#### CAN DRIVING AT THE SIMULATOR "DIAGNOSE" COGNITIVE IMPAIRMENTS?

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#### ABSTRACT

There is increasing concern and interest about the association of cognitive impairments and 1 2 driving performance among the elderly, and several recent studies have identified significant 3 driving performance deficits in cognitively impaired older people, measured by means of changes in driving simulator metrics. In this paper, it is attempted to reverse the question: can 4 driving at the simulator reveal the presence of cognitive impairments? This question has a two-5 fold interest: first, driving at the simulator may allow for the detection of subtle changes in 6 driving due to cognitive impairments imperceptible in one's daily routine; and second, driving 7 8 simulators may have potential of becoming in the future useful tools for the screening of older 9 individuals and assist clinicians both in the medical examination and the advice on whether to 10 continue driving. Data from a large interdisciplinary driving simulator study were analyzed by means of discriminant analysis techniques, in order to classify individuals as healthy or 11 12 cognitively impaired on the basis of their simulated driving performance. The analysis sample included 86 individuals, out of which 38 patients with Mild Cognitive Impairment (MCI) and 13 14 21 patients with Alzheimer's disease (AD). The results suggest that variables discriminating 15 between healthy and impaired individuals are average speed and headway, lateral position 16 variability, throttle position, reaction time and accident occurrence at incidents. The functions developed correctly classified more than 65% of the individuals, a share that dropped to around 17 18 60% when cross-validation analysis was implemented. Overall, although MCI and AD patients 19 had significant shares of misclassified cases, these misclassifications were mostly between the 20 one pathology and the other; very few pathological cases were classified as healthy, and all of 21 these concerned MCI patients. It is indicated that driving at the simulator may under certain 22 conditions assist in the screening for cognitive impairments.

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Key-words: driving simulator; cognitive impairments; MCI; Alzheimer's disease;
 discriminant analysis.

# 27

26 **BACKGROUND AND OBJECTIVES** 

28 Numerous studies have associated cognitive impairments among the elderly with driving 29 performance. Particular focus has been placed on Alzheimer's disease (AD), and Mild 30 Cognitive Impairment (MCI), i.e. the prodromal stage of many neurodegenerative diseases, 31 with prevalence estimated at least 10% among the elderly (1). The main purpose of these 32 studies was to assess fitness-to-drive and identify specific driving performance deficits and 33 risks due to the disease and the related cognitive impairments, following a formal diagnosis on 34 the basis of clinical, neurological and neuropsychological assessments.

35 Existing results have been largely consistent, with cognitively impaired people driving 36 at lower speeds, with increased variability in vehicle lateral position and / or wheel steering angle, difficulties in operating the gearbox, increased driving errors and violations, and slower 37 38 reaction time at incidents and / or brake response (2, 3, 4).

39 In this paper, the question is reversed: can driving at the simulator assist in the 40 screening for cognitive impairments, towards their diagnosis? In order to address with question, the simulated driving performance of 86 drivers aged older than 55 years (out of which 27 41 42 healthy controls, 38 MCI patients and 21 AD patients) was associated with their clinical 43 diagnosis, in order to attempt to classify the drivers into healthy or cognitively impaired groups 44 on the basis of their driving performance.

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#### 46 LITERATURE REVIEW

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48 Cognitive and driving impairments are strongly interrelated, with critical impact on the 49 mobility and quality of life of older individuals. A considerable amount of research is devoted 50 to the degree to which cognitive impairments affect driving, ranging from mild impairments 51 (MCI) and pre-dementia conditions, to dementing diseases, stroke, cerebrovascular disease, 52 Parkinson's disease etc.

53 Mild Cognitive Impairment (MCI), which is the prodromal stage of several dementing 54 diseases, has prevalence in persons older than 65 years of age ranging from 10% to 20% 55 (depending on the population studied and on the diagnostic criteria utilized) (1); however, its effect on driving ability has received less attention compared to other clinical groups, and is a 56 57 critical issue for further research (2, 4). Existing studies also indicate driving difficulties in 58 several driving performance measures and more errors between AD patients and cognitively 59 intact individuals (5, 6, 7, 8, 9, 10).

60 More specifically, the relationship between cognitive impairments and driving risks so far has mainly been investigated in on-road tests or driving simulators (11). Results clearly 61 establish that drivers with cognitive impairments may drive at – often dangerously – lower 62 speeds, have difficulty in positioning the vehicle on the lane and maintaining that position, may 63 64 have slower reaction time at unexpected events, may be more vulnerable to complex driving environments and more affected by in-vehicle or external distraction (12), may conduct more 65 66 driving errors and unintentional traffic violations etc. (13). However, older drivers with 67 cognitive impairments are often capable of self-regulating to some extent, and their driving 68 impairments are partly balanced by their reduced exposure (driving), especially in demanding 69 conditions (e.g. avoidance of motorways, night-time driving etc.) and the lower speeds (14).

70 It is suggested that preclinical dementia may have subtle cognitive and functional effects, which could combine to impair complex behaviors such as driving. Several researches 71 72 underline that emphasis should be placed on the early – and often preclinical – stages of the diseases, where cognitive impairments may be imperceptible in one's daily routine, and 73 74 undetectable with routine medical screening tools, yet already affecting driving ability (15). In 75 a recent study (16), for instance, a composite score reflecting psychometric functioning was

referring representation of the number of on-road driving errors, but AD biomarker patterns were identified and associated with these driving errors, suggesting the presence of AD pathology which would not be identified through standard tools. Consistent with this idea, postmortem studies of the brains of asymptomatic older drivers who were killed in car accidents found that many had underlying AD neuropathological changes (*17*).

Another recent study (*18*) presented an exploratory analysis of the extent to which differences between drivers with mild cognitive impairment and controls on a sign recall task in a fixed-base driving simulator could better predict whether a driver will be diagnosed with MCI, compared to self-reports of a decrease in driving proficiency or of avoidance of driving, or age alone. However, neither recall scores, nor self-reported frequency of avoiding driving, nor driver age predicted a clinical diagnosis of MCI, and only self-reported decline in global driving ability was significant.

88 Nevertheless, recent medical and neuropsychological research, underlines that there is 89 strong need for identifying sensitive tools to measure cognitive and functional changes in the 90 early stages, and although some have cautioned that it may not be feasible to assess functional 91 impairment at the earliest stages of the disease, the results suggest that driving tests on the road 92 or through simulation, may eventually provide such a measure. A driving simulation test in 93 particular, although often criticized for lacking the fidelity required for generalizing the results 94 with respect to driving performance (19), might provide more detailed information on the types 95 and importance of driving errors and could be repeated in other settings and with other samples 96 (16).

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## 98 DATA COLLECTION

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This research was implemented by an interdisciplinary team including transportation engineers of the Department of Transportation Planning and Engineering, of the National Technical University of Athens (NTUA), as well as neurologists and neuropsychologists of the University of Athens Medical School, at ATTIKON University General Hospital. The study was approved by the Ethics Committee of the "ATTIKON" University General Hospital. Informed consent was obtained from all individuals studied.

106 This large scale study had multiple objectives, namely testing the driving behavior of 107 different age groups, including young, middle-aged and older people, with emphasis and over-108 sampling of older people, both cognitively impaired and healthy. The total sample consists of 109 317 participants, out of which 105 were cognitively impaired older individuals. The diseases 110 diagnosed included mostly (75%) MCI, AD and Parkinson's disease, as well as a small share 111 on frontotemporal dementia (FTD), stroke, sleep disorders (RBD), multiple sclerosis (MS), depression etc.). All participants were recruited among patients of the 2<sup>nd</sup> Department of 112 113 Neurology of the University of Athens Medical School at ATTIKON University General 114 Hospital.

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## 116 Sampling frame

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For the purposes of the present analysis, a sample of 86 individuals aged >55 years old was selected from the total sample, including the respective healthy controls (27 individuals), the MCI (38 individuals) patients and the AD patients (21 individuals) explicitly diagnosed by the neurology / neuropsychology research teams. PD patients were excluded as in most cases they

did not present significant cognitive impairments; similarly, the remaining patients formed a

rather heterogeneous group of pathologies and were excluded to allow for a more focused

124 analysis.

125 In total, 59 of the participants were males and 25 were females. The gender distribution 126 of the control group was balanced, but males were over-represented in the MCI group and there 127 were no females in the AD group. Moreover, the mean age of the control group was 65 years, 128 while for the MCI and the AD groups the mean age was 70 and 75 years respectively. Females 129 had slightly lower mean age in all groups, with the same general trend of increasing age with 130 the presence of pathology (see Figure 1). It is noted that the distributions of gender and age 131 groups in this sample are representative of the prevalence of these pathologies in the general 132 population (1).

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#### Medical and neuropsychological assessment and diagnosis

A first assessment of the participants concerned the administration of a full clinical medical,
ophthalmological and neurological evaluation, in order to well document the characteristics of
each of their disorders as well as other related parameters of potential impact on driving (e.g.
use of medication affecting the Central Nervous System).

145 A second assessment concerned the administration of a series of neuropsychological 146 tests and psychological-behavioral questionnaires to the participants. The battery used covers 147 a large spectrum of Cognitive Functions: visuospatial and verbal episodic and working 148 memory, general selective and divided attention, reaction time, processing speed, psychomotor 149 speed, mental flexibility and task shifting etc. and included in total 13 tests (e.g. Mini Mental 150 State Examination, Clock Drawing Test, Semantic and Phonemic Fluency, Symbol Digit 151 Modalities Test - Written & Oral, Hopkins Verbal Learning Test-Revised, Trail Making Test 152 etc.) - for a detailed description the reader is referred to (20).

The driving assessment was carried out once the sample was classified into the 3 groups by the neurological and neuropsychological teams (AD, MCI or control group), on the basis of their diagnosis. All MCI patients had Clinical Dementia Rating (CDR) = 0.5 and all AD patients had CDR=1.0.

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#### 158 Driving Simulator assessment

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160 The NTUA driving simulator is a dynamic quarter-cab and consists of 3 wide screens 40",

161 driving position and support motion base. The dimensions at a full development are

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162 230x180cm, while the base width is 78cm and the total field of view is 170 degrees. The 163 simulator is validated against a real world environment, with satisfactory relative validity as 164 regards gender, age groups and area type i.e. urban or rural (*21*).

165 Patients were to carry out the simulator experiment while under their usual medication. 166 The driving simulator experiment started with a practice drive on the basis of several 167 quantitative and qualitative criteria of familiarization with the simulator (usually 10-15 168 minutes). Afterwards, all participants drove two sessions (approximately 20 minutes each). 169 Each session corresponded to a different road environment: a rural route (single carriageway, 170 lane width 3m, zero gradient and mild horizontal curves) and an urban route (dual carriageway, 171 separated by guardrails, lane width 3.5m, narrow sidewalks, commercial uses and roadside 172 parking).

173 In each road environment, there were 6 trials, under different traffic and cognitive 174 workload conditions. More specifically, traffic conditions tested included low traffic (ambient 175 vehicles' arrivals corresponding to an average traffic volume Q=300 vehicles/hour, i.e. drawn 176 from a Gamma distribution with mean m=12sec, and variance  $\sigma^2=6$  sec.) and high traffic 177 (ambient vehicles' arrivals corresponding to an average traffic volume of Q=600 vehicles/hour, 178 i.e. drawn from a Gamma distribution with mean m=6sec, and variance  $\sigma^2=3$  sec), whereas 179 cognitive workload conditions tested included undistracted driving, conversation with 180 passenger and mobile phone conversation. It is noted, however, that most of the participants 181 aged >55 years old reported that they never used their mobile phone while driving and preferred 182 not to use it during the simulator experiment.

183 During each trial, 2 unexpected incidents were scheduled to occur at fixed points along 184 the drive. More specifically, incidents in rural area concerned the sudden appearance of an 185 animal (deer or donkey) on the roadway, and incidents in urban areas concerned the sudden 186 appearance of an adult pedestrian, or of a child chasing a ball on the roadway. The hazard 187 appeared at the same location for the same trial (i.e. rural area, high traffic) but not at the same 188 location between the trials, in order to minimize learning effects. The moment that the hazard 189 appeared was defined on the basis of both the simulator vehicle speed and the time to collision 190 in order to have identical conditions for each participant as regards available reaction time (i.e. 191 no possibility for the incident to appear more closely or more suddenly to one participant than 192 to another).

193 In this research, the driving data of the rural area drive low traffic and undistracted 194 condition are used for the analysis, being the least demanding condition in terms of road 195 environment and participants' mental workload.

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# 197 ANALYSIS METHODOLOGY

# 198199 Research hypotheses

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201 Previous analyses of the experiment data revealed several driving deficits of cognitively 202 impaired older people. MCI and AD patients in particular were found to drive at lower speeds 203 and with increased headways from the leading vehicle, have longer reaction time and accident 204 risk at unexpected incidents, drive at lower gearbox position and with increased engine rounds 205 per meter (rpm), make more errors (e.g. unintentional lane departures, sudden braking, engine 206 stops etc.) (13). These results are exploited in the present research in order to investigate 207 whether driving simulator measures can predict the presence of cognitive impairments. 208 Two research hypotheses are tested, as follows:

• A "conservative" hypothesis is first examined, aiming to test whether the simulator may 210 be a screening tool for the presence of cognitive impairments in general, so that further

- 211 medical and neuropsychological tests may diagnose a specific pathology (MCI, AD or 212 other).
- 213 • A more ambitious hypothesis, aims to test whether driving at the simulator may identify 214 different pathologies; although from a medical viewpoint, it is hardly pertinent or 215 meaningful to attempt to identify specific pathologies from the driving simulator data, 216 previous analysis results suggest that there are different driving deficits associated with 217 different pathologies, and consequently it may be easier to identify specific conditions.

#### 219 **Discriminant Analysis**

 $D_i = \sum_{i=1}^p d_i Z_i$ 

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221 A discriminant analysis technique was used for the purposes of this research, which uses a 222 linear combination of predictors that characterizes or separates two or more classes of objects 223 or individuals, and explicitly attempts to model the difference between the classes. 224 Discriminant analysis is broken into a 2-step process: first, testing significance of a set of 225 discriminant functions, and second, classification of individuals. The first step is 226 computationally identical to MANOVA. One first performs the multivariate test, and, if 227 statistically significant, proceeds to see which of the variables have significantly different 228 means across the groups.

229 The discriminant function coefficients denote the unique contribution of each variable 230 to the discriminant function, while the structure coefficients denote the simple correlations between the variables and the functions. The discriminant function score for the  $i^{th}$  function is: 231

(1)

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235 Where Z is the score on each predictor, and  $d_i$  is the discriminant function coefficient. 236 Once the discriminant functions are determined and groups are differentiated, the utility of 237 these functions can be examined via their ability to correctly classify each data point to their a 238 priori groups. Classification functions are derived from the linear discriminant functions to 239 achieve this purpose. For unequal sample sizes  $n_i$  in each group the classification function has 240 the following form:

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$$242$$
  
 $\frac{243}{244}$ 

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 $C_j = c_{j0} + \sum_{i=1}^p c_{ij} x_i + ln\left(\frac{n_j}{N}\right)$ (2)

for the  $j^{th}$  group, j = 1...k, x are raw scores of each predictor,  $c_{jo}$  is a constant and N the total 245 246 sample size.

In this paper, the medical diagnosis was used as the dependent variable and the 247 248 simulator driving performance measures with proved association with cognitive impairments 249 were used as independent variables. Previous research with this dataset, as well as existing 250 results from other related studies, were used to select the independent variables among the 251 numerous simulator variables. The independent variables tested included: 252

- Average speed
  - Speed variability (StdSpeed)
  - Mean Lateral position (LateralPositionAverage)
- Lateral position variability (StdLateralPosition)
- 256 • Gearbox position (GearAverage)
- 257 • Gearbox Position Variability (StdGearAverage)
- 258 • Engine rounds per meter (RpmAverage)
- 259 • Engine rounds per meter variability (StdRpmAverage)
- 260 • Mean headway from lead vehicle (HWayAverage)

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- Steering angle (WheelAverage)
- Steering angle variability (StdWheelAverage)
- Number of engine stops (EngineStops)
- Number of hits of roadside bars (HitOfSideBars)
- Number of lane departures (OutsideRoadLines)
- Number of sudden brakes (SuddenBrakes)
- Number of speed limit violations (SpeedLimitViolation)
- High engine rounds per meter (HighRoundsPerMinute)
- Reaction time at first unexpected event (ReactionTime1)
  - Accident occurrence at first unexpected event (Acc.Prob.1)

In addition to these simulator metrics, the participant's age was included in the independent variables, to control for the positive relationship between age and pathology, which was also identifiable through the sampling process.

# 275 **RESULTS**

## 277 Identification of cognitive impairments

279 As a first step of the analysis, the conservative hypothesis was tested. For that purpose, 280 cognitively impaired individuals were grouped together and were tested against healthy 281 controls. The Wilks' lambda test of equality of group means suggested that the only variables 282 that significantly distinguished impaired from healthy individuals were age and reaction time 283 at incidents, which were consequently the only variables retained in the discriminant function. 284 This result suggested that the simulator metrics did not add to the identification of cognitive 285 impairments in general, since reaction time may be directly measured by several 286 neuropsychological tests.

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## 288 Identification of MCI or AD patients

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290 Next it was examined whether simulator metrics may identify cognitive impairments 291 specifically due to MCI or AD pathologies. In this case, the dependent variable had three 292 groups (controls, MCI and AD) and therefore two discriminant functions are estimated (the 293 number of discriminant functions examined is equal to the number of groups minus 1; however, 294 some discriminant dimensions may not be statistically significant.). The Wilks' Lambda and 295 F-tests for equality of group means presented in Table 1 suggest that the variables most likely 296 to discriminate groups are average speed, gearbox position, mean headway, reaction time at 297 incident, accident occurrence at incident, and age. Lateral position variability and the number 298 of sudden brakes are also marginally significant at 90% confidence level. 299

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#### TABLE 1 Tests of equality of group means (MANOVA) for the simulator metrics

	Wilks' Lambda	F	df1	Sig.
Age	,761	13,042	2	,000*
AverageSpeed	,870	6,184	2	,003*
StdevAverageSpeed	,961	1,666	2	,195
LateralPositionAverage	,968	1,378	2	,258
StdLateralPosition	,948	2,286	2	,108
GearAverage	,840	7,909	2	,001*
StdGearAverage	,974	1,089	2	,341
RpmAverage	,999	,059	2	,942
StdRpmAverage	,998	,069	2	,934
HWayAverage	,910	4,093	2	,020*
WheelAverage	,987	,555	2	,576
StdWheelAverage	,990	,399	2	,672
EngineStops	,973	1,158	2	,319
HitOfSideBars	,997	,114	2	,892
OutsideRoadLines	,974	1,095	2	,339
SuddenBrakes	,957	1,874	2	,160
SpeedLimitViolation	,972	1,214	2	,302
HighRoundsPerMinute	,994	,255	2	,775
ReactionTime 1	,781	11,634	2	,000*
Acc Prob 1	906	4 314	2	017*

303 \* Statistically significant at 95% confidence level

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305 On the basis of these significant and marginally significant variables, the discriminant functions were estimated. The best performing model was selected on the basis of both the discriminant 306 307 function performance and the classification results. In that model, lateral position variability 308 was retained being significant at 90%, while the number of sudden brakes was removed. Table 309 2 shows the quality of the discriminant functions; function 1 explains 88% of the total variance 310 and significantly differentiates the groups, as suggested by the Wilks' Lambda test. Function 2 311 does not appear to significantly further discriminate between groups, as suggested by the 312 Wilks' Lambda test and is therefore redundant.

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#### 314 TABLE 2 Eigenvalues and Wilks' Lambda tests of canonical discriminant functions.

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			Wilks'			
Function	Eigenvalue	% of Variance	Lambda	Chi-square	df	Sig.
1	,687a	87,9	,541	49,091	14	,000,
2	,095a	12,1	,914	7,233	6	,300

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317 Table 3 presents the discriminant functions coefficients and the respective structure matrix (i.e.

318 the pooled within-groups correlations between the variables and the discriminant function).

319 The latter is to be interpreted in the same way that factor loadings are interpreted in a factor

320 analysis, and therefore it is observed that age, average speed, gearbox position, reaction time

321 and accident occurrence at incidents are strongly correlated with discriminant function 1, while 322 mean headway and lateral position variability are strongly correlated with discriminant

323 function 2.

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# TABLE 3 Canonical discriminant function coefficients (left panel) and structure matrix (right panel)

	Coefficients		Correlations (structur matrix)	
Variables	Function 1	Function 2	Function 1	Function 2
Age	,492	-,844	,645*	-,546
AverageSpeed	-,497	-,348	,636*	,156
GearAverage	-,293	-,035	-,525*	-,116
ReactionTime 1	,396	,008	-,465*	-,025
Acc.Prob.1	,103	,544	,379*	,023
HWayAverage	-,138	,048	,353	,442*
StdLateralPosition	,268	,644	,231	,440*

328 \*Largest absolute correlation between variable and any discriminant function

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The classification function was estimated, with prior classification probabilities derived on the basis of the initial group sizes. Classification results are presented in Table 4. In total, the model correctly "diagnosed" 65.1% of all drivers, i.e. 67% of healthy controls, 68% of MCI patients and 57% of AD patients - it is noted however that another 38% of AD patients were misclassified as MCI, indicating that the pathology is highly identifiable also for this group, although not to its full extent. These results seem promising and suggest that driving simulator metrics may reveal cognitive impairments with driver age controlled for.

337 It is well known, however, that these classification results are an overestimation of the 338 actual potential of the model, as the classification is made on the same cases that were used to 339 develop the model. A cross-validation analysis is presented in the next section to assess this 340 effect.

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## 342 TABLE 4 Original vs. predicted group membership classification results

			Predicted			
			Control			
	-	Diagnosis	group	MCI	AD	Total
Original	Count	Control group	18	8	1	27
		MCI	10	26	2	38
		AD	1	8	12	21
	%	Control group	66,7	29,6	3,7	100,0
		MCI	26,3	68,4	5,3	100,0
		AD	4,8	38,1	57,1	100,0

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#### 346 Cross-validation

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Cross-validation was done in two steps; results are presented in Table 5. First, a leave-one-out classification was carried out, in which cases are classified with the discriminant function estimated on the basis of all other cases except this one. This provides a "correction" of the classification results. It is indicated (see top panel of Table 5) in this case that 59% of healthy controls are correctly classified (another 37% is falsely classified as MCI), 63% of MCI are correctly classified (another 10.5% is falsely classified as AD) and 47.6% of AD are correctly classified (another 47.6% is falsely classified as MCI).

355 As a second step, the sample was split in two parts, on the basis of a random (Bernoulli) 356 case selection process: a part of the sample (70% of cases) was selected for developing the model, while the remaining 30% of the sample (i.e. 5 controls, 14 MCI and 6 AD) was kept for 357 358 prediction on the basis of the model developed. The results (see bottom panel of Table 5) show 359 that the share of correct classification dropped for all groups, which was expected both because 360 of the smaller sample used to develop the discriminant function, and the removal of the bias in 361 the classification. In this case, 60% of controls, 43% of MCI and 33% of AD patients are correctly classified. Nevertheless, even in this case 71.5% in total of MCI patients are classified 362 363 as cognitively impaired (either as MCI or as AD) and all AD patients are classified as 364 cognitively impaired. Moreover, none of the control group are classified as AD.

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366TABLE 5 Model cross-validation - Original vs. predicted group membership367classification results - leave-one-out classification (top panel), unselected cases (top368panel).

Observed			Predicted	Predicted		
			Control			
		Diagnosis	group	MCI	AD	Total
Leave-one-out	Count	Control group	16	10	1	27
cross-validation*		MCI	10	24	4	38
		AD	1	10	10	21
	%	Control group	59,3	37,0	3,7	100,0
		MCI	26,3	63,2	10,5	100,0
		AD	4,8	47,6	47,6	100,0
Unselected cases**	Count	Control group	3	2	0	5
		MCI	4	6	4	14
		AD	0	4	2	6
	%	Control group	60,0	40,0	,0	100,0
		MCI	28,6	42,9	28,6	100,0
		AD	,0	66,7	33,3	100,0
*.Each case is class	ified by th	e functions derived f	from all cases	other than tha	at case.	
**. 30% of the initia	al sample	not used to derive the	e functions.			

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## 372 **DISCUSSION**

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374 The results of the discriminant analysis model development and validation did not support the

375 conservative research hypothesis that it would be easier (and more appropriate for a medical

viewpoint) to attempt to identify the presence of cognitive impairment in general rather than distinguish different pathologies. A model simply distinguishing healthy from impaired individuals did not achieve satisfactory performance, and the only variables that were found to discriminate were age and reaction time, not providing added value to what would be already known from basic medical screening of those individuals.

381 The more ambitious analysis attempting to discriminate between MCI and AD 382 pathologies rather surprisingly resulted in more robust models and satisfactory classification 383 of individuals. This may be attributed to the fact that these different pathologies present 384 different driving deficits: lower speed, slower reaction times and lower gearbox position are 385 common trends, but the effects are more pronounced on MCI patients than on AD patients, 386 while longer headways and increased lateral position variability are more specific to AD 387 patients. Consequently, the explicit separation of pathologies allowed for the contributions of 388 different simulator variables to the classification be more easily identified.

In this case, the classification results are encouraging, even when correcting for case selection bias. On the other hand, the classification results leads to returning to the conservative hypothesis: it is not possible and meaningful to use the classification results for "diagnosis", as only 50-60% of all cases are accurately classified. However, the misclassification occurs almost exclusively between "neighboring" groups, e.g. MCI classified as AD or vice-versa, healthy classified as MCI. Consequently, the model may be most useful for a general classification in cognitively impaired or not, with only an indication of specific pathology.

396 Therefore, the potential of identifying ("diagnosing") cognitive impairments through a 397 driving test alone appears to be significant. It is noted that no cognition measurements while 398 driving (e.g. memory, recall, recognition, attention) were included in this analysis; a recent 399 research on the potential of using such cognitive tasks in a driving simulator study to predict 400 cognitive impairments did not find significant effects (18). On the contrary, the "diagnoses" 401 obtained in this research were based on driving performance measures and errors alone. It is 402 underlined however that the experiment used in this research was not designed to help identify 403 cognitive impairments, but to assess the driving performance of individuals with a known 404 diagnosis. This analysis attempted to reverse the question and the results are encouraging that 405 a more focused driving test with an even larger sample might provide more insights.

406

# 407CONCLUSION408

This paper aimed to address the need for early detection of cognitive and driving impairments, by further exploring their correlation and their potential identification towards a medical screening diagnosis. There is increasing interest in such early detection tools, especially as it has been found that cognitively impaired individuals are often asymptomatic but their driving performance is very sensitive to this early onset of the diseases.

414 The results from using driving simulator metrics and individual age to discriminate 415 between healthy and cognitively impaired individuals under moderate traffic conditions 416 suggest that driving performance measures that successfully classify drivers are average speed, 417 headways, lateral position variability, incident reaction time, accident occurrence at incidents, 418 and gearbox position. The discriminant functions correctly "diagnosed" nearly 65% of all 419 drivers, with better rates for healthy or MCI drivers - it is noted however that the presence of 420 pathology was highly identifiable, as most misclassifications were between the one pathology 421 group and the other.

This paper of course does not suggest that driving at the simulator may substitute the formal medical and neuropsychological examination that is required for diagnosis. It is suggested that driving at the simulator may provide useful insight as per the driving 425 performance of older people, and as per their cognitive state through the observable driving426 performance deficits (which are due to their cognitive decline).

427 There is promising indication that the simulator may under certain conditions be used 428 as a "neuropsychological tool" revealing the presence of cognitive impairments and guiding to 429 further formal testing towards a diagnosis. Given that driving requires several cognitive skills, 430 the development of dedicated simulator tests allowing to examine specific cognitive domains 431 critical for safe driving but also associated with highly prevalent pathologies - often 432 undetectable in their early stages - might have a two-fold added value to assist clinicians, both 433 in the screening and examination process and in the provision of more targeted and 434 substantiated advice as regards driving.

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# 445 **REFERENCES**446

- Mielke, M.M., Vemuri, P., Rocca, W.A. Clinical epidemiology of Alzheimer's disease: assessing sex and gender differences. *Clinical Epidemiology* Vol. 6, 2014, pp. 37-48.
- Frittelli, C., Borghetti, D., Iudice, G., Bonanni, E., Maestri, M., Tognoni G., Pasquali,
  L., Iudice A. Effects of Alzheimer's disease and mild cognitive impairment on driving
  ability: a controlled clinical study by simulated driving test. *International Journal of Geriatric Psychiatry* Vol. 24, 2009, pp. 232-238.
- 3. Dawson, J.D., Anderson, S.W., Uc, E.Y., Dastrup, E., Rizzo, M. Predictors of driving safety in early Alzheimer disease. Vol. 72, 2009, pp. 521-527.
- 4. Kawano, N., Iwamoto, K., Ebe, K., Suzuki, Y., Hasegawa, J., Ukai, K., Umegaki, H.,
  457 Iidaka, T., Ozaki, N. Effects of mild cognitive impairment on driving performance in
  458 older drivers. *Journal of the American Geriatrics Society* Vol. 60 No7, 2012, pp.
  459 1379-1381.
- 460 5. Bieliauskas, L.A., Roper, B.R., Trobe, J., Green, P., Lacy, M. Cognitive measures,
  461 driving safety, and Alzheimer's disease. *The Clinical Neuropsychologist* Vol. 12 No2,
  462 1998, pp. 206-212.
- 463
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  465
- Fitten, L.J., Perryman, K.M., Wilkinson, C., et al. Alzheimer and vascular dementias
  and driving: a prospective road and laboratory study. *The Journal of the American Medical Association* Vol. 273, 1995, pp. 1360-1365.
- 469 8. Ott, B.R., Heindel, W.C., Papandonatos, G.D., Festa, E.K., Davis, J.D., Daiello, L.A.,
  470 Morris, J.C. A longitudinal study of drivers with Alzheimer disease. *Neurology* Vol.
  471 70, 2008, pp. 1171-1178.
- 472
  9. Uc, E.Y., Rizzo, M., Anderson, S.W., Shi, Q., Dawson, J.D. Driver route-following 473 and safety errors in early Alzheimer disease. *Neurology* Vol. 63, 2004, pp. 832-837.

474	10.	Uc, E.Y., Rizzo, M., Anderson, S.W., Shi, Q., Dawson, J.D. Unsafe rear-end collision
475		avoidance in Alzheimer's disease. Journal of the Neurological Sciences Vol. 251,
476		2006, pp. 35-43.
477	11.	Jongen, E., Brijs, T., Brijs, K., Lutin, M., Cuenen, A., Van Vlierden, K., and Wets, G.
478		Beyond summarized measures: Predictability of specific measures of simulated
479		driving by specific physical and psychological measures in older drivers. In:
480		Proceedings of the International Conference on Aging, Mobility and Quality of Life
481		(AMQol 2012), Michigan, USA, 24-26 June 2012.
482	12.	Cuenen, A., Jongen, E., Brijs, T., Brijs, K., Lutin, M., Van Vlierden, K., and Wets, G.
483		Does attention capacity moderate the effect of driver distraction in older drivers?
484		Accident Analysis and Prevention, Vol. 77, 2015, pp.12-20.
485	13.	Pavlou, D., Papadimitriou, E., Antoniou, C., Papantoniou, P., Yannis, G., Golias, J.,
486		Papageorgiou, S.G. Driving behavior of drivers with mild cognitive impairment and
487		Alzheimer's disease: a driving simulator study. Proceedings of the 94th Annual
488		meeting of the Transportation Research Board, Washington, January 2015.
489	14.	Breker, S., Henrikson, P., Falkmer, T., Bekiaris, E., Panou, M., Eeckhout, G., Siren,
490		A., Hakamies-Blomqvist, L., Middleton, H., Leue, E. Aged people Integration,
491		mobility, safety and quality of Life Enhancement through driving (AGILE)
492		Deliverable 1.1: Problems of elderly in relation to the driving task and relevant
493		critical scenarios, 2003.
494	15.	Snellgrove, C.A. <i>Cognitive screening for the safe driving competence of older people</i>
495		with mild cognitive impairment or early dementia. Australian Transport Safety
496		Bureau, Australia, 2005.
497	16.	Roe, C.M., Barco, P.P., Head, D.M., Ghoshal, N., Selsor, N., Babulal, G.M., Fierberg,
498		R., Vernon, E.K., Shulman, N., Johnson, A., Fague, S., Xiong, C., Grant, E.A.,
499		Campbell, A., Ott, B.R., Holtzman, D.M., Benzinger, T.L., Fagan, A.M., Carr, D.B.,
500		Morris, J.C. Amyloid Imaging, Cerebrospinal Fluid Biomarkers Predict Driving
501		Performance Among Cognitively Normal Individuals. Article in press, Alzheimer
502		Disease & Associated Disorders, 2016.
503	17.	Gerrie, C.A., Rodriguez, M., Sachdev, P., Duflou, J., Waite, P.M. Mild neuritic
504		changes are increased in the brains of fatally injured older motor vehicle drivers.
505		Accident Analysis and Prevention Vol.39, 2007, pp. 1114-1120
506	18.	Vardaki, S., Yannis, G., Antoniou, C., Pavlou, D., Beratis, I., Papageorgiou S.G. Do
507		simulator measures improve identification of older drivers with MCI? Proceedings of
508		the 94th Annual meeting of the Transportation Research Board, Washington, January
509		2015.
510	19.	Fisher, D.L., Rizzo, M., Caird, J.K., & Lee, J.D. (Eds). Handbook of Driving
511		Simulation for Engineering, Medicine, and Psychology. Boca Raton, FL, 2011, CRC
512		Press.
513	20.	Yannis, G., Golias, J., Antoniou, C., Papadimitriou, E., Vardaki, S., Papantoniou, P.,
514		Pavlou, D., Papageorgiou, S.G., Andronas, N., Papatriantafyllou, I., Liozidou, A.,
515		Beratis, I., Kontaxopoulou, D., Fragiadaki, S., Economou, A. Design of a large
516		driving simulator experiment on performance of drivers with cerebral diseases.
517		Proceedings of the 4th International Conference on Road Safety and Simulation,
518		Rome, October 2013
519	21.	Yannis, G., Papantoniou, P., Nikas, M. Comparative analysis of young drivers behavior
520		in normal and simulation conditions at a rural road. Proceedings of the 5th International
521		Conference on Road Safety and Simulation, Orlando, Florida, October 2015.
522		