinically important decline as one that was greater than or equal to 0.50 standard deviations.
[a]Lowest row percentages.

Table 4. Mean Number of Clinically Important Declines and Increases on the Eight SF-36 Scales, and Percentage of Participants Having Extensive Decline in HRQoL

Variable	Memory Intervention ($n = 542$)	Reasoning Intervention ($n = 531$)	Speed Intervention ($n = 543$)	Control Group ($n = 531$)	p
Number of clinically important increases	1.64	1.75	1.76	1.65	.493
Number of clinically important declines	2.35	2.39	2.08	2.25	.044
Participants with extensive decline in HRQoL (%)	28.0	26.7	19.5	25.8	.006

Notes: SF-36 = Short Form-36; HRQoL = health-related quality of life. We defined extensive decline in HRQoL as a decline of greater than or equal to 0.50 standard deviations on four or more of the eight SF-36 Scales.

Table 4 shows the mean total number of clinically important declines and increases on each of the eight SF-36 scales by treatment arm, as well as the percentage of participants who had extensive declines in HRQoL. Here we observed a statistically significant difference in the total number of clinically important declines, with participants in the speed-training treatment group averaging about 0.3 fewer declines on the eight SF-36 scale scores than their counterparts. More importantly, although 25.0% of the participants overall had extensive decline in HRQoL (i.e., clinically relevant declines on at least four of the eight SF-36 scales), the distribution of extensive decline was significantly different across the four treatment arms: 28.0% for participants in the memory group, 26.7% for participants in the reasoning group, 19.5% for participants in the speed group, and 25.8% for participants in the control group. This differential distribution was highly statistically significant ($p = .006$).

Multiple Logistic Regression

Table 5 contains the crude odds ratios (Models 1a and 1b) and AORs (Models 2a and 2b) obtained from the two multiple logistic regression models of extensive decline in HRQoL. We weighted one set of models (Models 1a and 2a) to adjust for potential attrition bias using the standard propensity score method; the other set of models (Models 1b and 2b) was unweighted. Models 1a and 1b provide the crude odds ratios for the four treatment arms (the control group is the reference category). As shown, and consistent with the above cross-classification results, participants in the speed-training group had lower odds of having extensive decline in HRQoL compared with the control group, with 37.6% lower odds in the weighted model (1a) and 31.4% lower odds in the unweighted model (1b). The risk of extensive decline in HRQoL for participants in the memory and reasoning training groups did not differ from that of participants in the control group (weighted or unweighted). When we added the 10 covariates into Models 2a and 2b, there was no appreciable change in the protective effect of being in the speed-training group. As is shown in Model 2a, among the covariates, age, race, education, and depressive symptoms had statistically significant effects, with a 2.9% increase in the odds for extensive decline associated with each year of age, 21.1% lower odds for Whites (compared with Blacks), a 6.8% decrease in the odds for extensive decline associated with each year of education, and a 2.2% decrease in the odds associated with each depressive symptom. The effects of the covariates shown in Model 2b (the unweighted analyses) were equivalent, although the marginally statistically significant effects of race and depressive symptoms shown in Model 2a were no longer statistically significant. Overall, Model 2a fit the data fairly well (Hosmer–Lemeshow statistic p value = .318; C statistic = .625).

Table 5. Crude and Adjusted Odds Ratios for Cognitive Interventions, and Adjusted Odds Ratios for Covariates, on Extensive Decline in HRQoL at 24 Months, Weighted and Unweighted to Adjust for Attrition Bias

Variable	Model 1a[a]	Model 1b[b]	Model 2a[a]	Model 2b[b]
Cognitive intervention				
Memory	1.077	1.129	1.149	1.188
Reasoning	0.995	1.047	1.014	1.074
Speed	0.624***	0.686**	0.643**	0.720*
Control (reference)	1.000	1.000	1.000	1.000
Covariate				
Age			1.029**	1.029**
Male			1.064	0.962
White			0.789*	0.799
Education			0.932**	0.927***
MMSE			0.977	0.978
ADLs			0.969	0.942
IADLs			0.988	0.988
EPT			0.983	0.979
CES-D			0.978*	0.979
Chronic conditions			1.065	1.043

Notes: HRQoL = health-related quality of life; MMSE = Mini-Mental State Examination; ADL = activity of daily living; IADL = instrumental ADL; EPT = Everyday Problems Test; CES-D = Center for Epidemiological Studies–Depression scale. We defined extensive decline in HRQoL as a decline of greater than or equal to 0.50 standard deviations on four or more of the eight Short Form-36 Scales.

[a]Weighted to adjust for attrition.

[b]Not weighted to adjust for attrition.

*$p < .05$; **$p < .01$; ***$p < .001$.

Discussion

ACTIVE is the largest randomized controlled trial yet conducted that focuses on improving cognitive performance among older adults (Jobe et al., 2001). Moreover, it is the first such trial specifically designed to avoid or postpone cognitive decline in normally functioning older adults in order to halt or slow the adverse consequences of such cognitive decline (including increases in basic, instrumental, and cognitive ADLs; lower HRQoL; and higher health services use; and nursing home placement). Previous research has shown that the three distinct cognitive interventions in ACTIVE were all successful in improving their proximal cognitive outcomes (Ball et al., 2002). We have shown here that the speed-of-processing training intervention was also successful in reducing extensive decline in HRQoL over the first 24 months of follow-up. Indeed, after adjustment for all of the covariates, participants in the speed-training arm of ACTIVE had 35.7% ($p = .006$) lower odds of experiencing extensive decline than participants in the control group.

The protective effect of the speed-training intervention, in the absence of benefits accruing from the reasoning- and memory-training arms, is not entirely surprising. As previously reported, speed training had a substantially greater effect on improving its proximal cognitive outcomes than did either of its counterparts (Ball et al., 2002). Specifically, 87% of the speed-, 74% of the reasoning-, and 26% of the memory-trained participants demonstrated reliable cognitive improvement (defined as a gain in score greater than or equal to at least one standard error of measurement) at the immediate post-test (Ball et al). Moreover, participants in the speed-training group who also received booster training had statistically significant improvements in ADL and IADL functioning 12 months after baseline, whereas participants in the reasoning- and memory-training groups did not.

Nonetheless, these findings beg an important question. What is it about speed-of-processing training that matters, at least in terms of HRQoL? Although the answer cannot be definitively determined from the ACTIVE study, it is likely that neurobiologic and psychosocial factors play important roles. Of the three cognitive interventions, speed of processing is the most clearly procedural. That is, speed of processing operates through sensory-motor elaboration and repetition, whereas the memory and reasoning interventions emphasize or require the explicit learning of new concepts. Procedural tasks have a broader pattern of regional brain activation (i.e., neostriatum and cerebellum in addition to neocortex) than do explicit memory tasks (Cabeza & Nyberg, 2000), and this may contribute to the greater sense of well-being captured by the HRQoL ratings. The psychosocial part of the explanation is that such improved brain activation or structure may delay the onset of (if not reduce the risk for) "slowing down," which is the single most dreaded fear of older adults, even though the majority of them clearly recognize that they will ultimately face "a slower pace of life" (Cape, 1983, p.18). Therefore, to the extent that participants in the speed-of-processing intervention delayed or avoided tempo reductions, these older adults were able to retain higher (i.e., baseline) perceptions of their HRQoL compared with their counterparts.

The failure of the memory and reasoning interventions to significantly reduce the risk of extensive decline in HRQoL warrants further comment. It is possible that these null findings may be somewhat artificial. First, although all three cognitive interventions were designed to have substantial comparability in terms of the number and length of sessions, there were differences in delivery structure. The speed-of-processing intervention involved more performance feedback from the trainer to the participant throughout the training process than did either the memory or reasoning interventions. Moreover, the feedback delivered in the speed-of-processing intervention was more concrete than that delivered in either the memory or reasoning interventions. Because the HRQoL measures were subjective self-evaluations, they may have been more sensitive to the increased and more concrete performance feedback associated with the speed-of-processing intervention. Second, although the 10-session standard delivery package was adequate for the speed-of-processing intervention, it may not have been sufficient to reach the necessary thresholds for either the memory or reasoning intervention. That is, the exposure (or training) threshold for producing the desired effect for the memory and reasoning interventions may require going well beyond 10 sessions. Although both of these possible explanations (i.e., differential performance feedback and differential training thresholds) for the null findings for the memory and reasoning interventions are plausible, they must be considered rather speculative, inasmuch as they cannot be addressed in these data.

We must recognize an important limitation in the design of the ACTIVE study. Although ACTIVE was a randomized controlled trial, which maximizes internal validity, its participants were not recruited to be representative of the population at large, which limits external validity (Shadish, Cook, & Campbell, 2002). Indeed, the exclusion criteria for ACTIVE intentionally screened out individuals with extant functional or cognitive decline. Because of this, ACTIVE participants were likely more resilient at baseline and less likely to decline by the time of the 24-month follow-up than the average older adult. One can observe this in the lack of functional decline in the control group. This possibility notwithstanding, 1 in 4 ACTIVE participants did experience extensive decline in HRQoL during the observation period. Thus, although it is clear that the ACTIVE interventions improved cognitive abilities and that these improvements continued through 24 months (Ball et al., 2002), most of the participants did not experience functional decline during this time. Therefore, it is possible that expected differential functional decline across treatment groups in the future, as this select cohort enters more fully into an age of functional loss, will contribute to additional and/or stronger observed protective effects against extensive decline in HRQoL.

What remains to be seen is whether the indisputable and protective effect of the speed-of-processing intervention on extensive decline in HRQoL reported here will be replicated when other, more objective outcomes are considered. After all, the SF-36 is a subjective and self-reported measure. This is not a criticism of the SF-36. Indeed, due to its very nature, researchers must assess HRQoL by using subjective self-reports, and postponing or eliminating declines in HRQoL among older adults is critically important. Nonetheless, one wonders whether the protective effect of the speed-of-processing intervention will translate into more appropriate and reduced levels of health services utilization and resource consumption and, ultimately, into greater longevity. Examining these more objective outcomes is the next step in the ACTIVE study.

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References

Aneshensel, C. S., Pearlin, L. I., & Schuler, R. H. (1993). Stress, role captivity, and the cessation of caregiving. *Journal of Health and Social Behavior, 34*, 54–70.

Ball, K., Berch, S. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske, M., et al. (2002). Effects of cognitive training interventions with older adults: A randomized controlled trial. *Journal of the American Medical Association, 288*, 2271–2281.

Braun, J. V., Wykle, M. H., & Cowling, W. R. (1988). Failure to thrive in older persons: A concept derived. *The Gerontologist, 28*, 809–812.

Brazier, J., Harper, R., & Jones, N. (1992). Validating the SF-36 Health Survey questionnaire: New outcome measures for primary care. *British Medical Journal, 305*, 160–164.

Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and MRI studies. *Journal of Cognitive Neuroscience, 12*, 1–47.

Cape, R. D. T. (1983). The geriatric patient. In R. D. T. Cape, R. M. Coe, & I. Rossman (Eds.), *Fundamentals of geriatric medicine* (pp. 17–24). New York: Raven Press.

Carmelli, D., Swan, G. E., LaRue, A., & Eslinger, P. J. (1997). Correlates of change in cognitive function in survivors from the Western Collaborative Group Study. *Neuroepidemiology, 16*, 285–295.

Cohen, J. (1969). *Statistical power analysis for the behavioural sciences.* London: Academic Press.

Cohen, R. A., Moser, D. J., Clark, M. M., Aloia, M. S., Cargill, B. R., Stefanik, S., et al. (1999). Neurocognitive functioning and improvement in quality of life following participation in cardiac rehabilitation. *American Journal of Cardiology, 83*, 1374–1378.

D'Agostino, R. B. (1998). Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Statistics in Medicine, 17*, 2265–2281.

Feinstein, A. R. (1999). Indexes of contrast and quantitative significance for comparisons of two groups. *Statistics in Medicine, 18*, 2557–2581.

Fillenbaum, G. (1988). *Multidimensional functional assessment of older adults: The Duke Older American Resources and Services procedures.* Hillsdale, NJ: Erlbaum.

Folstein, M. R., Folstein, S., & 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.

Fratiglioni, L., Paillard-Borg, S., & Winblad, B. (2004). An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurology, 3*, 343–353.

Hanley, J. A., & McNeil, B. J. (1982). The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology, 143*, 29–36.

Hosmer, D. W., & Lemeshow, S. (1989). *Applied logistic regression.* New York: Wiley.

Jobe, J. B., Smith, D. M., Ball, K., Tennstedt, S. L., Marsiske, M., Willis, S. L. et al. (2001). ACTIVE: A cognitive intervention trial to promote independence in older adults. *Controlled Clinical Trials, 22*, 453–479.

Kane, R. A., Kane, R. L., & Ladd, R. C. (1998). *The heart of long-term care.* New York: Oxford University Press.

Lloyd, A. J., Boyle, J., Bell, P. R., & Thompson, M. M. (2000). Comparison of cognitive function and quality of life after endovascular or conventional aortic aneurysm repair. *British Journal of Surgery, 87*, 443–447.

McHorney, C. A., Ware, J. E., & Raczek, A. E. (1993). The MOS 36-item Short-Form Health Survey (SF-36). II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical Care, 31*, 247–263.

Miller, G. A. (1956). The magic number seven plus or minus two: Some limits on our capacity for processing information. *Psychological Review, 63*, 81–97.

Morris, J., & Morris, S. (1997). ADL assessment for use with frail elders. *Journal of Mental Health and Aging, 3*, 19–45.

Morris, J. N., Fries, B. E., Steel, K., Ikegami, N., Bernabei, R., Carpenter, G. I., et al. (1997). Comprehensive clinical assessment in community settings: Applicability of the MDS-HC. *Journal of the American Geriatrics Society, 45*, 1017–1024.

Norman, G. R., Sloan, J. A., & Wyrwich, K. W. (2003). Interpretation of changes in health-related quality of life: The remarkable universality of half a standard deviation. *Medical Care, 41*, 582–592.

Pathy, M. S. J., Morley, J. E., & Sinclair, A. (Eds.). (2006). *Principles and practice of geriatric medicine* (4th ed.). New York: Wiley.

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

Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. *Biometrika, 70*, 41–55.

Rowe, J. W., & Kahn, R. L. (1998). *Successful aging*. New York: Pantheon.

Rubin, D. B. (1979). Using multivariate matched sampling and regression adjustment to control bias in observational studies. *Journal of the American Statistical Association, 74*, 318–324.

Shadish, W. R., Cook, T. D., & Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference.* Boston: Houghton Mifflin.

Sloan, J. A., Loprinzi, C. L., & Kuross, S. A. (1998). Randomized comparison of four tools measuring overall quality of life in patients with advanced cancer. *Journal of Clinical Oncology, 16*, 3662–3673.

Stewart, A. L., Hays, R. D., & Ware, J. E. (1988). The MOS Short-Form general health survey: Reliability and validity in a patient population. *Medical Care, 26*, 724–736.

Tarlov, A. R., Ware, J. E., & Greenfield, S. (1989). The Medical Outcomes Study: An application of methods for monitoring the results of medical care. *Journal of the American Medical Association, 262*, 925–934.

Testa, M. A. (1987). Interpreting quality of life clinical trial data for use in the clinical practice of antihypertensive therapy. *Journal of Hypertension, 5*, S9–S13.

Ware, J. E. (1996). The SF-36 Health Survey. In B. Spilker (Ed.), *Quality of life and pharmacoeconomics in clinical trials* (2nd ed., pp. 337–345). Philadelphia: Lippincott-Raven.

Ware, J. E., & Kosinski, M. (1999). *The SF-36 physical and mental health summary scales: A manual for users of version 1, second edition.* Boston: QualityMetric.

Ware, J. E., Kosinski, M., & Dewey, J. E. (2000). *How to score version 2 of the SF-36 Health Survey.* Boston: QualityMetric.

Ware, J. E., & Sherbourne, C. D. (1992). The MOS 36-item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Medical Care, 30*, 473–486.

Willis, S. L. (1994). Everyday cognitive competence in elderly persons: Conceptual issues and empirical findings. *The Gerontologist, 36*, 595–601.

Wolinsky, F. D. (2006). Functional assessment scales. In M. S .J. Pathy, J. E. Morley, & A. Sinclair (Eds.), *Principles and practice of geriatric medicine* (4th ed.) (pp. 1553–1563). New York: Wiley.

Wolinsky, F. D., Callahan, C. M., Fitzgerald, J. F., & Johnson, R. J. (1992). The risk of nursing home placement and subsequent death among older adults. *Journal of Gerontology: Social Sciences, 47*, S173–S182.

Wolinsky, F. D., Callahan, C. M., Fitzgerald, J. F., & Johnson, R. J. (1993). Changes in functional status and the risks of subsequent nursing home placement and death. *Journal of Gerontology: Social Sciences, 48*, S94–S101.

Wolinsky, F. D., Culler, S. D., Callahan, C. M., & Johnson, R. J. (1994). Hospital resource consumption among older adults: A prospective analysis of episodes, length of stay, and charges over a seven-year period. *Journal of Gerontology: Social Sciences, 49*, S240–S252.

Wolinsky, F. D., & Johnson, R. J. (1991). The use of health services by older adults. *Journal of Gerontology: Social Sciences, 46*, S345–S357.

Wolinsky, F. D., & Miller, D. K. (2006). Disability concepts and measurement: Contributions of the epidemiology of disability to gerontological inquiry. In J. M. Wilmoth & K. F. Ferraro (Eds.), *Gerontology: Perspectives and issues* (3rd ed.) (pp. 111–132). New York: Springer.

Wolinsky, F. D., Stump, T. E., & Callahan, C. M. (1997). Does being placed in a nursing home make you sicker and more likely to die? In S. L. Willis, K. W. Schaie, & M. Hayward (Eds.), *Societal mechanisms for maintaining competence in old age* (pp. 94–130). New York: Springer.

Wolinsky, F. D., Stump, T. E., & Johnson, R. J. (1995). Hospital utilization profiles among older adults over time: Consistency and volume among survivors and decedents. *Journal of Gerontology: Social Sciences, 50B*, S88–S100.

Wyrwich, K. W., Tierney, W. M., Babu, A. N., Kroenke, K., & Wolinsky, F. D. (2005). A comparison of clinically important differences in health-related quality of life for patients with asthma, lung disease, or heart disease. *Health Services Research, 40*, 577–591.

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