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The ACTIVE Cognitive Training Interventions and the Onset of and Recovery from Suspected Clinical Depression

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We evaluated the effects of the 3 cognitive interventions fielded in the Advanced Cognitive Training for Independent and Vital Elderly study on 2 subsets of participants—1,606 without and 424 with suspected clinical depression at baseline. In the former group, only the speed of processing (vs. no-contact control) intervention had a significant effect, with its participants being 38% less likely to develop suspected clinical depression at 1 year (adjusted odds ratio = 0.62; $p < .01$). None of the interventions had a significant effect on recovery from suspected clinical depression in the latter group. Although the etiological mechanism of the speed of processing's protective effect was not isolated, it may result from successful adaptation to age-related changes through selective optimization with compensation.

Key Words: ACTIVE—Depression—Randomized controlled trial—Speed of processing.

DEPRESSIVE symptoms involve both mood and malaise (i.e., feeling and bodily states; Mirowsky & Ross, 2003). Typical screening statements include "feeling sad, demoralized, lonely, helpless, or worthless, wishing you were dead, having trouble sleeping, crying, feeling everything is an effort, and not being able to get going" (Mirowsky & Ross, p. 23). These symptoms are common in the general population and are also prevalent among older adults (Anonymous, 1992; Blazer, 2003), especially those with health and functional limitations (Lyness et al., 2002; Nourhashemi et al., 2001). Among community-dwelling samples, the prevalence of current major depressive disorder in the elderly is estimated at 1%–5%, although rates in various patient samples range from approximately 5% to 15% (Hybels & Blazer, 2003). As would be expected, the prevalence of clinically significant depressive symptoms is much higher, with estimates ranging from 3% to 26% in community samples and 10%–30% in patient populations (Hybels & Blazer). Clinically depressed older adults have an increased risk of becoming frail (Fried et al., 2001; Penninx, Guralnik, Ferrucci et al., 1998) and of developing incident chronic diseases such as cancer (Penninx, Guralnik, Pahor et al., 1998), diabetes (Eaton, Armenian, Gallo, Pratt, & Ford, 1996), heart disease (Ferketich, Schwartzbaum, Frid, & Moeschberger, 2000), and stroke (Jonas & Mussolino, 2000), although the causal direction here has not been definitively demonstrated. Clinically depressed older adults are also at greater risk of adverse outcomes for existing comorbid conditions (Blazer, Hybels, & Pieper, 2001), lower health-related quality of life (HRQoL; Doraiswamy, Khan, Donahue, & Richard, 2002), and mortality (Ariyo et al., 2000).

Accordingly, gerontology and geriatrics have focused much attention on the recognition and treatment of depressive symptoms and clinical depression (Callahan, 2001; Callahan, Hendrie, & Tierney, 1996; Mulrow et al., 1995; Unutzer et al., 2003). In this article, we contribute to that literature by conducting a secondary analysis of data from the National Institutes of Health-funded, multisite, Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) randomized controlled trial (Jobe et al., 2001). Although ACTIVE was not designed to evaluate the effect of the cognitive interventions on the onset of or recovery from major depressive disorders, such data were collected at each assessment round.

ACTIVE hypothesized that each of its three intervention arms (memory, reasoning, and speed of processing) would have a direct effect on its targeted trained outcome (referred to as proximal outcomes) and nonspecific effects on each of its nontargeted untrained outcomes (via social contact mechanisms). It was further hypothesized that the effects of the ACTIVE interventions on both the primary and the secondary outcomes would be fully mediated (i.e., indirect only)

through the targeted trained (proximal) outcomes. Among the primary outcomes, the reasoning and memory interventions were expected to affect only everyday problem solving and activities of daily living (ADL) and instrumental activities of daily living (IADL) functioning, whereas the speed of processing intervention was hypothesized to have more diverse effects, including ADL and IADL functioning, everyday speed, and driving habits. All three ACTIVE interventions were expected to affect the secondary outcomes, including HRQoL, mobility, health services use, and expenditures.

In previous analyses, ACTIVE's memory, reasoning, and speed of processing interventions have been shown to have protective effects on both cognitive and functional outcomes (Ball et al., 2002; Willis et al., 2006). In addition, statistically and clinically significant effects of ACTIVE's speed of processing intervention, but not the memory or reasoning interventions, have been shown on many of the secondary or health outcomes. Indeed, relative to the no-contact control group, these findings include (a) a $244 per person-year (3%) reduction ($p = .012$) in predicted medical expenses at 1 year postbaseline (Wolinsky, Mahncke, Kosinksi et al., 2009); (b) a 38% reduction in the risk of global decline in HRQoL at 2 years postbaseline ($p = .004$) and a 26% reduction in the risk of global decline in HRQoL ($p < .038$) at 5 years postbaseline (Wolinsky et al., 2006a, 2006b); (c) a 30% reduction in the risk of clinically important worsening of depressive symptoms at both 1 year ($p = .012$) and 5 years ($p = .023$) postbaseline (Wolinsky, Vander Weg, Martin, Unverzagt, Ball et al., 2009); (d) improvements in self-rated health at 2, 3, and 5 years equivalent to at least half of the difference between "excellent" and "very good" responses ($p < .05$), which is known to be associated with a 0.8% "absolute" reduction in the 5 years mortality rate and a 10% "relative" mortality reduction (Wolinsky, Mahncke, Vander Weg et al., 2009); and (e) a 64% greater likelihood ($p < .05$) of improvements in internal locus of control (Lachman, Baltes, Nesselroade, & Willis, 1982) at 5 years postbaseline (Wolinsky, Vander Weg, Martin, Unverzagt, Willis et al., 2009a).

It is the findings on the reduced risks for those in the speed of processing intervention on worsening of depressive symptoms that motivated the present study. Those were the analyses that showed the speed of processing intervention substantially reduced the risk of a worsening of depressive symptoms, regardless of whether that worsening was defined as a 0.5 or 1.0 *SD* increment in symptoms. Here, we extend that research by taking the analyses to a more clinically relevant level. That is, we "drill down" to evaluate the effects of ACTIVE's three distinct cognitive interventions on what we believe are two clinically distinct subsets of participants. First, among participants who did not meet our criterion for suspected clinical depression at baseline, we evaluate the effects of ACTIVE's three cognitive training interventions on the onset of suspected clinical depression at 1 year. Second, among participants who did meet our criterion for suspected clinical depression at baseline, we evaluate the effects of ACTIVE's three cognitive training interventions on the recovery from suspected clinical depression at 1 year.

Although we examine here the effects of all three cognitive interventions, we a priori hypothesize that only speed of processing would have a protective effect against the onset of suspected clinical depression and an enhancing effect on recovery from suspected clinical depression. We hypothesize that these improvements delay the onset and/or reduce the risk of cognitive slowing, which Salthouse (1996, 2009) has championed as the most significant contributor to overall age-related cognitive decline. Although the etiological mechanism by which improved speed of processing might protect against the onset of suspected clinical depression or facilitate recovery from it is not established, that mechanism may result from enhancing the cognitive resources available to successfully manage or delay the declines commonly associated with aging through the adaptive processes of selection, optimization, and compensation (Baltes & Baltes, 1990). This possibility is entirely consistent with accumulating evidence suggesting that reduced processing speed is the core cognitive deficit observed among individuals with late-life depression (Sheline et al., 2006; Thomas & O'Brien, 2008).

Methods

Sample

All ACTIVE participants were aged 65 years and older and lived independently in the community. Each site developed its own recruitment strategy. From March 1998 through October 1999, a total of 4,970 potential participants were identified (Jobe et al., 2001). Of these, 905 (18%) were excluded due to poor vision, dependency in personal hygiene or dressing, cognitive impairment or dementia of the Alzheimer type, recent ischemic strokes, cancer or active cancer therapy-based reduced life expectancies, communication difficulties, short-term plans to move out of the area or other anticipated scheduling conflicts, or participation in prior cognitive training programs. Another 1,263 potential participants (25%) were unwilling to participate. The 2,802 remaining potential participants were screened, signed written Institutional Review Board-approved informed consent, and were enrolled in ACTIVE.

Randomization and Data Collection

All data collectors completed an intensive 4-day training workshop at the Coordinating Center, had to pass uniform certification requirements, and were subject to continuous quality improvement evaluation and review. Baseline data were collected after enrollment, and each of the six sites used a computerized program to randomly assign participants to the four study groups. Randomization was done immediately prior to the initiation of treatment in order to minimize dropout and potential imbalances between randomization and treatment. At follow-up, data collectors

were blinded to treatment assignment and reassessed participants immediately after training and at 1, 2, 3, and 5 years postbaseline. All analyses reported here, however, are limited to the baseline to 1-year follow-up because we hypothesized that this would best showcase the potential effects of the three interventions on suspected clinical depression. That is, suspected clinical depression is a chronic and recurring, if not cyclical, condition. Given the arbitrarily timed follow-up protocol in ACTIVE, the longer the follow-up period, the less readily interpretable the internal validity of results obtained beyond the first annual follow-up.

Interventions

The memory, reasoning, and speed of processing interventions each involved 10 standardized sessions that shared nine key elements (e.g., practice, individual, and group components; fostering self-efficacy; and social interaction) and involved 1-hr intervention sessions. The 10 sessions were spread over 6 weeks, with an optimum group size of 3–4 participants per group. The first five intervention sessions focused on strategy instruction and practice exercises, although the last five provided additional practice. Both the laboratory type and everyday activities used were well specified in trainer manuals, and the intervention trainers underwent extensive training, certification, and continuous quality improvement evaluation and review, with no cross-training permitted (Jobe et al., 2001). Inductive reasoning was the focus of "reasoning training," especially the ability to solve problems that required linear thinking, followed a serial pattern, and were manifested in executive functioning. Such problems included understanding the daily dosing pattern for prescription drugs or using a bus schedule to plan transportation needs. Verbal episodic memory was the focus of "memory training," especially using multiple mnemonic strategies for remembering lists, sequences of items, text material, and main ideas and story details. Sample problems included grocery shopping lists and visualizing and associating items to be remembered, such as "to-do" lists. Visual search and the ability to identify and locate visual information quickly in a divided attention format were the focuses of the computer-based "speed training." This involved systematically reducing the duration of the target stimulus, progressively increasing the divided visual attention difficulty level and field, and ultimately introducing auditory distraction.

Suspected Clinical Depression

As Blazer (2003, p. 249; see also Sachs-Ericsson & Blazer, 2006) has noted, "Clinicians and clinical investigators do not agree as to what constitutes *clinically significant* depression [emphasis added]." Formal diagnoses of major depressive disorder can only be made when one of the two core *Diagnostic and Statistical Manual of Mental Disorders, IV Edition* (DSM-IV) symptoms is consistently present (i.e., a general disinterest in most activities or a sad mood) for at least 2 weeks, along with at least four additional symptoms, including perceived worthlessness, diminished concentration or decision-making ability, psychomotor retardation or agitation, fatigue, altered sleep patterns, weight or appetite change, and suicidal ideation or recurrent thoughts of death (American Psychiatric Association [APA], 1994). Less severe levels of depression (i.e., minor, subsyndromal, or subthreshold depression) can be diagnosed if one of the core symptoms is consistently present for at least 2 weeks along with 1–3 additional symptoms (APA, 1994). "Suspected clinical depression" has routinely been operationalized, especially in large-scale epidemiological studies, as scores of 16 or more on the 20-item Center for Epidemiological Studies-Depression scale (CESD-20) because studies have shown that among participants with a CESD-20 score greater than or equal to 16, more than 80% are found to have clinical depression on subsequent, in-depth structured psychiatric interviews (Beekman et al., 1995; Blazer; Radloff, 1977; Sachs-Ericsson & Blazer, 2006).

In this study, we used the 12-item version of the Center for Epidemiological Studies-Depression scale (CESD-12), which is one of many short forms of the reliable and well-validated 20-item CESD (CESD-20) to measure suspected clinical depression (Mirowsky & Ross, 2003; Radloff, 1977; Ross, Mirowsky, & Huber, 1983). Like the CESD-20, the response set for the CESD-12 had four levels: *rarely or none of the time* (0), *some of the time* (1), *much of the time* (2), and *most or all of the time* (3). Thus, CESD-12 scores ranged from 0 (*no depressive symptoms acknowledged*) to 36 (*all 12 depressive symptoms acknowledged to occur most or all of the time*).

Although definitive evidence (such as receiver operating characteristics curve analyses) has not yet been demonstrated for a comparable (to the ≥ 16 on the CESD-20) suspected clinical depression cut-point on the CESD-12 and cannot be from the ACTIVE data, we proceeded as follows. Based on the high correlations between shorter versions of the CESD and the complete CESD-20 (which averaged 0.95 in all their gender and ethnic subgroups), Kohout, Berkman, Evans, and Cornoni-Huntley (1993) have suggested that "it would be feasible to use regression equations to estimate the 20×4 [CESD-20] scores from briefer forms to compare results across studies that use different forms." Kohout et al. noted that using *T*-score transformations would also be reasonable. Those approaches suggested a cut-point of about 9 on the CESD-11, which was one of the short forms Kohout et al. used. Alternatively, we note here that the cut-point of 16 on the CESD-20 represents 26% of the maximum symptom score and that a comparable relative cut-point on the CESD-12 would be about 9, which is the same cutoff used previously by Pascoe, Stolfi, and Ormond (2006) among others. Comparable criterion-based thresholds for case finding (i.e., screening) for primary care in older adults have been shown for 10-item versions of the CESD as well (see Andresen, Malmgren, Carter, & Patrick, 1994; Blank,

Gruman, & Robison, 2004; Irwin, Artin, & Oxman, 1999; Mulrow et al., 1995; Williams, Pignone, Ramirez, & Stellato, 2002). Thus, although certainly not definitive, a comparable relative cut-point on the CESD-12 for suspected clinical depression greater than or equal to 9 is reasonable.

Selection and Attrition Bias

To be included in our analytic sample for evaluating the onset ("incidence") of suspected clinical depression, participants had to have CESD-12 scores less than 9 at baseline and have complete data on depressive symptoms available at the 1-year follow-up. Of the 2,802 original ACTIVE participants, 1,606 (57%) met these criteria and were included in our analytic sample focusing on the incidence of suspected clinical depression. These inclusion restrictions created the potential for selection and attrition bias. Therefore, to maintain an intention-to-treat approach (attributing participants to the treatment group to which they were assigned regardless of treatment delivery and/or dosage and accounting for all participants in the analyses; Guyatt, Sackett, & Cook, 1993a, 1993b), we used a propensity score model to adjust for potential selection and attrition bias (D'Agostino, 1998; Robins, Rotnitzky, & Zhao, 1994; Rosenbaum & Rubin, 1983; Rubin, 1979) based on the explicit assumption that the missingness resulting from the selection and attrition bias were not associated with the observed outcome measures (i.e., it was missing at random; Carpenter, Pocock, & Lamm, 2002; Mallinckrodt, Lane, Schnell, Peng, & Mancuso, 2008). We estimated a multivariable logistic regression model of whether participants were included in the analytic sample and computed their predicted probability of inclusion (Hosmer & Lemeshow, 1989). This model included treatment group assignment and demographic; socioeconomic; and cognitive, health, and functional status measures at baseline (complete list available on request). The propensity score model fit the data very well (*C*-statistic = .78; Hosmer-Lemeshow statistic *p* value = .39; Hanley & McNeil, 1982; Hosmer & Lemeshow). Within each propensity score (predicted probability) quintile, we determined the average participation rate (i.e., inclusion in the analytic sample or *P*) and used the inverse (1/*P*) to weight the data. This gave greater influence to participants in the analytic sample most like those not included. We then adjusted the propensity score weights so that the final weighted *N* was equal to the actual number of participants in the analytic sample. For reference purposes, we also present the results without using the propensity-weighted approach to adjust for potential selection and attrition bias for any statistically significant effects that are observed.

To be included in our analytic sample for evaluating "recovery" from suspected clinical depression, participants had to have CESD-12 scores greater than or equal to 9 at baseline and have complete data on depressive symptoms available at the 1-year follow-up. Of the 2,802 original ACTIVE participants, 424 (15%) met these criteria and were included in our second analytic sample. These inclusion restrictions also created the potential for selection and attrition bias. Therefore, we used a second propensity score model to adjust for potential selection and attrition bias (D'Agostino, 1998; Robins et al., 1994; Rosenbaum & Rubin, 1983; Rubin, 1979) to maintain an intention-to-treat approach (Guyatt et al., 1993a, 1993b). Using the procedures described above, we estimated a second propensity score model, which also fit the data very well (*C*-statistic = .81; Hosmer-Lemeshow statistic *p* value = .48; Hanley & McNeil, 1982; Hosmer & Lemeshow, 1989). Within each propensity score quintile, we again determined the average participation rate (*P*) and used the inverse (1/*P*) to weight the data, adjusting the propensity score weights so that the final weighted *N* was equal to the actual number of participants in this second analytic sample. Again, for reference purposes, we also present the results without using the propensity-weighted approach for any statistically significant observed effects.

Analytic Method

We used multivariable logistic regression (Hosmer & Lemeshow, 1989) to model the effects of the three treatment groups on (a) incidence of suspected clinical depression between the baseline and the 1-year follow-up ($N = 1,606$) and (b) the recovery from suspected clinical depression between the baseline and the 1-year follow-up ($N = 424$). Both of our intention-to-treat analyses had three steps. The first included only three dummy variables, contrasting each treatment group with the no-contact control group (Model 1). On the second step, the baseline CESD-12 score was added to ensure that the results were not sensitive to baseline values (Model 2). On the final step, we introduced the change in the Useful Field of View (UFOV) composite test (Ball, Beard, Roenker, Miller, & Griggs, 1988), which was the proximal (or targeted and trained) outcome for the speed of processing intervention (Model 3). We did this to determine whether the effect of the speed of processing intervention was fully mediated (i.e., indirect only) through changes in the UFOV test (i.e., was it just a mediated effect, as expected by ACTIVE's theoretical model) or whether it had a direct (i.e., nonmediated) effect on other indirect components as well.

Results

Evaluating the Incidence of Suspected Clinical Depression

Descriptive.—Of the 1,606 participants included in the analytic sample for the onset of suspected clinical depression, there were 409, 385, 407, and 405 in the memory, reasoning, speed of processing, and no-contact control groups, respectively. After weighting the data to

Table 1. Adjusted Odds Ratios (AORs) Obtained from Multiple Logistic Regression Models of the Onset (i.e., incidence) of Suspected Clinical Depression (i.e., CESD-12 scores ≥9) Between the Baseline and the 1-Year Follow-Up Among ACTIVE Participants Without Suspected Clinical Depression at Baseline (i.e., CESD-12 scores ≤ 8) (N = 1,606)

Risk factor	Model 1 AORs	Model 2 AORs	Model 3 AORs
Treatment group			
Memory	0.71	0.74	0.76
Reasoning	0.91	0.91	0.91
Speed of processing	0.62**	0.58**	0.53**
Baseline CESD-12 score	—	1.33***	1.33***
1-year change in the UFOV composite (per 10 ms)			1.00

Notes: CESD-12 = 12-item version of the Center for Epidemiological Studies-Depression scale; UFOV = Useful Field of View.

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

adjust for potential selection and attrition bias (weighted N = 1,606), the mean age at baseline was 74, 25% were men, 26% were Black, and the average educational attainment was 13.6 years. The mean Mini-Mental State Examination (MMSE) score at baseline was 27, the average number of ADLs with difficulty was 0.3 (out of three tasks), the average number of IADLs performed with any level of assistance or supervision was 1.2 (out of seven tasks), the mean number of chronic conditions was 2.2, 14% reported being in fair or poor (vs. excellent, very good, or good) health, and the mean score on the UFOV composite test was 908 ms. The mean CESD-12 score at baseline was 3.3 (range = 0–8), with 19% having no symptoms (i.e., a CESD-12 score of 0). By the 1-year follow-up, 288 (18%) met criteria for suspected clinical depression (i.e., had CESD-12 scores ≥ 9). Contrary to our hypotheses, however, the average UFOV composite test improvement did not differ between those who developed suspected clinical depression (a 136 ms improvement) versus those who did not (a 139 ms improvement; p > .80).

Multivariable regressions.—Table 1 contains the results obtained from the intention-to-treat multivariable logistic regression analyses. Relative to the no-contact control group, only the speed of processing intervention had a statistically significant effect on the onset (i.e., incidence) of suspected clinical depression between the baseline and the 1-year follow-up (Model 1), lowering the odds of that occurring by 38% (adjusted odds ratio [AOR] = 0.62; p < .01). Adjustment for baseline CESD-12 scores (Model 2) did not alter this protective effect (AOR = 0.58; p < .01). Similarly, adjustment for changes in the UFOV composite test (Model 3) did not mediate this protective effect at all (AOR = 0.53; p < .01). Moreover, changes in the UFOV composite test were not significantly related to the onset of suspected clinical depression. Finally, when we replicated these analyses without using the propensity score method to adjust for potential selection and attrition bias, equivalent (robust) results were obtained (AOR = 0.65; p < .05).

Additional analyses (data not shown) in which the speed of processing (rather than the no-contact control) group was used as the reference category (i.e., in head-to-head comparisons with each of the three other study groups) showed that the speed of processing group was significantly protected from the onset of suspected clinical depression relative to the reasoning group (p = .05) but not (p = .30) relative to the memory group. It should, however, be emphasized that the memory group was not statistically significantly different from the no-contact control group. To calibrate the magnitude of the mean baseline to 1-year change in CESD-12 scores, we conducted similar analysis (data not shown) using multivariable linear regression. Those results indicated that the mean change (partial unstandardized B coefficient) from baseline to the 1-year follow-up was significant only for the speed of processing group as well, indicating a mean decline (relative to the no-contact control group) of 0.88 points on the CESD-12 (p < .01).

Evaluating Recovery from Suspected Clinical Depression

Descriptive.—Of the 424 participants included in the analytic sample for evaluating recovery from suspected clinical depression, there were 97, 113, 110, and 104 in the memory, reasoning, speed of processing, and no-contact control groups, respectively. After weighting the data to adjust for potential selection and attrition bias, the mean age at baseline was 74, 19% were men, 32% were Black, and the average educational attainment was 13.4 years. The mean MMSE score was 27, the average number of ADLs with difficulty was 0.3 (out of three tasks), the average number of IADLs performed with any level of assistance or supervision was 1.5 (out of seven tasks), the mean number of chronic conditions was 2.2, and 16% reported being in fair or poor (vs excellent, very good, or good) health. Consistent with others who have noted an association between late-life depression and reduced processing speed (e.g., Butters et al., 2004; Den Hartog, Derix, Van Bemmel, Kremer, & Joiles, 2003; Simons et al., 2009), the mean score on the UFOV composite test at baseline was 1,027 ms, reflecting a 119 ms slower average speed than what was found among participants without suspected clinical depression (p < .001). The mean CESD-12 score at baseline was 11.3 (range = 9–34). By the 1-year follow-up, 266 (63%) no longer met the criteria for suspected clinical depression (i.e., had CESD-12 scores <9). Although the average UFOV composite test improvement was associated with recovery, that association was the opposite of what was expected. That is, those who recovered from suspected clinical depression had 47 ms lower improvement in processing speed than those who did not recover (143 vs 190 ms improvements; p < .001).

Table 2. Adjusted Odds Ratios (AORs) Obtained from Multiple Logistic Regression Models of the Recovery from Suspected Clinical Depression (i.e., CESD-12 scores ≤8) Between Baseline and the 1-Year Follow-Up Among ACTIVE Participants With Suspected Clinical Depression at Baseline (i.e., CESD-12 scores ≥9) (N = 424)

Risk factor	Model 1 AORs	Model 2 AORs	Model 3 AORs
Treatment group			
Memory	0.61	0.66	0.76
Reasoning	1.04	1.25	1.69
Speed of processing	0.47**	0.47**	0.67
Baseline CESD-12 score	—	0.86***	0.85***
1-year change in the UFOV composite (per 10 ms)			1.02**

Notes: CESD-12 = 12-item version of the Center for Epidemiological Studies-Depression scale; UFOV = Useful Field of View.

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

Multivariable regressions.—Table 2 contains the results obtained from the intention-to-treat multivariable logistic regression analyses. Relative to the no-contact control group, only the speed of processing intervention had a statistically significant effect on recovery from suspected clinical depression between the baseline and the 1-year follow-up, lowering the odds of that occurring by 53% (Model 1 AOR = 0.47; p < .01). Adjustment for baseline CESD-12 scores (Model 2) did not alter this recovery inhibiting effect (AOR = 0.47; p < .01). However, adjustment for changes in the UFOV composite test (Model 3) did fully mediate this protective effect (AOR = 0.67; p > .20). Moreover, changes in the UFOV composite test were significantly related to recovery from suspected clinical depression, although that relationship was the opposite of our expectations (i.e., reduced speed of processing enhanced the likelihood of recovery). Finally, when these analyses were replicated without using the propensity score method to adjust for potential selection and attrition bias, the results were less robust and not statistically significant.

Given the surprising direction of the speed of processing and change in UFOV composite test effects on recovery from suspected clinical depression, as well as their lack of robustness when selection and attrition bias adjustments were not made, post hoc sensitivity analyses were conducted. These involved using different cut-points on the CESD-12 of 10, 11, 12, 13 (1.5 *SD* above the baseline mean), and 14 for suspected clinical depression with and without adjustment for selection and attrition bias. Those results (data not shown) suggested that the findings shown in Table 2 were probably an artifact of using the CESD-12 threshold of greater than or equal to 9 in these data with adjustment for selection and attrition bias. That is, the effect of assignment to the speed of processing intervention was not statistically significant in any of these sensitivity analyses.

Discussion

In this study, we have shown significant differences by treatment intervention group in the incidence of suspected clinical depression (i.e., having CESD-12 scores ≥ 9) between the baseline and the 1-year follow-up among the 1,606 participants who did not meet the criteria for suspected clinical depression at baseline. The speed of processing treatment group was 38% (AOR = 0.62; p < .01) less likely than the no-contact control group to develop suspected clinical depression. In contrast, the memory and reasoning interventions were not significantly different from the no-contact control group. Based on the prevalence of clinically relevant levels of depressive symptoms in the no-contact control group at the 1-year follow-up (i.e., 21%), this represents an "attributable (i.e., absolute) risk reduction" (ARR) of 8%. In other words, for every 12.5 participants randomized to the speed of processing intervention, the development of suspected clinical depression was avoided for one person (number needed to treat = 1/ARR; Guyatt et al., 1993b).

We did not, however, find significant differences by treatment intervention group in the recovery from suspected clinical depression between the baseline and the 1-year follow-up among the 424 participants who had suspected clinical depression at baseline. This is not surprising given the compelling evidence for "the efficacy of antidepressant medications (both alone and in combination with psychotherapy) in the treatment of older adults with major depression" (Sachs-Ericsson & Blazer, 2006, p. 1178). Indeed, antidepressants (specifically, the general class of selective serotonin reuptake inhibitors, and more particularly, citalopram) are recognized as the treatment of first choice for moderate to severe depression in older adults (Blazer, 2003; Sachs-Ericsson & Blazer). Although cognitive behavioral and interpersonal therapies have also been shown to be efficacious, this is mostly true in combination with antidepressant medications (Reynolds et al., 1999; Thompson, Coon, Gallegher-Thompson, Sommer, & Koin, 2001).

There are two main classes of potential mechanisms by which the speed of processing intervention may have protected against the incidence of suspected clinical depression. The first includes "indirect" mechanisms in which the protection against the onset of suspected clinical depression is fully mediated by a behavior or function that is directly improved by speed of processing training. It was hypothesized that changes in UFOV composite test scores would be the primary mediator. Additional potential mediators known to be affected by speed of processing training that could plausibly affect depressive symptoms include HRQoL (Wolinsky et al., 2006a, 2006b), driving behaviors (Roenker et al., 2003), and timed IADLs (Edwards et al., 2002, 2005; Willis et al., 2006). In the above and additional analyses (data not shown), however, we found no evidence of such mediation effects associated with UFOV, HRQoL, or timed IADL changes (data on changes in driving behavior were not available).

The second class potential of mediators includes "direct" mechanisms in which the protection is caused directly by

the effect of speed of processing training on brain functions or processes related to mood. Candidate mechanisms here would include the enhancement of neuromodulatory system function through intensive activation of attention and reward systems during procedural learning (Gold, 2003; Wise, 2004). Alternatively, it could be that the processing speed intervention helps to preserve or enhance cognitive resources that facilitate the use of adaptive processes (such as selection, compensation, and optimization) in response to the developmental changes and demands associated with aging (Baltes & Lang, 1997; Lang, Rieckmann, & Baltes, 2002). Unfortunately, data to evaluate these potential direct mechanisms are not available in ACTIVE. Thus, further research is warranted.

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