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► **To cite this version:**

Hannes Devos, Maud Ranchet, Deborah Backus, Matt Abisamra, John Anschutz, et al.. Determinants of On-road Driving in Multiple Sclerosis. Archives of Physical Medicine and Rehabilitation, 2017, 98 (7), pp.1332-1338.e2. 10.1016/j.apmr.2016.10.008 . hal-01475850v3

**HAL Id: hal-01475850**

**<https://hal.science/hal-01475850v3>**

Submitted on 21 Jun 2017

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# Accepted Manuscript



Determinants of On-road Driving in Multiple Sclerosis

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PII: S0003-9993(16)31226-6

DOI: [10.1016/j.apmr.2016.10.008](https://doi.org/10.1016/j.apmr.2016.10.008)

Reference: YAPMR 56715

To appear in: *ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION*

Received Date: 12 September 2016

Accepted Date: 18 October 2016

Please cite this article as: Devos H, Ranchet M, Backus D, Abisamra M, Anschutz J, Allison Jr. CD, Mathur S, Akinwuntan AE, Determinants of On-road Driving in Multiple Sclerosis, *ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION* (2016), doi: 10.1016/j.apmr.2016.10.008.

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**Manuscript title.** Determinants of On-road Driving in Multiple Sclerosis

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**Running head (21 characters):** On-road driving in MS

**Acknowledgments:** The authors thank all participants for their time and effort. We also thank Erin Neal, B.S. for technical assistance with data collection and Li Fang Zhang, M.S., for assistance with data analysis.

**Funding:** This work was supported by the National Multiple Sclerosis Society [grant number AG4674A1/1]. The Authors declare that there is no conflict of interest.

## 1 **Abstract**

2 *Objective:* To investigate the cognitive, visual, and motor deficits underlying poor performance  
3 on different dimensions of on-road driving in individuals with multiple sclerosis (MS).

4 *Design:* Prospective cross-sectional study

5 *Setting:* MS Clinic and Driving Simulator Lab

6 *Participants:* A total of 102 active drivers with various types of MS.

7 *Interventions:* Not applicable

8 **Main outcome measure:** Off-road cognitive, visual and motor functions, as well as 13 specific  
9 driving skills. These skills were categorized into hierarchic clusters of operational, tactical,  
10 visuo-integrative, and mixed driving. Stepwise regression analysis was employed to determine  
11 the off-road functions influencing performance on the on-road test and each cluster.

12 *Results:* Visuospatial function ( $p=0.002$ ), inhibition ( $p=0.008$ ), binocular acuity ( $p=0.04$ ),  
13 vertical visual field ( $p=0.02$ ), and stereopsis ( $p=0.03$ ) best determined variance in total on-road  
14 score (unadjusted  $R^2=0.37$ ). Attentional shift ( $p=0.0004$ ), stereopsis ( $p=0.007$ ), glare recovery  
15 ( $p=0.047$ ), and use of assistive devices ( $p=0.03$ ) best predicted the operational cluster  
16 (unadjusted  $R^2=0.28$ ). Visuospatial function ( $p=0.002$ ), inhibition ( $p=0.002$ ), reasoning  
17 ( $p=0.003$ ), binocular acuity ( $p=0.04$ ), and stereopsis ( $p=0.005$ ) best determined the tactical  
18 cluster (unadjusted  $R^2=0.41$ ). The visuo-integrative model (unadjusted  $R^2=0.12$ ) comprised  
19 binocular acuity ( $p=0.007$ ) and stereopsis ( $p=0.045$ ). Inhibition ( $p=0.0001$ ) and binocular acuity  
20 ( $p=0.001$ ) provided the best model of the mixed cluster (unadjusted  $R^2=0.25$ ).

21 *Conclusions:* Our results provide more insights into the specific impairments that influence  
22 different dimensions of on-road driving and may be used as a framework for targeted driving  
23 intervention programs in MS.

24 **Key words:** multiple sclerosis; vision; neuropsychology; rehabilitation; driving

25

26 **Abbreviations:**

27 DA, divided attention

28 EDSS, Expanded Disability Status Scale

29 MS, multiple sclerosis

30 MMSE, Mini-Mental State Examination

31 RA, risk assessment

32 ROCF, Rey Osterrieth Complex Figure

33 PASAT, paced auditory serial addition test

34 SA, selective attention

35 SDSA, stroke drivers screening assessment

36 SDMT, symbol digit modalities Test

37 SOP, speed of processing

38 TMT, trail making test

39 TRIP, test ride for investigating practical fitness-to-drive

40 UFOV, Useful Field of View

41 VIF, variance inflation factor

42

## 43 **Introduction**

44

45 The cognitive, visual, motor, and behavioral impairments associated with multiple sclerosis (MS)  
46 eventually affect the ability to drive safely.<sup>1</sup> Nevertheless, about 77% of individuals with MS  
47 continue driving after diagnosis.<sup>2</sup> Those who continue to drive do so less frequently than drivers  
48 with no neurological conditions,<sup>2</sup> and are at an increased risk for car crashes.<sup>3</sup>

49

50 Between 6% and 38% of drivers with MS fail a formal road test.<sup>1,4-7</sup> Yet, these studies used a  
51 dichotomous decision of fitness-to-drive as the main outcome measure which does not reflect the  
52 different skill set needed to safely drive a car in a highly interactive traffic situation.<sup>1,4-6</sup> The road  
53 test consists of different sections assessing distinct driving skills.<sup>8</sup> Previous studies in drivers  
54 with other neurological conditions found that distinct cognitive, visual, and motor functions  
55 impact different dimensions of on-road driving performance.<sup>9-13</sup> In Parkinson's disease, severity  
56 of motor symptoms and slow reaction time correlated with operational driving skills such as  
57 maintaining lane position, whereas cognitive functions related to more complex driving skills  
58 including turning left.<sup>11</sup>

59

60 Understanding which cognitive, motor, and visual functions affect specific domains of on-road  
61 driving can inform the design of off-road screening tests for evaluation of fitness-to-drive and  
62 interventions for specific driving difficulties in MS. Therefore, the aim of this study was to  
63 determine the critical impairments in cognitive, visual, and motor functions that lead to poor on-

64 road driving performance in MS. Similar to our work in other neurological conditions,<sup>9,11,13,14</sup> we  
65 hypothesized that visual functions will impact all aspects of on-road driving, motor and  
66 cognitive functions will influence basic on-road driving skills, whereas cognitive functions will  
67 determine complex on-road driving skills in MS.

68

## 69 **Methods**

70

### 71 *Subjects*

72

73 Participants were recruited from the Andrew C. Carlos MS Institute at Shepherd Center in  
74 Atlanta, GA and Augusta University MS Center in Augusta, GA from August 2013 to October  
75 2015. Inclusion criteria were (1) diagnosis of MS; (2) scores on the Expanded Disability Status  
76 Scale (EDSS) between 1 and 7;<sup>15</sup> (3) age between 25-75 years; (4) valid driver's license; (5)  $\geq 5$   
77 years driving experience; (6) drive at least once a month in the previous year; and (7) meet the  
78 minimum visual requirements to drive in accordance with GA laws (binocular acuity  $\geq 20/60$  and  
79 peripheral vision  $\geq 140$  degrees). Exclusion criteria were (1) score  $< 24$  on Mini Mental State  
80 Examination (MMSE);<sup>16</sup> (2) fluctuations in medication and dosage in the month preceding the  
81 study; (3) exacerbation of symptoms within a month preceding the study; and (4) any other  
82 neurological condition, acute psychiatric disorder, or drug and alcohol abuse as determined by  
83 the referring neurologist.

84



85 All study protocols were approved by the Institutions' Review Boards. Written informed consent  
86 was obtained.

87

88 *Off-road test battery*

89

90 Demographic, clinical, and driving characteristics. Age, gender, education, disease duration,  
91 disease severity (EDSS), type of MS (relapsing-remitting; primary progressive; secondary  
92 progressive), driving experience, annual mileage, and number of traffic tickets and crashes in the  
93 last 5 years were collected. We also administered the Hospital Anxiety and Depression Scale  
94 (HADS)<sup>17</sup> and the Modified Fatigue Impact Scale (MFIS).<sup>18</sup>

95

96 Cognitive tests. The cognitive tests are widely used in MS research, evaluate different cognitive  
97 domains, and have been found to predict fitness-to-drive in previous research.<sup>1,6,10,19-21</sup>

98

99 The Useful Field of View (UFOV) consists of three subtests that evaluate speed of processing  
100 (SOP), divided attention (DA), and selective attention (SA) in milliseconds.<sup>a</sup> The risk assessment  
101 (RA) score for prospective car crashes ranges from 1 (very low) to 5 (very high).<sup>22</sup>

102

103 The Rey Osterrieth Complex Figure (ROCF)–copy test measures visuospatial and  
104 visuoconstructive abilities on a score ranging from 0 to 36.<sup>23</sup>

105

106 The Symbol Digit Modalities Test (SDMT) evaluates visual search and working memory.

107 Number of correct responses in 90 seconds was the outcome variable.<sup>24</sup>

108

109 The Trail Making Test part A (TMT A) assesses visuomotor tracking and working memory. The

110 TMT B additionally evaluates attentional shift. Time to completion and number of errors were

111 recorded.<sup>25</sup>

112

113 The Stroop test included the color, word, and color-word subtests. The color and word subtests

114 evaluate speed of processing. The color-word subtest assesses response inhibition and cognitive

115 flexibility. The number of errors in a time limit of 45 seconds was the main outcome.

116

117 The Stroke Driver Screening Assessment (SDSA) for MS<sup>20</sup> consists of four tests. The dot

118 cancellation test measures visual scanning and sustained attention. Time to completion and

119 number of errors were recorded. The directions and compass tests measure reasoning skills.

120 Correct answers were scored on a scale ranging from 2 to 32. The road sign recognition test

121 evaluates visual comprehension and traffic knowledge. The scale ranges from 0 to 12.

122

123 The Paced Auditory Serial Addition Test (PASAT-3 seconds) evaluates working memory,

124 auditory information processing speed and flexibility, as well as arithmetic ability. Number of

125 correct responses was recorded.<sup>26</sup>

126

127 Visual tests. Scores on binocular acuity (far, mid (26''), and near distance), peripheral vision  
128 (horizontal and vertical), color perception (red/green and blue/violet), stereopsis (depth  
129 perception), glare recovery, and contrast sensitivity were dichotomized into pass-fail scores  
130 according to the Keystone Vision Screener cut-off values.<sup>b</sup>

131  
132 Motor tests. The motor assessment included the 25-foot walk test,<sup>26</sup> the 9-hole pegtest,<sup>26</sup> and the  
133 Barthel Index.<sup>27</sup> The use of assistive devices (yes/no) was also documented.

134  
135 *Road test*

136  
137 The main outcome was score on the Test Ride for Investigating Practical fitness-to-drive  
138 (TRIP).<sup>8,28</sup> The TRIP consists of 13 items and 49 sub-items, each scored on a 4-point ordinal  
139 scale. The total TRIP score was the sum of all item scores and ranged from 49 to 196. All 13  
140 items were mapped onto a theoretical framework of hierarchic driving skills according to  
141 Michon<sup>29</sup> and adapted by De Raedt and Ponjaert-Kristofferson.<sup>28</sup> The operational cluster  
142 comprised lateral position on the road at speed (I) below and (II) above 45 m/h, and (III)  
143 mechanical operations.<sup>28,29</sup> The tactical cluster consisted of speed adaptations at speed (IV)  
144 below and (V) above 45 m/h, headway distance to the lead car at speed below (VI) and (VII)  
145 above 45 m/h, and (VIII) lane position change.<sup>28,29</sup> The visuo-integrative cluster included (IX)  
146 anticipation and perception of road signs and traffic signals, (X) visual behavior and  
147 communication with other road users, and (XI) traffic insight, understanding, and quality of

148 traffic participation.<sup>28</sup> Finally, the mixed cluster included the items (XII) joining the traffic  
149 stream and (XIII) turning left.<sup>28</sup> The items in the mixed cluster encompassed a combination of  
150 operational, tactical, and visuo-integrative skills. For example, left-turn maneuvers were rated on  
151 operational skills (e.g., signal indicator use); tactical skills (e.g., gap acceptance to opposing  
152 traffic); and visuo-integrative skills (e.g., checking mirrors and blind spots).

153

154 Each participant's practical fitness-to-drive was evaluated in a vehicle with automatic  
155 transmission, adapted with dual controls, and registered with the GA Department of Driver  
156 Services. Assistive devices were installed in the car if needed (e.g., spinner knob). The road test  
157 course traversed rural, urban, and interstate roadways and took approximately 45 minutes to  
158 complete. The TRIP checklist was administered immediately after completion of the road test by  
159 certified driving instructors or driving rehabilitation specialists. All driving assessors attended a  
160 one-day workshop where the reliability of TRIP scoring was established through video review of  
161 four drives.

162

163 *Statistical analysis*

164

165 Kolmogorov-Smirnov tests were used to determine normality of the variables. Pearson  
166 correlations ( $r$ ) were calculated between on-road scores and normally distributed off-road  
167 variables. On-road scores were correlated with off-road ordinal variables and not normally  
168 distributed ratio variables using Spearman rho ( $\rho$ ). Correlations ( $r/\rho$ ) were considered weak  
169 below 0.10, moderate between 0.10 and 0.49 and strong between 0.50 and 1.00.<sup>30</sup> Independent

170 variables were entered into a multivariate stepwise linear regression analyses with a select entry  
171 ( $p < 0.15$ ) and retain ( $p < 0.05$ ) level for each of the five on-road models: (1) total TRIP score; (2)  
172 operational cluster; (3) tactical cluster; (4) visuo-integrative cluster; and (5) mixed cluster. We  
173 verified the collinearity between independent variables by correlation analysis ( $r/\rho > 0.40$ ) and  
174 calculating variance inflation factors (VIF). A VIF score of 10 or higher was considered to  
175 indicate substantial collinearity.<sup>31</sup> P values  $< 0.05$  were considered significant. All statistical  
176 analyses were performed with SAS®, version 9.4.<sup>c</sup>

177

## 178 **Results**

179

180 Table 1 shows that the majority (86%) of the 102 participants was female and presented with no  
181 to limited functional (e.g., Barthel Index) and cognitive disability (e.g., MMSE). Eight (8%)  
182 drivers required car modifications (spinner knob or hand controls). Scores on the cognitive tests  
183 are presented in Supplementary Table 1.

184

185 *Insert Table 1 here*

186

187 *Total on-road score*

188

189 Overall, most drivers with MS achieved submaximal performance on the road test (Table 2).

190

191

192

*Insert Table 2 here*

193

194 Weak to moderate correlations were found between performance in off-road tests and total TRIP  
195 scores (Table 3). The magnitude of correlations of the significant variables ranged between 0.21  
196 (UFOV RA and Stroop color-word) and 0.40 (traffic tickets and TMT B time). Among the  
197 descriptive variables, education and number of traffic tickets correlated significantly with total  
198 TRIP scores. In the cognitive domain, all variables were associated with total TRIP scores,  
199 except for MMSE, Stroop color and word subtests, and number of errors on TMT A, TMT B,  
200 and dot cancellation. In the visual domain, binocular acuity at mid-distance, peripheral visual  
201 field, and stereopsis correlated with on-road scores. The 9-hole peg test was the only variable in  
202 the motor domain that correlated with total TRIP scores.

203

204

*Insert Table 3 here*

205

206 Regression analysis showed that total TRIP scores were determined by a combination of five  
207 cognitive and visual functions: ROCF, Stroop color-word, binocular acuity at mid-distance,  
208 vertical visual field, and stereopsis (Table 4).

209

210 *Insert Table 4 here*

211

212 *Operational cluster*

213

214 Table 3 shows that the magnitude of significant correlations between off-road variables and the  
215 operational cluster ranged between 0.21 (TMT B errors and UFOV SA) and 0.37 (TMT B time  
216 and 9-hole peg test).

217

218 The regression analysis constituted a multidimensional model of four variables in the cognitive,  
219 visual, and motor domains to determine scores on the operational cluster: TMT B errors,  
220 stereopsis, glare recovery, and use of assistive devices (Table 4).

221

222 *Tactical cluster*

223

224 Table 3 shows that the magnitude of significant correlations between off-road variables and the  
225 tactical cluster ranged between 0.20 (ROCF) and 0.32 (digit symbol).

226 A combination of ROCF, directions, Stroop color-word, mid-distance acuity, and stereopsis  
227 explained 41% of the variance in the tactical driving cluster (Table 4).

228

229 *Visuo-integrative cluster*

230

231 Table 3 shows that the magnitude of significant correlations between off-road variables and the  
232 visuo-integrative cluster ranged between 0.22 (education and road sign recognition) and 0.32  
233 (TMT B time and vertical visual field).

234

235 Only binocular acuity at mid-distance and stereopsis were retained in the model, explaining 12%  
236 of the variance in the visuo-integrative cluster (Table 4).

237

238 *Mixed cluster*

239

240 The magnitude of significant correlations between off-road variables and the mixed cluster  
241 ranged between 0.22 (road sign recognition) and 0.36 (mid-distance acuity). Compared with the  
242 other on-road clusters, fewer off-road variables correlated significantly with the mixed cluster  
243 (Table 3).

244

245 Only binocular acuity at mid-distance and Stroop color-word were retained in the multivariate  
246 regression analysis, explaining 25% of the variance in the mixed cluster (Table 4).

247



248 Supplementary Table 2 shows the correlation matrix between the cognitive, visual, and motor  
249 tests and the 13 on-road items.

250

## 251 **Discussion**

252

253 This study focused on identifying the critical impairments in cognitive, visual, and motor  
254 functions underlying poor on-road driving in MS. To capture the different dimensions of on-road  
255 driving, we mapped the TRIP items onto an existing theoretic framework of hierarchic driving  
256 skill consisting of operational, tactical, visuo-integrative, and mixed clusters.<sup>28,29</sup>

257

258 This cohort of drivers with MS performed equally well on the same checklist of on-road driving  
259 performance used to investigate driving difficulties in Parkinson's disease, stroke, and  
260 Huntington's disease.<sup>13,14,32</sup> Similar to these studies, our results support the notion that visual,  
261 cognitive, and motor impairments differently affect distinct on-road driving skills.<sup>10,11,13</sup>

262

263 General disease descriptors (e.g., disease duration, EDSS) or demographic information (e.g., age)  
264 were not retained as determinants in any of the on-road driving models once cognitive, visual,  
265 and motor functions were added. This finding extends empirical evidence that disease status and  
266 age alone fail to inform clinical decisions regarding fitness-to-drive in MS.

267 Visuospatial ability (ROCF), response inhibition (Stroop color-word) and visual functions (mid-

268 distance binocular acuity, vertical visual field, and stereopsis) constituted the best model to  
269 explain total on-road scores in drivers with MS. Two systematic reviews recommended ROCF as  
270 a valid screening tool for fitness-to-drive after stroke.<sup>33,34</sup> Akinwuntan et al. found the ROCF to  
271 be univariately correlated with pass-fail driving status in MS.<sup>1</sup> Stroop color-word reflects  
272 executive functions such as response inhibition, which has shown to be impaired in MS.<sup>35,36</sup>

273

274 Total on-road scores were also determined by tests assessing mid-distance binocular acuity,  
275 vertical visual field, and stereopsis, which highlight the importance of visual functions for  
276 driving. About 38% of all states rely solely on visual criteria to determine medical clearance,  
277 despite lack of evidence of a relationship between visual acuity and car crashes in the general  
278 population.<sup>37</sup> Yet, Shultheis et al. failed to find significant associations between visual acuity,  
279 horizontal visual field and driving outcomes in MS.<sup>38</sup> The inclusion of other visual tests and the  
280 use of a standardized on-road test rather than self-report of driving behavior may be the reason  
281 for the inconsistency of our results with previous findings.<sup>38</sup>

282

283 Visual functions continued to be important determinants of each on-road driving cluster,  
284 emphasizing the importance of intact vision across all hierarchic levels of driving skill. Mid-  
285 distance acuity and peripheral visual field were even sole determinants of the visuo-integrative  
286 cluster. By contrast, motor functions, indexed by the use of assistive devices, in combination  
287 with shifting of attention, stereopsis, and glare recovery, showed to correlate only with  
288 operational driving items in the multivariate model. Operational driving skills require intact  
289 motor functions to operate the steering wheel and pedals and keep the car under control.<sup>29</sup>

290

291 Finally, ROCF, Stroop color-word, mid-distance acuity, directions tests and stereopsis explained  
292 41% of the total variance in the tactical cluster, which was higher than any of the other clusters  
293 of driving skill. These findings reveal the major role of cognitive functions, especially  
294 visuospatial (ROCF) and executive functions (Stroop color-word, directions) in tactical driving  
295 skills, such as speed adaptation or lane changing. Other studies support the use of the directions  
296 test to predict fitness-to-drive in MS.<sup>6,19,20</sup>

297

298 Clinically, this research highlights the importance of assessing specific cognitive and visual  
299 functions to determine driving abilities in individuals with MS. However, some  
300 neuropsychological tests widely used in the clinic (MMSE, PASAT) have limited ability to  
301 predict on-road driving. We recommend the use of ROCF and the Stroop test to assess  
302 visuospatial functions and response inhibition as well as stereopsis and vertical visual field to  
303 assess visual functions in drivers with MS.

304

305 Detailed study of the factors underlying impaired on-road driving in MS also opens avenues for  
306 rehabilitation. Cognitive rehabilitation shows promising evidence to improve attention, executive  
307 functions, and memory in MS.<sup>39</sup> Remedial interventions to improve these cognitive functions  
308 may translate to improvements in on-road driving. Yet, the few intervention studies that focused  
309 on remedial training of driving-related cognitive functions in patients with stroke found limited  
310 carry-over to on-road driving.<sup>40</sup> Our results suggest that targeted training of visuomotor tracking  
311 and attentional shift may result in improvements in operational driving skills, whereas training of

312 visuospatial functions and response inhibition may transfer to improvements in tactical driving  
313 skills.

314

315 Visual scanning strategies, extra mirrors, or corrective glasses may compensate for visual field  
316 and binocular acuity loss whereas teaching drivers to maintain proper headway distance may  
317 help with impairments in stereopsis. These compensational strategies may result in  
318 improvements in tactical, visuo-integrative, and mixed driving skills. Physical therapy can help  
319 to improve performance on operational driving skills such as applying the emergency brake or  
320 controlling the steering wheel. Alternatively, the car may be equipped with a spinner knob, hand  
321 brakes, or left sided gas pedal to compensate for muscle weakness or spasticity. None of these  
322 proposed interventions have been tested in a controlled experiment. One pilot study found that  
323 five hours of simulator-based driving training improved working memory, visual scanning, color  
324 perception, and fatigue in 36 individuals with relapsing-remitting MS.<sup>41</sup>

325

326 The strength of the current study is that we included a broad off-road assessment battery to  
327 determine performance in hierarchic driving clusters in a large sample of active drivers with MS.  
328 Our findings lend to a theoretic framework for remedial training of targeted driving skills.

329

330 *Study limitations*

331

332 The study has several limitations, including the lack of an age- and sex-matched control group.

333 We therefore cannot determine whether this cohort of drivers with MS showed impaired driving  
334 skills compared to controls and whether the determinants of on-road driving are inherent to MS.  
335 However, for the clinical purpose of this study, i.e., to provide a framework for driving screening  
336 and interventions in individuals with MS, a comparison to a control group was not deemed  
337 necessary.

338

339 Similar to previous studies,<sup>13,14,19,32</sup> the variance explained by the visual, cognitive, and motor  
340 tests remained moderate, even though cognitive and visual tests that were underexplored in  
341 previous studies were added to this broad off-road assessment battery. One of the reasons for the  
342 moderate variance explained by the cognitive functions may be that this cohort of drivers with  
343 MS did not show substantial cognitive deficits. They achieved similar scores on the MMSE,  
344 PASAT, TMT A and B, and ROCF when compared to norm values.<sup>42-45</sup> Since we included a  
345 broad assessment battery, some of the analyses were exploratory. For this purpose, we did not  
346 control for multiple comparisons.

347

348 Although the TRIP is a reliable<sup>8</sup> and valid<sup>46</sup> questionnaire widely used to assess practical fitness-  
349 to-drive, we do not have any quantitative measures from the vehicle (e.g. driving speed, lane  
350 position). Further studies should consider the inclusion of quantitative measures of naturalistic  
351 driving.

352

353 **Conclusions**

354

355 Our findings showed that on-road driving performance in MS is affected by a combination of  
356 cognitive, visual, and, to a lesser extent, motor functions. We recommend that screening tests  
357 should broadly assess multiple domains of cognitive and visual sensory functions rather than  
358 narrowly targeting one single domain. A detailed decomposition of the critical cognitive, visual  
359 or motor impairments underlying impaired performance on different hierarchic layers of driving  
360 in MS may provide a framework of targeted rehabilitation interventions. These intervention  
361 strategies should be tested in a randomized controlled trial.

362

### 363 Suppliers

- 364 a. Useful Field of View, Visual Awareness Research Group, Inc, Punta Gorda, FL.
- 365 b. Keystone Vision Screener, Keystone View, Reno, NV.
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367

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Table 1. Demographic and clinical characteristics (n =102)

Variable	Mean (SD)	Range
Age, years	47.91 (8.71)	25 – 65
Driving experience, years	31.06 (8.87)	10 – 49
	Median (Q1 – Q3)	
Annual mileage, 1000 miles/y	2.80 (1.04 – 10.00)	0.2 – 55
Tickets in last five years, n	0 (0 – 1)	0 – 4
Crashes in last five years, n	1 (0 – 1)	0 – 2
EDSS, /10	5 (4 – 7)	2 – 7
Disease duration, y	9 (5 – 14)	0 – 37
Barthel Index, /100	95 (90 – 100)	65 – 100
MMSE, /30	30 (30 – 30)	24 – 30
HADS depression, / 21	5 (2 – 7)	0 – 18
HADS, anxiety, / 21	7 (4 – 10)	0 – 19
MFIS, /84	39.77 (15.88)	29 – 51
	N (%)	
Sex, female	88 (86)	N/A
Type of MS (RRMS; PPMS; unknown)	91 (89); 10 (10); 1 (1)	N/A

Abbreviations: EDSS, Expanded Disability Status Scale; HADS, Hospital Anxiety and Depression Scale; MMSE, Mini-Mental State Examination; N/A, not applicable; RRMS, relapsing remitting multiple sclerosis; PPMS; primary progressive multiple sclerosis.

Table 2. Performance in Test Ride for Investigating Practical fitness-to-drive (n =102)

Variable	Mean (SD)	Scale range
<i>Total on-road score</i>	184.15 (13.48)	49 – 196
<i>Operational cluster</i>	24.57 (5.04)	7 – 28
I. Lateral position on the road at speed < 45 mph	6.39 (2.33)	2 – 8
II. Lateral position on the road at speed > 45 mph	6.76 (2.21)	2 – 8
III. Mechanical operations	11.49 (1.38)	3 – 12
<i>Tactical cluster</i>	49.50 (3.37)	13 – 52
IV. Speed adaptations at speed < 45 mph	7.33 (1.07)	2 – 8
V. Speed adaptations at speed > 45 mph	7.09 (1.28)	2 – 8
VI. Headway distance at speed < 45 mph	7.73 (1.07)	2 – 8
VII. Headway distance at speed > 45 mph	7.81 (0.70)	2 – 8
VIII. Lane position change	19.61 (1.50)	5 – 20
<i>Visuo-integrative cluster</i>	52.61 (4.92)	14 – 56
IX. Anticipation and perception of road signs and traffic lights	15.14 (2.00)	4 – 16
X. Visual behavior and communication	30.00 (3.20)	8 – 32
XI. Traffic insight, understanding, and quality of traffic participation	7.47 (1.10)	2 – 8
<i>Mixed cluster</i>	57.46 (4.06)	15 – 60
XII. Joining the traffic stream	23.00 (2.36)	6 – 24
XIII. Turning left	34.57 (2.53)	9 – 36

Table 3. Correlation matrix of on-road total TRIP score and clusters with performance on off-road battery<sup>a</sup>

Descriptive	Total score		Operational		Tactical		Visuo-integrative		Mixed	
	r/ρ	p	r/ρ	p	r/ρ	p	r/ρ	p	r/ρ	p
Age	-0.02	0.82	-0.01	0.92	0.06	0.55	-0.02	0.87	-0.09	0.35
Education	0.26	<b>0.01</b>	0.09	0.35	0.15	0.13	0.22	<b>0.03</b>	0.13	0.19
Disease duration	-0.07	0.50	-0.11	0.28	-0.02	0.85	-0.09	0.39	0.004	1.00
EDSS	-0.14	0.15	-0.14	0.17	-0.07	0.48	-0.03	0.74	-0.17	0.10
Type of MS	-0.04	0.66	0.06	0.58	-0.11	0.25	0.03	0.75	-0.11	0.29
HADS, depression	-0.11	0.16	-0.12	0.15	-0.11	0.16	-0.14	0.12	-0.14	0.12
HADS, anxiety	-0.11	0.19	-0.13	0.15	-0.17	0.10	-0.13	0.12	-0.17	0.10
MFIS	-0.01	0.89	-0.09	0.37	0.004	0.96	-0.02	0.86	0.09	0.40
Driving experience	0.09	0.35	0.07	0.50	0.14	0.17	0.09	0.35	0.004	0.97
Annual mileage	-0.15	0.14	0.05	0.62	-0.26	<b>0.01</b>	-0.14	0.19	-0.07	0.49
Traffic tickets	-0.40	<b>&lt;0.0001</b>	-0.31	<b>0.002</b>	-0.22	<b>0.02</b>	-0.26	<b>0.01</b>	-0.24	<b>0.01</b>
Traffic crashes	0.007	0.94	0.07	0.48	0.03	0.77	-0.08	0.42	-0.01	0.54
<b>Cognitive</b>										
MMSE	0.18	0.08	0.13	0.21	0.11	0.28	0.09	0.39	0.14	0.16
UFOV, SOP	-0.23	<b>0.02</b>	-0.06	0.52	-0.21	<b>0.04</b>	-0.23	<b>0.02</b>	-0.15	0.15
UFOV, DA	-0.33	<b>0.0009</b>	-0.27	<b>0.006</b>	-0.19	0.06	-0.31	<b>0.002</b>	-0.18	0.07
UFOV, SA	-0.27	<b>0.01</b>	-0.21	<b>0.03</b>	-0.17	0.09	-0.25	<b>0.01</b>	-0.14	0.17
UFOV, RA	-0.21	<b>0.03</b>	-0.13	0.19	-0.15	0.13	-0.24	<b>0.02</b>	-0.14	0.16
ROCF	0.24	<b>0.02</b>	0.15	0.13	0.20	<b>0.05</b>	0.18	0.07	0.25	<b>0.01</b>
SDMT	0.28	<b>0.004</b>	0.17	0.10	0.32	<b>0.001</b>	0.16	0.12	0.28	<b>0.005</b>
TMT A, errors	0.07	0.49	0.09	0.38	0.03	0.76	0.02	0.85	0.11	0.25
TMT B, time	-0.40	<b>&lt;0.0001</b>	-0.37	<b>0.0002</b>	-0.29	<b>0.004</b>	-0.32	<b>0.001</b>	-0.17	0.09
TMT B, errors	-0.14	0.16	-0.21	<b>0.03</b>	-0.04	0.72	-0.15	0.14	-0.02	0.81
Dot cancellation time	-0.23	<b>0.02</b>	-0.16	0.11	-0.21	<b>0.03</b>	-0.16	0.09	-0.17	0.09
Dot cancellation errors	-0.01	0.94	-0.005	0.96	0.13	0.21	-0.006	0.95	-0.04	0.74
Stroop color	0.09	0.39	0.12	0.25	0.06	0.57	-0.006	0.96	0.11	0.31
Stroop word	-0.15	0.17	0.11	0.3	-0.17	0.14	-0.11	0.35	-0.23	<b>0.045</b>
Stroop C/W	-0.21	<b>0.04</b>	-0.02	0.83	-0.23	<b>0.02</b>	-0.09	0.39	-0.22	<b>0.03</b>
Directions	0.28	<b>0.004</b>	0.17	0.10	0.31	<b>0.001</b>	0.15	0.12	0.28	<b>0.005</b>
Compass	0.29	<b>0.004</b>	0.30	<b>0.002</b>	0.29	<b>0.003</b>	0.15	0.12	0.17	0.09
Road Sign Recognition	0.29	<b>0.003</b>	0.30	<b>0.002</b>	0.24	<b>0.02</b>	0.22	<b>0.02</b>	0.22	<b>0.03</b>
PASAT	0.14	0.24	0.08	0.48	0.04	0.71	0.18	0.11	0.18	0.11
<b>Visual</b>										
Acuity, far	-0.04	0.70	0.006	0.95	-0.07	0.47	-0.06	0.56	-0.09	0.38
Acuity, mid	-0.30	<b>0.003</b>	-0.08	0.45	-0.22	<b>0.03</b>	-0.29	<b>0.004</b>	-0.36	<b>0.0002</b>
Acuity, near	-0.09	0.37	-0.003	0.97	0.009	0.93	-0.11	0.29	-0.20	0.05
Peripheral, horizontal VF	0.11	0.31	0.08	0.46	0.13	0.20	0.03	0.74	0.02	0.84
Peripheral, vertical VF	-0.24	<b>0.02</b>	-0.20	0.05	-0.15	0.14	-0.32	<b>0.002</b>	-0.09	0.36
Color perception, R/G	-0.14	0.18	-0.04	0.70	-0.10	0.33	-0.16	0.12	-0.17	0.10
Color perception, B/V	-0.19	0.06	-0.22	<b>0.03</b>	-0.07	0.50	-0.12	0.25	-0.10	0.31
Stereopsis	-0.26	<b>0.01</b>	-0.28	<b>0.01</b>	-0.26	<b>0.01</b>	-0.07	0.50	-0.08	0.43

Glare recovery	-0.13	0.20	-0.27	<b>0.01</b>	-0.15	0.14	0.04	0.71	0.05	0.62
Contrast sensitivity	-0.07	0.47	-0.16	0.12	0.006	0.96	0.06	0.53	0.006	0.95
<b>Motor</b>										
Barthel	-0.03	0.77	0.08	0.44	0.03	0.74	-0.07	0.50	-0.04	0.70
25-foot walk	-0.11	0.31	-0.16	0.11	-0.02	0.86	0.007	0.94	-0.09	0.33
9-hole peg dominant	-0.32	<b>0.001</b>	-0.37	<b>0.0001</b>	-0.17	0.10	-0.13	0.21	-0.17	0.08
Assistive device	-0.21	0.09	-0.24	<b>0.02</b>	-0.10	0.58	-0.05	0.80	-0.16	0.42

Abbreviations: B/V, blue-violet; DA, divided attention; C/W, color-word; EDSS, Expanded Disability Status Scale; HADS, Hospital Anxiety and Depression Scale; MMSE, Mini-Mental State Examination; MS, multiple sclerosis; PASAT, paced auditory serial addition test; RA, risk assessment; R/G, red/green; ROCF, Rey-Osterrieth Complex Figure; SA, selective attention; SOP, speed of processing; SDMT, symbol digit modalities test; TMT, Trail Making Test; UFOV, Useful Field Of View; VF, visual field.

Table 4. Results of the five multivariate linear regression analysis models

Dependent variable	Independent variables	beta value	t-value	p-value
Total TRIP score	ROCF	0.92	3.90	0.0002
	Stroop color-word errors	-8.30	-2.70	0.008
	Acuity mid-distance	-5.55	-2.06	0.04
	Vertical VF	-6.72	-2.43	0.02
	Stereopsis	-5.25	-2.21	0.03
Operational cluster	TMT B errors	-0.86	-3.67	0.0004
	Stereopsis	-2.90	-2.76	0.007
	Glare recovery	-3.30	-2.01	0.047
	Assistive device (yes/no)	2.65	2.24	0.03
Tactical cluster	ROCF	0.20	3.21	0.002
	Stroop color-word errors	-2.60	-3.27	0.002
	Directions	0.20	3.38	0.001
	Acuity mid-distance	-1.39	-2.05	0.04
	Stereopsis	-1.78	-2.89	0.005
Visuo-integrative cluster	Acuity mid-distance	-3.22	-2.75	0.007
	Vertical VF	-2.50	-1.82	0.045
Mixed cluster	Stroop color-word errors	-4.29	-4.06	0.0001
	Acuity mid-distance	-2.85	-3.32	0.001

Abbreviations: ROCF, Rey-Osterrieth Figure of Rey; TMT, Trail Making Test; TRIP, Test Ride for Investigating Practical fitness-to-drive; VF, visual field