Cognitive Training Decreases Motor Vehicle Collision Involvement of Older Drivers

Karlene Ball, PhD,* † Jerri D. Edwards, PhD, † Lesley A. Ross, PhD, * † and Gerald McGwin, Jr., MS, PhD† §

OBJECTIVES: To test the effects of cognitive training on subsequent motor vehicle collision (MVC) involvement of older drivers.

DESIGN: Randomized, controlled, multisite, single-blind clinical trial.

SETTING: Community-dwelling seniors at four U.S. sites: Birmingham, Alabama; Baltimore, Maryland; Indianapolis, Indiana; and State College, Pennsylvania.

PARTICIPANTS: Nine hundred eight older drivers (mean age 73.1; 18.6% African American) who were randomized to one of three cognitive interventions or a control condition.

INTERVENTIONS: Up to 10 sessions of cognitive training for memory, reasoning, or speed of processing.

MEASUREMENTS: State-recorded MVC involvement up to 6 years after study enrollment.

RESULTS: Speed-of-processing and reasoning training resulted in lower rates of at-fault collision involvement over the subsequent approximately 6-year period than controls. After adjusting for age, sex, race, education, mental status, health, vision, depressive symptoms, and testing site, participants randomized to the speed-of-processing and reasoning interventions had an approximately 50% lower rate (per person-mile) of at-fault MVCs than the control group (rate ratio (RR) = 0.57, 95% confidence interval (CI) = 0.34–0.96 for speed of processing), and (RR = 0.50, 95% CI = 0.27–0.92 for reasoning). There was no significant difference observed for the memory group.

CONCLUSION: Cognitive speed-of-processing and reasoning training resulted in a lower at-fault MVC rate in older drivers than in controls. Considering the importance of driving mobility, the costs of crashes, and the benefits of cognitive training, these interventions have great potential to sustain independence and quality of life of older adults. More research is needed to understand the effects of different types and quantities of training. J Am Geriatr Soc 58:2107–2113, 2010.

Key words: older drivers; interventions; cognitive training transfer; motor vehicle collisions; ACTIVE study
result in less difficulty in instrumental activities of daily living (IADLs) as indicated by self-ratings 5 years after training. In ACTIVE, memory, reasoning, and speed-of-processing training also positively affected self-reported health-related quality of life. In two different studies, speed-of-processing training was associated with immediate improvements in performance of IADLs as measured with the Timed IADL Test, a performance-based assessment that measures speed and accuracy across four IADL domains.21

Of particular interest is research showing that speed-of-processing training results in better UFOV test performance, which has a well-established relationship with processing and MVC involvement. For example, it has been demonstrated that in older drivers with significantly slower speed of processing, cognitive speed-of-processing training not only enhanced UFOV test performance, but also resulted in better on-road driving safety. Specifically, older drivers randomized to speed-of-processing training experienced significantly fewer dangerous on-road maneuvers (an action requiring the front-seat driving instructor to take control of the vehicle to avoid a crash or an action that led to another driver altering the course of their vehicle to avoid a crash) immediately after training—an improvement that endured 18 months later. The speed-trained older drivers made significantly fewer dangerous maneuvers immediately and 18 months after training than at baseline and made significantly fewer dangerous maneuvers than a control group of older drivers who received traditional driver education and simulator training 18 months after training. Whether speed-of-processing training, or any other cognitive intervention, reduces MVC involvement of older drivers has never been evaluated.

The analyses presented here examine the effect of three cognitive interventions on the subsequent at-fault MVC involvement of older drivers using data from the ACTIVE clinical trial. ACTIVE is the first multisite, randomized, controlled trial to examine the long-term effects of cognitive training on the everyday abilities of relatively healthy older adults and the first clinical trial to examine the effect of cognitive training on state-recorded MVC records.

Based upon the strong relationship between speed of processing and MVCs in older adults, as well as prior results that speed training enhances on-road driving safety, it was hypothesized that cognitive speed-of-processing training would result in a lower rate of MVC involvement of older drivers. Considering that some driving outcomes have also been related to cognitive reasoning and memory performance, it was possible that memory and reasoning training might also positively affect the rate of MVC involvement, especially considering the association between these abilities and everyday functioning.

METHODS
Participants
The ACTIVE sample consisted of older adults living independently who were recruited across six sites from healthcare clinics, senior housing sites, senior centers, senior citizen organizations, local churches, community centers, wellness and service programs, and state driver registration lists. Participants were interviewed over the telephone to confirm eligibility. In addition to being available throughout the study period, inclusion criteria included aged 65 and older, no evidence of substantial functional (<2 activities of daily living (ADL) disabilities) or cognitive decline (Mini-Mental State Examination (MMSE) score > 23), and no self-reported diagnosis of Alzheimer’s disease or any other health conditions with potential concomitant functional decline or higher mortality risk. Individuals with severe losses in vision (acuity worse than 20/50) or hearing (self-report), or communicative difficulties (based on the interviewer’s perception that participant could understand and be understood by others) that would interfere with study participation were excluded. None of the participants reported recently participating in any cognitive training studies. Participants were paid for their participation at each testing visit.

Information pertaining to MVC involvement, the primary outcome of interest, was available from only four of the six testing sites: Alabama, Indiana, Maryland, and Pennsylvania. Only participants from these four sites who reported that they were currently driving at baseline, drove at least 1,000 miles per year, and did not complete booster training (additional training sessions intended to increase the durability of the intervention) are included in these analyses (N = 908). The booster training sessions were approximately 90 minutes in length, involved more practice of the same tasks used in training, and were administered 1 and 3 years after the initial intervention. Participants who completed booster training were excluded from analyses for several reasons. First, given the design of the ACTIVE trial, only participants who completed eight of the 10 initial training sessions were eligible for booster training. Thus, boosted participants were by definition adherent to the intervention, and they were excluded from analyses to ascertain the true intention-to-treat effect of up to 10 sessions of each intervention. Because the booster sessions were administered 1 and 3 years after initial training, the effect of any booster training may lag behind that of the initial training. Future work will evaluate the effect of booster sessions over an equivalent period of time, as well as the timing of the effect of training on driving outcomes, following the 10th annual follow-up of ACTIVE, which is currently in progress.

Nine hundred eight drivers from the four sites had complete data and met the inclusion criteria. This subsample consisted of 73.0% females and 18.1% African Americans and had an overall age range of 65 to 91, with an average age of 73.1 at baseline. Characteristics of the sample are reported in Table 1.

Study Design
ACTIVE is a multisite, randomized, controlled, single-blind trial with three treatment arms and a no-contact control group. The institutional review boards at all sites approved the study protocol, and a Data Safety and Monitoring Board monitored the trial. Written informed consent was obtained. Participants were randomized by computer to one of the four conditions. Participants completed individual and group assessments at baseline; immediately after training (or an equivalent delay for controls); and
at 1, 2, 3, and 5 years. Testers were blind to treatment assignment.

Interventions
Participants were randomized to one of four conditions: a no-contact control or one of three intervention conditions (memory, reasoning, or speed-of-processing training). Each of the three interventions was designed to target a specific cognitive ability: memory, reasoning, or speed of processing. Trainers led interventions, which were conducted in small groups of two to four participants at the study sites during approximately 70-minute sessions over a period of 5 to 6 weeks. In each intervention condition, 10 initial training sessions were administered and occurred twice a week over a 5-week period. Memory training involved teaching mnemonic strategies (organization, visualization, association) for remembering verbal material (e.g., word lists, texts).26 For participants, were taught how to form visual images and make mental associations to enhance word recall and taught strategies for organizing word lists into meaningful categories to enhance retention of the information. Reasoning training involved teaching strategies for finding the pattern in a letter or word series (e.g., a c e g i . . .) and identifying the next item in the series.27 Exercises focused on understanding patterns in everyday life such as travel schedules. These exercises included abstract reasoning and everyday problem solving. Speed-of-processing training involved practice of visual attention skills and the ability to identify and locate visual information quickly in increasingly demanding visual displays. Participants practiced speeded visual tasks on a computer; difficulty was increased each time a participant achieved criterion performance on a particular task. For example, participants were asked to identify an object on a computer screen at increasingly brief exposures, followed by dividing attention between two tasks, then performing both tasks in the presence of distractions (with the primary modification being display speed).19,22 Each intervention involved a maximum of 10 sessions. On average, participants in each of the three training conditions completed nine training sessions (range 0–10).

Measures

Demographics
Several demographic factors that could affect the rate of MVC involvement were included in analyses: age, sex, race, education, depressive symptoms, and location, as indicated by test site.

Self-Rated Health
Participants rated their health on a scale of 1 (excellent) to 5 (poor). Prior research has demonstrated that using this single-item measure of self-rated health is reliable and valid.28

Vision
Far visual acuity was measured using a light box with the ETDRS chart using standard procedures. Participants were tested at a distance of 10 feet, with corrective lenses when applicable. Scores were assigned using a method described previously,16 which provides credit for each letter correctly identified. Scores can range from 0 to 90, with higher scores indicating better acuity.

Mental Status
The MMSE was used to assess mental status and to exclude participants with probable dementia. The questions measured attention, memory, language, orientation, and construction skills, with scores ranging from 0 (poor cognitive function) to 30 (high cognitive function).23 Participants were required to have a score of 23 or higher for inclusion in the study.

Mileage
Participants reported the number of miles that they drove per week on the Mobility Driving Habits Questionnaire,29 which was used to calculate the dependent variable of interest, rate of MVCs per person-mile driven. Prior work has indicated that older adults’ self-reports of mileage are reliable and valid,30 and this technique has been used in several prior studies.5,13,31

Depressive Symptoms
The 12-item short-form Center for Epidemiologic Studies Depression Scale32 was used to quantify the frequency of depressive symptoms experienced in the prior week.

Table 1. Descriptive Characteristics of the Sample According to Group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controls</th>
<th>Reasoning Training</th>
<th>Memory Training</th>
<th>Speed-of-Processing Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>298 (72.9)</td>
<td>133 (76.0)</td>
<td>103 (71.0)</td>
<td>129 (72.1)</td>
</tr>
<tr>
<td>Caucasians, n (%)</td>
<td>335 (81.9)</td>
<td>143 (81.7)</td>
<td>116 (80.0)</td>
<td>150 (83.8)</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>73.0 ± 5.5</td>
<td>73.3 ± 5.9</td>
<td>72.9 ± 5.7</td>
<td>72.8 ± 5.4</td>
</tr>
<tr>
<td>Education, years, mean ± SD</td>
<td>13.3 ± 2.6</td>
<td>13.5 ± 2.7</td>
<td>13.5 ± 2.6</td>
<td>13.6 ± 2.7</td>
</tr>
<tr>
<td>Self-rated health, mean ± SD (range 1–5)*</td>
<td>2.6 ± 0.9</td>
<td>2.6 ± 0.8</td>
<td>2.7 ± 0.9</td>
<td>2.4 ± 0.9</td>
</tr>
<tr>
<td>Visual acuity, mean ± SD (range 0–90)†</td>
<td>73.5 ± 11.5</td>
<td>74.8 ± 9.6</td>
<td>72.3 ± 12.5</td>
<td>73.2 ± 11.4</td>
</tr>
<tr>
<td>Centers for Epidemiologic Studies Depression Scale score, mean ± SD*</td>
<td>9.6 ± 3.8</td>
<td>10.6 ± 3.9</td>
<td>9.4 ± 3.4</td>
<td>9.9 ± 3.8</td>
</tr>
<tr>
<td>Mini-Mental State Examination Score, mean ± SD (range 23–30)†</td>
<td>27.4 ± 2.0</td>
<td>27.5 ± 1.9</td>
<td>27.6 ± 1.95</td>
<td>27.5 ± 2.0</td>
</tr>
<tr>
<td>Miles driven per year, mean ± SD</td>
<td>5,483 ± 5,130</td>
<td>4,929 ± 4,107</td>
<td>4,996 ± 5,015</td>
<td>5,083 ± 4,365</td>
</tr>
</tbody>
</table>

* Lower scores reflect better ratings.
† Higher scores reflect better performance.
SD = standard deviation.
Participants rated the frequency with which they experienced 12 symptoms such as feeling down or blue on a scale of 0 to 3, with higher total scores reflecting more depressive symptoms.

Outcome Measures
The primary outcome of interest for this analysis was a state-recorded MVC. Information regarding such outcomes was obtained from the Departments of Motor Vehicles in the states of Alabama, Indiana, Maryland, and Pennsylvania. For each MVC, whether the study participant was deemed at fault was obtained from the MVC report. The police officer completing the report makes a determination of fault based upon information received regarding the circumstances of the incident and the role of the driver(s). Only MVCs that occurred after enrollment in ACTIVE were used in this analysis.

Analyses
A Poisson regression model using generalized estimating equations (GEEs) was used to calculate crude and adjusted rate ratios (RRs) and 95% confidence intervals (CIs) for the association between ACTIVE training and at-fault MVC rates per person-year and person-mile of travel. GEEs were used to account for the clustering of repeated MVC events in study participants. Person-years was calculated for each participant as the time between the date of randomization and the date of driving cessation, death, or December 31, 2004, whichever came first. This measure of exposure is thus based only on the number of days each participant could have driven during the follow-up period. Person-miles of travel was calculated by multiplying each participants’ person-years by their self-reported annual mileage during the period of follow-up. This adjustment is needed to reflect the fact that person-time may fail to reflect differences in opportunity for an MVC. Crude and adjusted RRs were calculated, the latter being adjusted for age at baseline, sex, education, depressive symptoms, site location, vision, and mental status. \( P < 0.05 \) (two-sided) was considered statistically significant.

RESULTS
The drivers included in analyses \((N = 908)\) did not significantly differ from the drivers excluded from analyses \((n = 828)\) in age at baseline, education, visual function, miles driven at baseline, depressive symptoms, mental status, or self-rated health (all \( P > 0.05 \)).

Table 2 presents the total number of at-fault MVCs and the accumulated follow-up (in years and miles) for each of the study groups. Overall, 85% of the sample remained crash free, 12% of the sample experienced one crash, and 3% experienced more than one crash, regardless of fault; 11% of the sample experienced one at-fault crash, and 2% experienced more than one at-fault crash.

Table 3 presents the unadjusted and adjusted RRs and 95% CIs for at-fault MVCs based upon chronological time and driving exposure. Regardless of the metric used, there was no significant association with memory training. Participants randomized to speed-of-processing training experienced a significantly lower rate of at-fault MVCs per year of driving exposure \((RR = 0.55, 95\% CI = 0.33–0.92)\) or per person mile driven \((RR = 0.58, 95\% CI = 0.35–0.97)\). These associations were largely unchanged after adjustment for age at baseline, sex, race, education, location, visual acuity, health, depression, and mental status \((RR = 0.52, 95\% CI = 0.31–0.87\) and \(RR = 0.57, 95\% CI = 0.34–0.96\).

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Table 2. Total and At-Fault Collisions, Person-Time, and Person-Miles According to Group

<table>
<thead>
<tr>
<th>Factor</th>
<th>Control n = 409</th>
<th>Memory Training n = 175</th>
<th>Reasoning Training n = 145</th>
<th>Speed-of-Processing Training n = 179</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total collisions</td>
<td>92</td>
<td>31</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>At-fault collisions</td>
<td>75</td>
<td>28</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Person-time, years</td>
<td>2,135.3</td>
<td>929.1</td>
<td>767.9</td>
<td>929.8</td>
</tr>
<tr>
<td>Person-miles</td>
<td>11,943,285.8</td>
<td>4,770,414.7</td>
<td>3,868,571.5</td>
<td>4,966,644.0</td>
</tr>
<tr>
<td>At-fault crashes/year</td>
<td>0.035</td>
<td>0.030</td>
<td>0.023</td>
<td>0.019</td>
</tr>
<tr>
<td>At-fault crashes/mile</td>
<td>0.000000628</td>
<td>0.00000587</td>
<td>0.00000465</td>
<td>0.00000362</td>
</tr>
</tbody>
</table>

Table 3. Association Between Intervention Group and Motor Vehicle Collision (MVC) Involvement

<table>
<thead>
<tr>
<th>At-Fault MVC</th>
<th>Memory Training</th>
<th>Reasoning Training</th>
<th>Speed-of-Processing Training</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude</td>
<td>Adjusted*</td>
<td>Crude</td>
</tr>
<tr>
<td>Person-time</td>
<td>0.86 (0.56–1.32)</td>
<td>0.82 (0.53–1.27)</td>
<td>0.67 (0.40–1.12)</td>
</tr>
<tr>
<td>Person-miles</td>
<td>0.93 (0.61–1.44)</td>
<td>0.93 (0.60–1.45)</td>
<td>0.74 (0.44–1.24)</td>
</tr>
</tbody>
</table>

Control = reference.

* Adjusted for age, sex, race, education, Mini-Mental State Examination score, self-rated health status, vision, depression, and site.
Participants randomized to reasoning training had a significantly lower rate of at-fault MVCs per year of driving exposure (RR = 0.44, 95% CI = 0.24–0.82) or person-miles driven (RR = 0.50, 95% CI = 0.27–0.92) only after adjustment for age at baseline, sex, race, education, location, visual acuity, health, depression, and mental status (Table 3).

DISCUSSION

The ACTIVE study is the first large-scale, randomized trial to show that cognitive training improves cognitive function of older adults for up to 5 years. This was true for speed-of-processing, reasoning, and memory training, and the enduring cognitive benefits are remarkable given the modest amount of training received. The results of these analyses, as well as previously published findings, provide evidence that improvements in cognitive function translate to enhanced everyday functioning for older adults. Specifically, reasoning training has been found to protect against decline in self-reported IADLs, and additional booster training (after the 10 initial sessions) resulted in a significant improvement on the performance-based functional measure of everyday speed for the speed-of-processing-trained group. Prior research has indicated that cognitive training is also protective against declines in health-related quality of life (for memory, reasoning, and speed training) and speed-of-processing training enhances the efficiency and accuracy of performance of tasks instrumental to independence. Although speed of processing in particular has previously been related to crash involvement, all three of the cognitive abilities trained in ACTIVE have been associated with everyday functioning. Similarly, a different study found that cognitive reasoning affected later driving behaviors of older adults. Furthermore, maintained driving over time was related to reasoning performance in prior analyses of the ACTIVE data.

Analyses presented here indicate that speed-of-processing training reduced at-fault MVC risk (unadjusted and adjusted models), consistent with past results demonstrating better driving performance after training as indicated by on-the-road driving safety. Analyses also show that reasoning training reduced at-fault MVC risk when adjusting for relevant covariates. Paired with prior results, the present results indicate that there are numerous potential benefits of cognitive speed-of-processing and reasoning training as interventions for older adults.

The results presented in Table 3 indicate that RRs for MVC involvement are lower for all intervention groups than for the control group but only significantly so for the speed-training group for at-fault MVC involvement (unadjusted and adjusted models) and the reasoning training group for at-fault MVC in adjusted models. Associations are typically weaker for “any MVC,” because many of these incidents may have nothing to do with the functional capabilities of the participant driver. That is, they include a substantial number of collisions that can be partly or wholly attributed to the actions of other drivers. If an association exists, it is more likely to be observed when outcomes are limited to at-fault MVCs.

For reasoning training, a similar pattern is observed, although differences in at-fault MVCs are statistically significant only in the adjusted models. A follow-up analysis revealed that participants randomized to reasoning training reported significantly higher depression scores (F = 3.04, degrees of freedom = 3,904, P = .03), and also reported less exposure (person-time and person-miles) than the other three groups. Once depression was added as an additional covariate to the adjusted models, the relationships between reasoning training and MVC became statistically significant.

In addition, results are consistent with the degree of cognitive training gain found in ACTIVE. Effect sizes at immediate posttest indicated 0.26 standard deviations improvement in memory for memory-trained participants as compared to controls, 0.48 standard deviations improvement in reasoning for reasoning-trained participants, and 1.46 standard deviations improvement in speed for speed-of-processing-trained participants. This suggests that cognitive improvement is a mediating factor in the MVC reduction results, although mediation analyses would be necessary to confirm this. It is possible that, if greater training gains could be achieved, possibly through more initial training or continued booster training, more transfer would be observed to everyday tasks such as driving.

Initial reports from the ACTIVE trial indicated that evidence for transfer of the effects of cognitive training to everyday function was modest and was not observed until the 5-year follow-up. Two reasons were postulated for these findings. First, prior research has demonstrated that there is typically a lag between cognitive decline and decline in everyday function. Thus, if cognitive ability can be maintained through training, this might delay or protect participants against difficulties in performing everyday tasks. Furthermore, with respect to the ACTIVE trial, participants with suspected cognitive or ADL decline were excluded from enrollment. Thus, the more-advantaged nature of the ACTIVE sample no doubt delayed the onset of functional ability decline in the control group. Because the ACTIVE participants as a group were not already experiencing everyday functional limitations, training may have served a protective effect, maintaining driving competence relative to a delayed decline in the control group. The results indicate that, overall, older drivers randomized to speed-of-processing or reasoning training experienced lower rates of at-fault crashes over a 6-year period. Further research with a larger sample is needed to determine at what point in time training significantly affects crash rates, as well as the durability of training.

Although many physicians, scientists, and policy-makers focus efforts on the identification of unsafe older drivers, the ACTIVE results presented here raise the matter as to whether all older drivers might benefit from cognitive training. Scarce resources to identify “high risk” drivers might be better spent in providing interventions to postpone cognitive decline to begin with. Physicians and other healthcare providers may want to consider the potential benefits of speed-of-processing training for older drivers, which include prolonged driving mobility, lower risk of driving cessation, and greater driving safety. The potential benefits of reasoning training for improving driving outcomes warrant further investigation.

Physicians should also know that there are other potential benefits of speed-of-processing and reasoning
training as well. Speed-of-processing and reasoning training have been associated with maintained health-related quality of life. In addition to improving speed and accuracy of IADL performance, speed training has been protective against depressive symptoms, may potentially decrease healthcare costs, and is associated with enhanced locus of control. These results, paired with the present findings, provide evidence that cognitive training can transfer beyond the ability trained. Further research is needed to understand not only the mechanisms of effective cognitive training techniques, but also the complex interrelationships between the cognitive, well-being, and everyday functional benefits that may be associated with cognitive training gains.

There are some limitations of the study that should be noted. The health measures were somewhat limited. No quantitative health rating scale or any indices of cumulative illness were available, although prior research has consistently indicated that cognitive performance is more strongly associated with MVC involvement than medical conditions or physical functioning.

CONCLUSION

Data from the ACTIVE trial have demonstrated that cognitive speed-of-processing and reasoning training result in a lower rate of at-fault MVC involvement in older drivers over a 6-year period. Older drivers as a group have higher MVC rates per mile driven and are more likely to be injured or killed from such MVCs than younger drivers. Thus, as the proportion of older drivers in the U.S. population increases over the next 25 years, there is some concern that there will be increases in traffic fatalities. The cost of MVCs for older persons is not only represented in property damage, but is significantly more costly than that of younger individuals because of higher rates of injuries and fatalities, as well as healthcare costs, in the older population. Thus, effective methods of reducing MVC involvement in this increasingly large segment of the driving population will not only ensure a safer future for all drivers on the road, but also has the potential to improve public health overall.

Taking into account these results, the best policy for helping older drivers is to offer effective interventions. Considering the importance of driving mobility, the costs of MVC involvement, and the many potential benefits of cognitive training, evidence-based cognitive training programs have great potential to sustain independence and improve quality of life of older adults.

ACKNOWLEDGMENTS

We would like to acknowledge and thank the entire ACTIVE team. The ACTIVE investigators included: Hebrew Senior Life—John N. Morris, PhD (PI), Richard N. Jones, ScD; Indiana University School of Medicine—Frederick W. Unverzagt, PhD; Johns Hopkins University—George W. Rebok, PhD; New England Research Institutes (Data Coordinating Center)—Sharon L. Tennstedt, PhD; Pennsylvania State University—Sherry L. Willis, PhD; University of Alabama at Birmingham—Karlene Ball, PhD; University of Florida/Wayne State University—Michael Marsiske, PhD; National Institutes of Health—Kathy Mann Koepke, PhD, National Institute of Nursing Research, and Jonathan King, PhD, National Institute on Aging (NIA).

Conflict of Interests: Karlene Ball owns stock in the Visual Awareness Research Group (formerly Visual Awareness, Inc.), and Posit Science, Inc., the companies that market the UFOV Test and speed-of-processing training software. Posit Science acquired Visual Awareness, and Dr. Ball continues to collaborate on the design and testing of these assessment and training programs as a member of the Posit Science Scientific Advisory Board. Jerri Edwards has worked as a limited consultant for Visual Awareness, Inc. and Posit Science.

ACTIVE is supported by grants from the NIA and the National Institute of Nursing Research to Hebrew Senior Life (U01 NR04507), Indiana University School of Medicine (U01 NR04505), Johns Hopkins University (U01AG14260), New England Research Institutes (U01 AG14282), Pennsylvania State University (U01 AG14263), University of Alabama at Birmingham (U01 AG14289), and University of Florida (U01AG14276). Funds to obtain the accident reports and support the analysis of mobility outcomes were provided by a grant from the NIA (R03 AG023078).

Author Contributions: Dr. McGwin had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Ball, Edwards, Ross, McGwin. Acquisition of data: Ball, McGwin (driving records), Analysis and Interpretation of data: Ball, Edwards, McGwin. Drafting of the manuscript: Ball, Edwards, Ross, McGwin. Critical revision of the manuscript for important intellectual content: Ball, Edwards, Ross, McGwin. Statistical analysis: McGwin, Administrative, technical or material support: Ball, Edwards, Ross, McGwin. Study supervision: Ball, Edwards, McGwin.

Sponsor’s Role: Representatives of the NIA and the National Institute for Nursing Research were directly involved in the design of the ACTIVE trial, interpretation of the data, and review and approval of the manuscript. These representatives also monitored the conduct of the study, collection, management, and analysis of the data.

REFERENCES