



HAL
open science

Determinants of On-road Driving in Multiple Sclerosis

Hannes Devos, Maud Ranchet, Deborah Backus, Matt Abisamra, John Anschutz, Allison Jr. C. Dan, Mathur Sunil, Abiodun E. Akinwuntan

► **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, 2016, 10.1016/j.apmr.2016.10.008 . hal-01475850v2

HAL Id: hal-01475850

<https://hal.science/hal-01475850v2>

Submitted on 21 Apr 2017 (v2), last revised 21 Jun 2017 (v3)

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Accepted Manuscript



Determinants of On-road Driving in Multiple Sclerosis

Hannes Devos, PhD, Maud Ranchet, PhD, Deborah Backus, PT, PhD, Matt Abisamra, OTR/L, CDRS, John Anschutz, ATP, RET, C. Dan Allison, Jr., MS, OTR/L, ATP, CDRS, Sunil Mathur, PhD, Abiodun E. Akinwuntan, PhD, MPH, MBA

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.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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

Names and institutional affiliations of the authors.

Hannes Devos, PhD,^{1,2} Maud Ranchet, PhD,^{2,3} Deborah Backus, PT, PhD,⁴ Matt Abisamra, OTR/L, CDRS,⁴ John Anschutz, ATP, RET,⁴ C. Dan Allison, Jr., MS, OTR/L, ATP, CDRS,⁴ Sunil Mathur, PhD,⁵ Abiodun E. Akinwuntan, PhD, MPH, MBA^{2,6}

¹ Department of Physical Therapy and Rehabilitation Science, School of Health Professions, University of Kansas Medical Center, KS

² Department of Physical Therapy, College of Allied Health Sciences, Augusta University, Augusta, GA

³ French Institute of Science and Technology for Transport, Development and Networks (IFSTTAR), Laboratory of Ergonomic and Cognitive Sciences for Transports (TS2-LESCOT), Bron, France

⁴ Shepherd Center, Atlanta, GA

⁵ Biostatistics Department, Medical College of Georgia, Augusta University, Augusta, GA

⁶ Dean's Office, School of Health Professions, University of Kansas Medical Center, Kansas City, KS

Name and address for corresponding author

Hannes Devos, University of Kansas Medical Center, School of Health Professions, Department of Physical Therapy and Rehabilitation Science, 3901 Rainbow Boulevard, Mailstop 2002, Kansas City, KS 66160

Tel 913-588-2840

Fax 913-588-6910

E-mail: hdevos@kumc.edu

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.¹ Nevertheless, about 77% of individuals with MS
47 continue driving after diagnosis.² Those who continue to drive do so less frequently than drivers
48 with no neurological conditions,² and are at an increased risk for car crashes.³

49

50 Between 6% and 38% of drivers with MS fail a formal road test.^{1,4-7} 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.^{1,4-6} The road
53 test consists of different sections assessing distinct driving skills.⁸ 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.⁹⁻¹³ 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.¹¹

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,^{9,11,13,14} 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;¹⁵ (3) age between 25-75 years; (4) valid driver's license; (5) ≥ 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 ≥ 140 degrees). Exclusion criteria were (1) score < 24 on Mini Mental State
80 Examination (MMSE);¹⁶ (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)¹⁷ and the Modified Fatigue Impact Scale (MFIS).¹⁸

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.^{1,6,10,19-21}

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.^a The risk assessment
101 (RA) score for prospective car crashes ranges from 1 (very low) to 5 (very high).²²

102

103 The Rey Osterrieth Complex Figure (ROCF)–copy test measures visuospatial and
104 visuoconstructive abilities on a score ranging from 0 to 36.²³

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.²⁴

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.²⁵

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 MS²⁰ 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.²⁶

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.^b

131
132 Motor tests. The motor assessment included the 25-foot walk test,²⁶ the 9-hole pegtest,²⁶ and the
133 Barthel Index.²⁷ 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).^{8,28} 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 Michon²⁹ and adapted by De Raedt and Ponjaert-Kristofferson.²⁸ 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.^{28,29} 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.^{28,29} 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.²⁸ Finally, the mixed cluster included the items (XII) joining the traffic
149 stream and (XIII) turning left.²⁸ 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 (ρ). Correlations (r/ρ) were considered weak
169 below 0.10, moderate between 0.10 and 0.49 and strong between 0.50 and 1.00.³⁰ 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.³¹ P values < 0.05 were considered significant. All statistical
176 analyses were performed with SAS®, version 9.4.^c

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.^{28,29}

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.^{13,14,32} Similar to these studies, our results support the notion that visual,
261 cognitive, and motor impairments differently affect distinct on-road driving skills.^{10,11,13}

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.^{33,34} Akinwuntan et al. found the ROCF to
271 be univariately correlated with pass-fail driving status in MS.¹ Stroop color-word reflects
272 executive functions such as response inhibition, which has shown to be impaired in MS.^{35,36}

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.³⁷ Yet, Shultheis et al. failed to find significant associations between visual acuity,
279 horizontal visual field and driving outcomes in MS.³⁸ 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.³⁸

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.²⁹

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.^{6,19,20}

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.³⁹ 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.⁴⁰ 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.⁴¹

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,^{13,14,19,32} 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.⁴²⁻⁴⁵ 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 reliable⁸ and valid⁴⁶ 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.
- 366 c. SAS, version 9.1, SAS Institute, Inc, Cary, NC.

367

368 References

- 369 1. Akinwuntan AE, Wachtel J, Rosen PN. Driving simulation for evaluation and
370 rehabilitation of driving after stroke. *JStroke Cerebrovasc Dis* 2012;21:478-86.
- 371 2. [Ryan KA, Rapport LJ, Telmet Harper K, Fuerst D, Bieliauskas L, Khan O et al. Fitness to](#)
372 [drive in multiple sclerosis: Awareness of deficit moderates risk. *J Clin Exp Neuropsychol*](#)
373 [2009;31\(1\):126-39.](#)

- 374 3. Dehning M, Kim J, Nguyen CM, Shivapour E, Denburg NL. Neuropsychological
375 Performance, Brain Imaging, and Driving Violations in Multiple Sclerosis. Arch Phys Med
376 Rehabil 2014;95(10):1818-23.
- 377 4. [Devos H, Akinwuntan AE, Gelinas I, George S, Nieuwboer A, Verheyden G. Shifting up
378 a gear: considerations on assessment and rehabilitation of driving in people with neurological
379 conditions. An extended editorial. Physiother Res Internat 2012;17\(3\):125-31.](#)
- 380 5. Schultheis MT, Weisser V, Ang J, Elovic E, Nead R, Sestito N et al. Examining the
381 Relationship Between Cognition and Driving Performance in Multiple Sclerosis. Arch Phys Med
382 Rehabil 2010;91(3):465-73.
- 383 6. [Lincoln NB, Radford KA. Cognitive abilities as predictors of safety to drive in people
384 with multiple sclerosis. Mult Scler 2008;14\(1\):123-8.](#)
- 385 7. [Ranchet M, Akinwuntan AE, Tant M, Neal E, Devos H. Agreement between physician's
386 recommendation and fitness-to-drive decision in multiple sclerosis. Arch Phys Med Rehabil
387 2015;96\(10\):1840-4.](#)
- 388 8. [Akinwuntan AE, DeWeerd W, Feys H, Baten G, Arno P, Kiekens C. Reliability of a
389 road test after stroke. Arch Phys Med Rehabil 2003;84\(12\):1792-6.](#)
- 390 9. [Devos H, Ranchet M, Emmanuel Akinwuntan A, Uc EY. Establishing an evidence-base
391 framework for driving rehabilitation in Parkinson's disease: A systematic review of on-road
392 driving studies. NeuroRehabilitation 2015;37\(1\):35-52.](#)
- 393 10. [Aksan N, Anderson SW, Dawson J, Uc E, Rizzo M. Cognitive functioning differentially
394 predicts different dimensions of older drivers' on-road safety. Accid Anal Prev 2015;75:236-44.](#)

- 395 11. Devos H, Vandenberghe W, Tant M, Akinwuntan AE, De Weerd W, Nieuwboer A et al.
396 Driving and off-road impairments underlying failure on road testing in Parkinson's disease. *Mov*
397 *Disord* 2013;28(14):1949-56.
- 398 12. Barco PP, Baum CM, Ott BR, Ice S, Johnson A, Wallendorf M et al. Driving errors in
399 persons with dementia. *J Am Geriatr Soc* 2015;63(7):1373-80.
- 400 13. Devos H, Tant M, Akinwuntan AE. On-road driving impairments and associated
401 cognitive deficits after stroke. *Cerebrovasc Dis* 2014;38(3):226-32.
- 402 14. Devos H, Nieuwboer A, Vandenberghe W, Tant M, De Weerd W, Uc EY. On-road
403 driving impairments in Huntington disease. *Neurology* 2014;82(11):956-62.
- 404 15. [Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability](#)
405 [status scale \(EDSS\). *Neurology* 1983;33\(11\):1444-52.](#)
- 406 16. Folstein MF. The Mini-Mental State Examination. *Arch Gen Psychiatry* 1983;40(7):812.
- 407 17. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr*
408 *Scand* 1983;67(6):361-70.
- 409 18. Tellez N, Rio J, Tintore M, Nos C, Galan I, Montalban X. Does the Modified Fatigue
410 Impact Scale offer a more comprehensive assessment of fatigue in MS? *Mult*
411 *Scler*2005;11(2):198-202.
- 412 19. [Akinwuntan AE, Devos H, Stepleman L, Casillas R, Rahn R, Smith S et al. Predictors of](#)
413 [driving in individuals with relapsing-remitting multiple sclerosis. *Mult Scler* 2013;19\(3\):344-50.](#)
- 414 20. Akinwuntan AE, O'Connor C, McGonegal E, Turchi K, Smith S, Williams M et al.
415 Prediction of driving ability in people with relapsing-remitting multiple sclerosis using the stroke
416 driver screening assessment. *Int J MS Care* 2012;14(2):65-70.

- 417 21. [Shawaryn MA, Schultheis MT, Garay E, Deluca J. Assessing functional status: exploring](#)
418 [the relationship between the multiple sclerosis functional composite and driving. Arch Phys Med](#)
419 [Rehabil 2002;83\(8\):1123-9.](#)
- 420 22. [Ball KK, Roenker DL, Bruni JR. Developmental Changes in Attention and Visual Search](#)
421 [throughout Adulthood. The Development of attention - Research and Theory. Elsevier BV; 1990.](#)
422 [p 489-508.](#)
- 423 23. [Rey A. L'examen psychologique dans les cas d'encephalopathie traumatique. Arch](#)
424 [Psychol 1941;28:215-85.](#)
- 425 24. [Wechsler D. Wechsler Adult Intelligence Scale. San Antonio, TX: The Psychological](#)
426 [Corporation; 1997.](#)
- 427 25. [Reitan R. Trail Making Test Manual for Administration and Scoring. Tucson, AZ: Reitan](#)
428 [Neuropsychology Laboratory; 1986.](#)
- 429 26. [Cutter GR, Baier MS, Rudick RA, Cookfair DL, Fischer JS, Petkau J, et al. Development](#)
430 [of a Multiple Sclerosis Functional Composite as a clinical trial outcome measure. Brain](#)
431 [1999;122: 101-12.](#)
- 432 27. [Mahoney F, Barthel D. Functional evaluation: The Barthel Index. Maryland State Med J](#)
433 [1965;14:61-5.](#)
- 434 28. [De Raedt R, Ponjaert-Kristoffersen I. Predicting at-fault car accidents of older drivers.](#)
435 [Accid Anal Prev 2001;33\(6\):809-19.](#)
- 436 29. [Michon JA. Explanatory pitfalls and rule-based driver models. Accid Anal Prev](#)
437 [1989;21\(4\):341-53.](#)
- 438 30. [Cohen J, Cohen P, West S, Aiken L. Applied multiple regression/correlation analysis for](#)
439 [the behavioral sciences \(3rd ed.\). Psychology Press 2002.](#)

- 440 31. Belsley DA, Kuh E, Welsch RE. Regression Diagnostics. Wiley Series in Probability and
441 Statistics. John Wiley & Sons, Inc.; 1980.
- 442 32. Devos H, Vandenberghe W, Tant M, Akinwuntan AE, De Weerdts W, Nieuwboer A et al.
443 Driving and off-road impairments underlying failure on road testing in Parkinson's disease. *Mov*
444 *Disord* 2013; 28(14):1949-56.
- 445 33. Marshall SC, Molnar F, Man-Son-Hing M, Blair R, Brosseau L, Finestone HM et al.
446 Predictors of Driving Ability Following Stroke: A Systematic Review. *Topics in Stroke*
447 *Rehabilitation* 2007;14(1):98-114.
- 448 34. Hird MA, Vetivelu A, Saposnik G, Schweizer TA. Cognitive, On-road, and Simulator-
449 based Driving Assessment after Stroke. *J Stroke and Cerebrovasc Dis* 2014;23(10):2654-70.
- 450 35. Genova HM, DeLuca J, Chiaravalloti N, Wylie G. The relationship between executive
451 functioning, processing speed, and white matter integrity in multiple sclerosis. *J Clin Exp*
452 *Neuropsychol* 2013;35(6):631-41.
- 453 36. Vitkovitch M, Bishop S, Dancy C, Richards A. Stroop interference and negative priming
454 in patients with multiple sclerosis. *Neuropsychologia* 2002;40(9):1570-6.
- 455 37. Owsley C, Wood JM, McGwin G. A roadmap for interpreting the literature on vision and
456 driving. *Surv Ophthalmol* 2015;60(3):250-62.
- 457 38. Schultheis MT, Manning K, Weisser V, Blasco A, Ang J, Wilkinson ME. Vision and
458 Driving in Multiple Sclerosis. *Arch Phys Med Rehabil* 2010;91(2):315-7.
- 459 39. Rosti-Otajärvi EM, Hämäläinen PI. Neuropsychological rehabilitation for multiple
460 sclerosis. *Cochrane Database Syst Rev*. Wiley-Blackwell; 2014.
- 461 40. George S, Crotty M, Gelinias I, Devos H. Rehabilitation for improving automobile driving
462 after stroke. *Cochrane Database Syst Rev*. Wiley-Blackwell; 2014.

- 463 41. Akinwuntan AE, Devos H, Baker K, Phillips K, Kumar V, Smith S et al. Improvement of
464 Driving Skills in Persons With Relapsing-Remitting Multiple Sclerosis: A Pilot Study. Arch
465 Phys Med Rehabil 2014;95(3):531-7.
- 466 42. Bravo G, Hebert R. Age- and education-specific reference values for the Mini-Mental
467 and modified Mini-Mental State Examinations derived from a non-demented elderly population.
468 IntJ Geriatr Psychiatry 1997;12(10):1008-18.
- 469 43. Wiens AN, Fuller KH, Crossen JR. Paced Auditory Serial Addition Test: adult norms and
470 moderator variables. J Clin Exper Neuropsychol 1997;19(4):473-83.
- 471 44. Tombaugh TN. Trail Making Test A and B: Normative data stratified by age and
472 education. ArchClin Neuropsychol 2004;19(2):203-14.
- 473 45. Fastenau PS, Denburg NL, Hufford BJ. Adult norms for the Rey-Osterrieth complex
474 figure test and for supplemental recognition and matching trials from the extended complex
475 figure test. Clin Neuropsychol 1999;13(1):30-47.
- 476 46. Akinwuntan AE, De Weerd W, Feys H, Baten G, Arno P, Kiekens C. The validity of a
477 road test after stroke. Arch Phys Med Rehabil 2005;86(3):421-6.
- 478
- 479
- 480

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^a

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	0.01	0.09	0.35	0.15	0.13	0.22	0.03	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	0.01	-0.14	0.19	-0.07	0.49
Traffic tickets	-0.40	<0.0001	-0.31	0.002	-0.22	0.02	-0.26	0.01	-0.24	0.01
Traffic crashes	0.007	0.94	0.07	0.48	0.03	0.77	-0.08	0.42	-0.01	0.54
Cognitive										
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	0.02	-0.06	0.52	-0.21	0.04	-0.23	0.02	-0.15	0.15
UFOV, DA	-0.33	0.0009	-0.27	0.006	-0.19	0.06	-0.31	0.002	-0.18	0.07
UFOV, SA	-0.27	0.01	-0.21	0.03	-0.17	0.09	-0.25	0.01	-0.14	0.17
UFOV, RA	-0.21	0.03	-0.13	0.19	-0.15	0.13	-0.24	0.02	-0.14	0.16
ROCF	0.24	0.02	0.15	0.13	0.20	0.05	0.18	0.07	0.25	0.01
SDMT	0.28	0.004	0.17	0.10	0.32	0.001	0.16	0.12	0.28	0.005
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	<0.0001	-0.37	0.0002	-0.29	0.004	-0.32	0.001	-0.17	0.09
TMT B, errors	-0.14	0.16	-0.21	0.03	-0.04	0.72	-0.15	0.14	-0.02	0.81
Dot cancellation time	-0.23	0.02	-0.16	0.11	-0.21	0.03	-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	0.045
Stroop C/W	-0.21	0.04	-0.02	0.83	-0.23	0.02	-0.09	0.39	-0.22	0.03
Directions	0.28	0.004	0.17	0.10	0.31	0.001	0.15	0.12	0.28	0.005
Compass	0.29	0.004	0.30	0.002	0.29	0.003	0.15	0.12	0.17	0.09
Road Sign Recognition	0.29	0.003	0.30	0.002	0.24	0.02	0.22	0.02	0.22	0.03
PASAT	0.14	0.24	0.08	0.48	0.04	0.71	0.18	0.11	0.18	0.11
Visual										
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	0.003	-0.08	0.45	-0.22	0.03	-0.29	0.004	-0.36	0.0002
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	0.02	-0.20	0.05	-0.15	0.14	-0.32	0.002	-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	0.03	-0.07	0.50	-0.12	0.25	-0.10	0.31
Stereopsis	-0.26	0.01	-0.28	0.01	-0.26	0.01	-0.07	0.50	-0.08	0.43

Glare recovery	-0.13	0.20	-0.27	0.01	-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
Motor										
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	0.001	-0.37	0.0001	-0.17	0.10	-0.13	0.21	-0.17	0.08
Assistive device	-0.21	0.09	-0.24	0.02	-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