# *VALIDATION OF A COGNITIVE SCREENING BATTERY TO PREDICT FITNESS-TO-DRIVE IN INDIVIDUALS WITH MULTIPLE SCLEROSIS: A PRELIMINARY REPORT*

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**Summary:** In a previous study, we identified five cognitive tests that together predicted the outcome of a comprehensive driving evaluation of 44 individuals with multiple sclerosis (age = 46 ± 11 years, 84% females) with 91% accuracy, 70% sensitivity, and 97% specificity. In this study, we sought to validate the predictive accuracy of the five tests in a different cohort of individuals with multiple sclerosis. Sixty-three participants (age = 49 ± 9 years, 89% females) were administered the five cognitive tests. Participants were also administered a standardized practical on-road driving test. Performance on the road test was judged by completing a 16-item checklist of very important driving skills. A raw score of 45 or more out of 50 maximum points was classified as “pass” and below 45 as “fail”. Performance on the five cognitive tests was used to predict the pass/fail outcome of the on-road test. Study results showed that all five variables each had significant association with the on-road test raw score. The five tests together explained 44% of the variance of the pass/fail classification. Participants’ “pass” or “fail” performance on the road test was predicted with 83% accuracy, 67% sensitivity, and 85% specificity. The short battery of five tests appears to be a valid predictor of fitness-to-drive of individuals with multiple sclerosis and more accurate at predicting individuals who will pass the on-road evaluation (85% specificity) than those who will fail (67% sensitivity).

## INTRODUCTION

Multiple Sclerosis (MS) is a neurodegenerative disease that sometimes affects driving-related visual (van Diemen et al, 1992; Schultheis et al, 2010), physical (Stouquart-Elsankari et al, 2010), and cognitive skills (Akinwuntan et al, 2013; Lincoln & Radford, 2008). While the majority of drivers with MS continue to drive safely on the road, some limit their driving or discontinue driving altogether (Niewoehner & Thomas, 2011). Current practices to determine the fitness-to-drive of individuals with MS employ the use of many visual and cognitive tests, which on an average take three hours or more to complete, cost between $300 and $600, and in some cases lead to erroneous judgments. We embarked on a series of studies to develop a short but highly predictive battery of tests that can be used to screen for MS patients whose driving performance can be accurately predicted using a short battery versus those who need anextensive evaluation. In the first study of the series, we identified five cognitive tests from 24 physical, visual, and cognitive tests that together predicted the on-road driving performance of MS patients with 91% accuracy, 70% sensitivity, and 97% specificity. The five tests included the Stroop Color test (Stroop, 1935), the Direction, Compass, and Road Sign Recognition tests of the Stroke Driver Screening Assessment battery (Akinwuntan et al,. 2013a; 2013b), and the Speed of Processing sub-test of the Useful Field of View (UFOV) test (Ball et al, 1990). The study included 44 participants with diagnosis of relapsing–remitting MS: age = 46 ± 11 years, 84% females and whose disease severity were classified as being between stages 1 and 7 according to the Expanded Disability Status Scale Expanded Disability Status Scale (EDSS) (Kurtzke, 1983). Each participant had a valid driver license, ≥ 5 years of driving experience, drove at least once a month in the last 1 year, and met minimum legal visual requirements to drive in accordance with Georgia laws (Akinwuntan et al, 2013a). In this report, we present the preliminary findings of an on-going study to validate the predictive accuracy of the battery of five tests in a new cohort of individuals with MS. Cross-validation is the most effective method to complete the task because of identifying the best predictors of fitness-to-drive of individuals with MS. A model that only fits the population on which it was identified is not sufficient to change current clinical practice. Based on the outcome of the first study in the series, we hypothesized that performance on the five tests will predict participants' performance on a standardized road test with at least 90% accuracy.

## METHODS

### Participants

Currently, 63 individuals have participated in the study. Each participant was required to: (1) be diagnosed with any type of MS with an EDSS between 3-7, (2) be between 25 and 75 years of age with a valid driver's license and ≥ 5 years of driving experience, (3) drive at least once a month in the last year, (4) be on stable medications and dosage (including steroids, benzodiazepines, or other cognition altering medications), and (5) have no exacerbation of symptoms within a month preceding and during the study. Exclusion criteria included history of traumatic brain injury (TBI), stroke, Parkinson's disease (PD), acute psychiatric disorders, drug and alcohol abuse and any change in medication within a month prior to inclusion in the study. To ensure comprehension of study instructions, anyone who scored ≤ 23 on the Mini-Mental State Examination (MMSE) was also excluded.

### The five cognitive tests (predictor variables)

*Stroop Color:* The Stroop Color and Word Test is a test of speed of cognitive processing, mental flexibility, and executive function. It is simple and quick to administer with established reliability and validity (Lezak et al, 2004). The Stroop Color test was a reading test in which participants were required to read out ink colored blocks (blue, red, green) in a time limit of 45 seconds. The Stroop Color test assesses speed of information processing and executive functions.

*SDSA – Square Matrix Direction, Square Matrix Compass, and Road Sign Recognition:* The SDSA battery consists of four tests that together measure driving-related attention, concentration, and executive reasoning abilities (Akinwuntan et al, 2013a; 2013b). The four tests include dot cancellation test, square matrix direction test, square matrix compass test, and road sign recognition test. However, only three of the tests made up part of the five cognitive tests being validated in this study. The square matrix direction and the square matrix compass tests both involved correctly placing 16 cards, each containing pictures of two vehicles traveling in different directions, on 16 squares arranged in a four-by-four matrix. Each correctly placed card, determined by directional arrows (square matrix direction test) or compass cards (square matrix compass test) placed by the side of each square, earned two points. Participants had 5 minutes to complete each of the two tests. The road sign recognition test involved placing the correct traffic sign from 19 available traffic signs on one of 12 traffic situations, shown on cards placed in front of the participant, in a maximum time of 3 minutes. One point was given for each correctly placed traffic sign.

*UFOV - Speed of Processing:* The UFOV test is a computer-administered and computer-scored test of speed of processing visual information and attention. It a test that has being shown to be predictive of risk for traffic crashes in neurologically impaired drivers (Uc et al, 2006). The 3-subtest computer-based touch-screen version of the test was used in this study. In the speed of processing subtest, the task was to identify either a car or truck that appeared in a box in the center of the touch-screen. The speed of presentation of the target varied between 40 and 240 milliseconds. The subtest ended when the presented target can no longer be identified with 75% accuracy.

**On-road test (outcome measure)**

Each participant's performance on a standardized road test was evaluated in a vehicle with automatic transmission, adapted for safety (dual-controls), and registered with the GA Department of Driver Services. The road test course traversed rural, urban, and interstate roadways and took approximately 45 minutes to complete. The test was administered by a certified driver evaluator with over 33 years of experience in the assessment of older, disabled, and novice drivers. The driver evaluator took notes during the tests and completed a 16-item checklist immediately after the test. The checklist consisted of 10 general driving behavior items (approaching traffic signs, checking blind spots, speeding, braking, lane keeping, lane changing, staying in center of lane, following, signaling, and right of way) and the accuracy of execution of three left and three right turns. A maximum score of 50 points was obtainable on the road test. A score of 45 or more out of a maximum of 50 points on the road test was classified as 'Pass' (no major concerns) and others as 'Fail' (concerns with some aspects of driving) as is done during the real-life official evaluation of individuals who have experienced a neurological condition such as stroke, Parkinson's disease, and MS by the certified driver evaluator. All test administrators were blinded to performance on all other tests not administered by them. Consent process and all study protocols were approved by the Institutional Review Board of Georgia Regents University.

**Data Analysis**

The normality of the variables in this study was investigated using the Kolmogorov-Smirnov test. Demographic, physical, visual and cognitive variables of this study cohort (***validation***

***cohort***) were compared to those of the previous study cohort (***original cohort***) to identify differences between the two cohorts using Chi-Square or Wilcoxon-Rank Sum for non-parametric data and two-sample t-test for parametric data. The relationship between the five predictor variables and the on-road test raw scores was compared using Pearson r correlation statistic. To determine variance of the road test outcome explained by performance on the five cognitive tests identified in the previous study, a logistic regression analysis was done. The five tests were also entered into a discriminant function analysis to derive the equation that best predicted the 'pass' or 'fail' outcome of the on-road test. All statistical analyses were carried out using Statistical Analysis Software with the threshold for significance testing set at $p \leq 0.05$.

## RESULTS

Sixty-three participants (age = 49 ± 9 years, 89% females) met all study criteria, consented, and were included in this study. Comparison of the demographic, MS severity (EDSS), physical functioning (Barthel Index), and cognitive variables of the previous study cohort and those of the present study cohort showed some significant differences between the two cohorts (Table 1).

**Table 1. Original cohort versus validation cohort comparisons**

| Variable | Original Cohort | Validation Cohort | Statistic | p-Value |
|---|---|---|---|---|
| Age, mean (SD) | 45.7 (11.1) | 49.0 (8.7) | t=-1.76 | 0.08 |
| Sex, n (%) | | | $\chi^2$=0.25 | 0.61 |
| Male | 7 (16) | 7 (11) | | |
| Female | 37 (84) | 56 (89) | | |
| Driving experience, median (IQR) | 28 (19.5-36) | 33 (25-38) | W=2090.5 | 0.07 |
| Annual Mileage, median (IQR) | 12000 (7300-15000) | 1450 (650-6440) | W=3300 | <0.0001* |
| Years of MS, median (IQR) | 6 (3.5-12.5) | 10.5 (5-15.5) | W=1982 | 0.01* |
| EDSS, median (IQR) | 3 (2-4.5) | 6 (4.5-6) | W=1441 | <0.0001* |
| Barthel Index, , median (IQR) | 100 (95-100) | 95 (90-100) | W=2806 | 0.008* |
| MMSE, median (IQR) | 30 (29-30) | 30 (29.5-30) | W=2290 | 0.40 |

**Key:** SD = standard deviation; IQR = interquartile range; t = t-test; $\chi^2$ = Chi-Square; W = Wilcoxon-Rank Sum; * = significant variable.

In comparison to the original cohort, the validation cohort drove fewer miles yearly ($p < 0.0001$), had a longer duration of MS ($p = 0.01$), had higher EDSS scores ($p < 0.0001$), and scored lower on the Barthel Index ($p = 0.008$).

**Table 2: Correlation between the five predictor variables and the on-road test raw score**

| Variable | Pearson correlation | p-Value |
|---|---|---|
| Stroop Color | 0.27 | 0.03 |
| SDSA - Square Matrix Direction | 0.47 | <0.0001 |
| SDSA - Square Matrix Compass | 0.46 | 0.0001 |
| SDSA - Road Sign Recognition | 0.65 | <0.0001 |
| UFOV- Speed of Processing | -0.29 | 0.02 |

Key: SDSA = Stroke Driver Screening Assessment; UFOV = Useful Field of View

Performance on each of the five cognitive tests correlated significantly with the raw score of the on-road test (Table 2). The logistic regression analysis revealed that performance of the five tests together explained 44% of the variance in the pass/fail outcome of the on-road test.

**Table 3. Validation study: Predicted versus actual performance on the road test**

| | On-Road | |
|---|---|---|
| **Predicted** | Fail | Pass |
| Fail | 6 | 8 |
| Pass | 3 | 46 |

Predictive Accuracy = (6+46) / (6 + 8 + 3 + 46) = 83%
Positive Predictive Value = (6) / (6 + 8) = 43%
Negative Predictive Value = (46) / (3 + 46) = 94%
Sensitivity = (6) / (6 + 3) = 67%
Specificity = (46) / (8 + 46) = 85%
The prediction equation generated from the discriminant analysis including the five tests predicted participants' "pass" or "fail" performance on the road test with 83% accuracy, 67% sensitivity, and 85% specificity. The positive and negative predictive values were 43% and 94% respectively (Table 3).

## DISCUSSION

In this preliminary report, we sought to validate the predictive accuracy of the five cognitive tests identified in a previous study (Akinwuntan et al, 2013a) as predictive of the driving performance of individuals with MS in a new cohort of individuals with MS. Our findings showed that the battery of five cognitive tests, including the Stroop Color test, the Direction, Compass, and Road Sign Recognition tests of the SDSA battery, and the Speed of Processing subtest of the UFOV test, appears to be a very good predictor of the on-road driving ability of individuals with MS. The three primary cognitive domains assessed by the five tests are some of the most important cognitive skills required for safe driving. These cognitive domains include executive function, attention, and speed of processing visual information. Attention and executive function skills are very crucial in a highly risky and multitasking activity such as driving and have been shown several times to be predictive of on-road performance of individuals with stroke (Devos et al, 2011), Parkinson's disease (Devos et al, 2007), and dementia (Lincoln et al, 2006) as well. It is estimated that more than 90% of the sensory input required to drive is visual related (Taylor, 1987). It is thus understandable that the ability to process multiple visual stimuli in good time during the performance of a dynamic and highly time-dependent activity like driving is important. That the five tests can together be administered in less than 45 minutes, should cost less than current cost for extended driving evaluations, and is at least 83% accurate makes the findings of this preliminary report highly clinically relevant.

The predictive accuracy of 83% in this study is less than the ≥ 90% stated in the hypothesis. This finding can be attributed to the differences in the cohort of individuals with MS in this study and the previous one (Akinwuntan et al, 2013a). In this study, individuals with all types of MS and with moderate disability in one functional system; or mild disability in three or four functional systems, though fully ambulatory (EDSS = 3) to those unable to walk beyond 5 meters even with aid (EDSS = 7) were included. In the previous study (Akinwuntan et al, 2013a), only individuals with Relapsing-Remitting MS and with only minimal signs of one functional system but no disability (EDSS = 1) to those with minimal disability in two functional systems (EDSS = 2.5) were included.

As in many studies on the prediction of driving performance of individuals with a neurological condition (Akinwuntan et al, 2006; 2007), the battery was better at predicting those who will perform well (specificity) on an on-road evaluation of driving ability than those who will perform poorly (sensitivity). It is very likely that the unequal distribution of pass/fail (54/9) performance on the road tests affected our finding, which is a limitation of the study. The observed distribution was primarily due to the inclusion criterion that required participants to possess a valid driver license. Possession of a valid license was to ensure that it was legal to test participants on public roads. The very high negative predictive value (94%) of the prediction, which means that 94% of those predicted pass actually passed, is of high ecological importance and relevance. The decision to advice on the continuation of performing a highly risky task such as driving needs to be as accurate as possible. A finding that could tend to dampen the desire to routinely use this short battery of test clinically is that eight of the 14 (57%) participants who were predicted to fail passed the on-road test, which represents a positive predictive value of 43%. On the contrary, it is better to be more cautious and advice an individual who has only fairly good performance on the tests, as was the case with the eight participants, to undergo further testing than to be immediately advised to continue driving. In spite of the impressive predictive accuracy of the battery, we recommend that a fail outcome should only be interpreted as the need perform a more extensive evaluation to more accurately determine the driving ability of the individual. We must also reiterate that this is only the preliminary report of an on-going study, although we do not expect that the findings of the study, when completed, will be significantly different from the current findings.

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