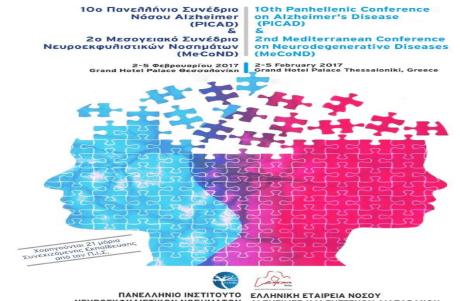
Drivers with AD and MCI: The predictive value of neurological and neuropsychological measures



NEYPOEKΦΥΛΙΣΤΙΚΩΝ ΝΟΣΗΜΑΤΩΝ PANHELLENIC INSTITUTE OF NEURODEGENERATIVE DISEASES (P.I.N.Dis.)

EΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ ΝΟΣΟΥ ALZHEIMER ΚΑΙ ΣΥΓΓΕΝΩΝ ΔΙΑΤΑΡΑΧΩΝ GREEK ASSOCIATION OF ALZHEIMER'S DISEASE AND RELATED DISORDERS

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Senior drivers: general information

- **13%** of drivers > 65 years old (2009)
- 23% increase between 1999 and 2009
- Elderly individuals keep their driving license longer and drive larger distances
- During 2013, 6.500 older drivers lost their lives in car accidents (Eurostat, 2014)
- Life loss in elderly represent the 26% of all road fatalities in the EU (Eurostat, 2014)
- <u>The percentage of older drivers that are at risk due to</u> <u>cognitive or physical impairments remains unknown</u>

Cognitive functions critical for safe driving

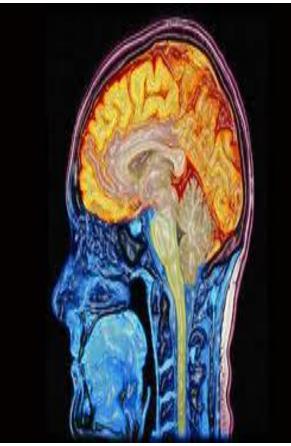
1. Attention

2. quick perception of the environment

- 3. Executive functions
- 4. process multiple simultaneous environmental cues
- 5. make rapid, accurate and safe decisions
- 6. Visuo-spatial skills
- 7. position the car accurately on the road
- 8. manoeuvre the vehicle correctly
- 9. judging distances and predicting the development of traffic situations

10.Memory 11.journey planning 12.adapting behaviour

(Reger et al., 2004)



Cognitive Disorders and Driving

Alzheimer disease and accident risk

AD patients are 2.5 to 4.7 times more likely to be involved in a car crash than age-matched controls

(Brown and Ott 2004; Dobbs et al. 2002; Ernst et al. 2010; Withaar et al. 2000, Brorsson, 1989; Massie & Campbell, 1993; Tuokko et al., 1995)

But ~ 50% of patients with AD continue driving for at least three years after their initial diagnosis (Adler and Kuskowski 2003; Seiler et al.2012, Johansson and Lundberg, 1997; Dubinsky et al., 1992; Rizzo et al., 2001; Charlton et al., 2004; Uc et al., 2005; Uc et al., 2006; Ott 2008; Ernst et al. 2010)

However, certain drivers with AD maintain adequate driving fitness at the initial stages of the disease (Carr et al., 2000; Perkinson et al., 2005)

Driving Predictors-Alzheimer Disease

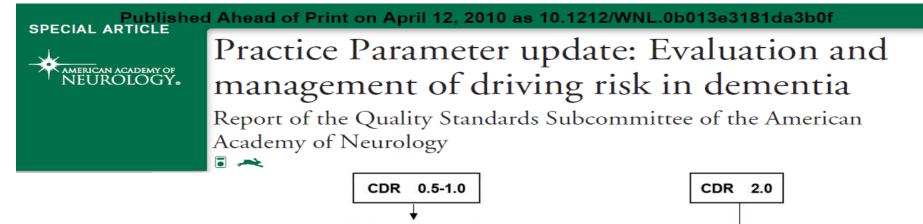
Performance on neuropsychological measures assessing

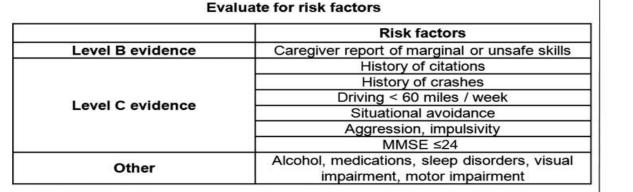
- visuospatial skills,
- attention,
- executive functioning
- And probably memory

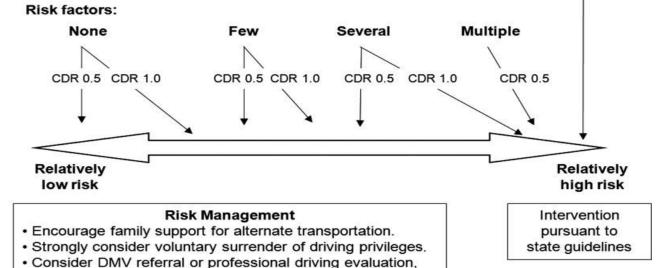
Appear to be related with the driving fitness of patients with

<u>AD</u> (Brown et al., 2005; Grace et al., 2005; Ott et al., 2008; Uc et al., 2005)

Neuropsychological and neurological measures in combination with driving evaluations (on-road or simulator environment) could be used for providing effective recommendations in drivers with AD (Frittelli et al., 2009; Ott et al., 2008; Ott et al., 2003; Rizzo et al., 1997)







based on state guidelines.

MCI and driving: a controversial issue



Wadley et al., 2009
 on-road

- Devlin et al., 2012 simulator
- Jeong et al., 2012 questionnaire

- Snellgrove et al., 2005
 on-road (50% of MCI failed the on-road test)
- Kawano et al., 2012 simulator
- O' Connor et al., 2010 questionnaire

Predictors of driving behavior in MCI

- Measures associated with driving performance in patients with MCI
- Cognitive domains:
- mental flexibility (TMT-B)
- Inhibitory control (modified Stroop test)
- visual attention (TMT-A)
- When controlling for memory impairment, TMT-B seemed to be the best predictor

(Kawano et al., 2012)

Interdisciplinary Research Project 2012-2015

- Driving simulator experiment focusing on drivers with cognitive disorders [MCI (N=59), AD (N=25), PD (N=25)]
- Majority of drivers >55 years old (<u>N=154</u>)
- Cognitively healthy drivers of similar age and driving experience were also included
- Interdisciplinary research team (neurologists, psychiatrists, neuropsychologists, transportation research scientists





Procedure

- Part 1. Medical, Clinical & Neurological evaluation
 Attikon General Hospital, (~1,5 hours)
- Part 2. Neuropsychological Assessment Attikon General Hospital, (~2 hours)
- Questionnaire on driving habits At home (~20 minutes)
- Part 3. Driving simulation experiment NTUA Driving Simulator (~1,5 hour)



 Part 1B. Medical evaluation, Part 2B. Neuropsychological Assessment Attikon General Hospital, (~1 hours)

Medical/Neurological Assessment

Comprehensive Clinical Evaluation (general medical and neurological)

- Present & past history, pharmacological treatment, life habits (alcohol consumption, smoking, etc)
- Detailed neurological examination (neurological signs: markers for a disease)
- Psychiatric assessment for depression, anxiety, behavioral disturbances
- Ophthalmological evaluation: visual acquity, visual fields, fundoscopy



 Motor ability-tests in Fitness to Drive: Specific clinical tests examining motor control, balance, visual fields etc. related to driving skills

Neuropsychological Assessment

General Cognitive Functioning : MMSE, MOCA

Working memory/attention: Letter-Number Sequencing, Spatial Span, Spatial Addition (WMS), Neuropsychological Assessment Battery - Driving Scenes Test.

Episodic Memory: Hopkins Verbal Learning Test, Brief Visuospatial Memory Test.

Visual Perception: Benton's Judgment of Line Orientation, Witkin's Embedded Figure Test.

Executive function/processing speed: Frontal Assessment Battery, Trail Making Test, Comprehensive Trail Making Test, Symbol Digit Modalities Test.

Computerized tests: Useful Field of View, Psychomotor Vigilance Test.

Outcome Measures

Indexes of Driving Performance

- a) Average Speed
- b) Speed Variation
- c) Lateral Position
- d) Variation of Lateral Position
- e) Headway Distance
- f) Variation of Headway Distance
- g) Hits of side bars
- h) Speed limit violations
- i) Accident Risk
- j) Reaction time



Driving Simulator Environment: Urban and Rural Area

Driving Simulator Assessment:

- Rural and urban area
- two traffic scenarios (low and high traffic volumes)
- three distraction conditions (undistracted driving, driving while conversing with a passenger and driving while conversing on a mobile phone)

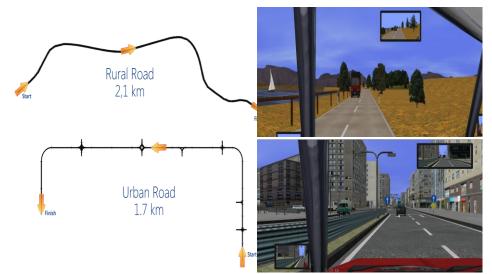


Figure 1. The two plans of the driving routes (rural and urban) and two screenshots for each driving environment



Figure 2. Two incidents screenshots - donkey entering the road in rural area and a child chasing a ball in urban area

MCI & driving: current findings



Sokratis Papageorgiou¹, <u>Ion Beratis¹</u>, Nikolaos Andronas¹, Alexandra Economou², Dimosthenis Pavlou³, Anastasios Bonakis¹, George Tsivgoulis¹, Leonidas Stefanis¹, George Yannis³

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Results (Average Speed)

Outcome: Driving Speed

Predictors:

(1st level) general cognitive functioning (MMSE)

(2nd level) balance and movement coordination (**Tandem Walking**, β =-.63, p=.007)

The model explained 55.9% of the variance in average driving speed

*R*²=.559, *F*(2,13)=8.25, *p*=.005.

 In the cognitively intact group the same regression model did not contribute to the prediction of average driving speed

*R*²=.166, *F*(2,11)=1.10, *p*=.368

Normal Group (*Mean*=43.62, *SD*=7.33) vs MCI Group(*Mean*=42.24, *SD*=7.46) • *t*(28)=.51, *p*=.614

Results (Number of Crashes)

Outcome: Number of Crashes

Predictors:

(1st level) general cognitive functioning (**MMSE**) (2nd level) visuospatial memory (**BVMT_Recognition**, β =-.40, *p*=.056) and

speed of **attention** (UFV_1, β =.48, *p*=.027)

The model explained 77.3% of the variance in number of crashes

*R*²=.773, *F*(3,10)=11.35, *p*=.001

• In the cognitively intact group the same regression model did not contribute to the prediction of number of crashes

*R*²=.279, *F*(3,10)=1.29, *p*=.330

Normal Group (*Mean*=.43, *SD*=.65) vs MCI Group(*Mean*=.56, *SD*=.81) • *t*(28)=.49, *p*=.25

Results (Reaction Time)

Outcome: Reaction Time

Predictors:

(1st level) general cognitive functioning (**MMSE**)

(2nd level) information processing speed (SDMT, β =-.60, *p*=.014) and balance and movement coordination (Tandem Walking_RNC, β =.54, *p*=.007)

The model explained 73.2% of the variance in reaction time

R² = .732, F(3,12)=10.92, p=.001

 In the cognitively intact group the same regression model did not contribute to the prediction of reaction time

*R*²=.119, *F*(3,10)=.45, *p*=.772

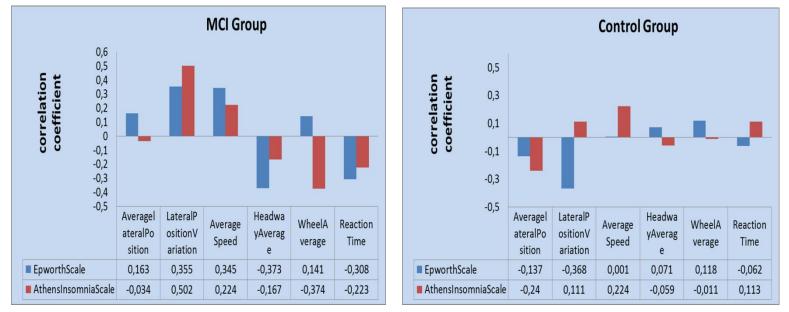
Normal Group (*Mean*=1.78, *SD*=.28) vs MCI Group (*Mean*=1.89, *SD*=.46) *t*(28)=.80, *p*=.43

The role of sleeping abnormalities on the driving performance of individuals with Mild Cognitive Impairment

I. N. Beratis, N. Andronas, E. Papadimitriou, D. Kontaxopoulou, S. Fragkiadaki, C. Koros, A.Bonakis, A. Economou, S. G. Papageorgiou (EAN Berlin 2015)

- 27 cognitively intact individuals (Age: 63.4±7.2 years)
- <u>33 individuals with MCI (Age: 66.4±7.4 years)</u>

Figure 1. Correlation coefficients between driving indexes and sleeping abnormalities in the control and MCI group



- The current findings indicate a stronger association between sleeping abnormalities and driving behavior in the MCI group as compared to the group of cognitively intact individuals
- In the MCI group, sleepiness was positively associated with lateral position variation and average speed, and negatively associated with average headway distance
- In the MCI group, insomnia symptoms were positively associated with lateral position variation, and negatively with the average wheel position

Driving in Mild Cognitive Impairment: The role of depressive symptoms.

Beratis IN¹, Andronas N¹, Kontaxopoulou D¹, Fragkiadaki S¹, Pavlou D², Papatriantafyllou J¹, Economou A³, Yannis G², Papageorgiou SG¹.

Author information

Abstract

OBJECTIVES: Previous studies indicate a negative association between depression and driving fitness in the general population. Our goal was to cover a gap in the literature and to explore the link between depressive symptoms and driving behavior in individuals with Mild Cognitive Impairment (MCI) through the use of a driving simulator experiment.

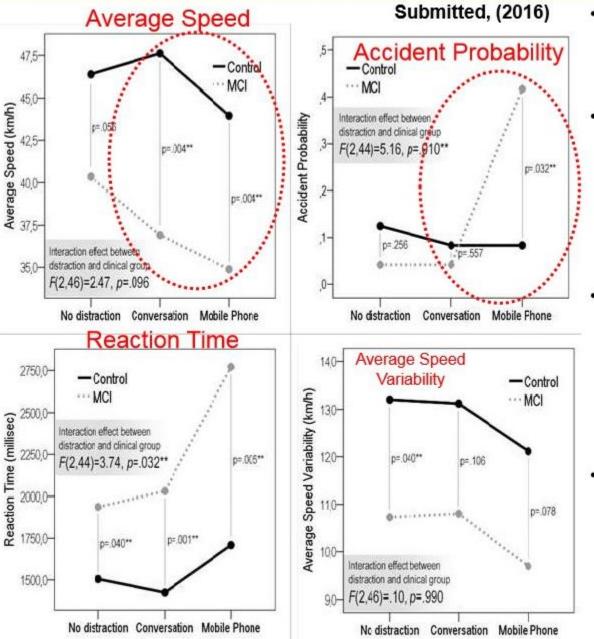
METHODS: Twenty-four individuals with MCI (Age: Mean = 67.42, SD = 7.13) and 23 cognitively healthy individuals (Age: Mean = 65.13, SD = 7.21) were introduced in the study. A valid driving license and regular car use served as main inclusion criteria. Data collection included a neurological/neuropsychological assessment and a driving simulator evaluation. Depressive symptomatology was assessed with the Patient Health Questionnaire (PHQ-9).

RESULTS: Significant interaction effects indicating a greater negative impact of depressive symptoms in drivers with MCI than in cognitively healthy drivers were observed in the case of various driving indexes, namely average speed, accident risk, side bar hits, headway distance, headway distance variation, and lateral position variation. The associations between depressive symptoms and driving behavior remained significant after controlling for daytime sleepiness and cognition.

CONCLUSIONS: Depressive symptoms could be a factor explaining why certain patients with MCI present altered driving skills. Therefore, interventions for treating the depressive symptoms of individuals with MCI could prove to be beneficial regarding their driving performance.

Mild Cognitive Impairment and driving: Does in-vehicle distraction affect driving performance?

Ion N. Beratis, Dimosthenis Pavlou, Eleonora Papadimitriou, Nikolaos Andronas, Dionysia Kontaxopoulou, Stella Fragkiadaki, George Yannis, S. G. Papageorgiou



- The mixed ANOVA revealed a greater effect of distraction on MCI patients.
- Specifically, the use of mobile phone induced a more pronounced impact on reaction time and accident probability in the group of patients, as compared to healthy controls.
- Also, a greater negative effect of "conversing with passenger" was observed in the group of drivers with MCI, but of a lesser extent than in the case of the mobilephone condition.
- Notably, the aforementioned findings were observed despite the effort of the drivers with MCI to apply a compensatory strategy by reducing significantly their speed.

AD & driving: current findings

Mini Mental State Examination and Montreal Cognitive As sessment: which is the best predictor of Driving Ability?

D. Kontaxopoulou⁴, I. N. Beratis¹, S. Fragkiadaki⁴, N. Andronas⁴, D. Pavlou², G. Yannis², J. Pap atria ntafy 11ou2, L. Stefan is4, A. Economou4, S. G. Papa geor giou4

2nd University Department of Neurology "Attiken" University General Hespital, "Department of Transportation Planning & Engineering, National Technical University of Athena, "General Heapital of Athena G. Generatata, "Department of Paye hology, National and Kapedistian University of Athens





INTRODUCTION

Table 1. Correlations between MMSE, MoCA and Driving Indexes in aMCI patients

Min i Men tal State Examination (MM SE) and Montreal Cognitive Assessment (MoCA) are the most commonly used screening tests for the evaluation of general cognitive ability. Previous research sugglests that MIMSE and MoCA could be used as predictors of driving a bility.

In regards to M MSE, previous studies which have investigated performance on the MMSE in relation to driving abilities have revealed contradictory results. Although the inconsistency of the MMSE as a predictor of driving ability is shown in a number of studies (Adlen et al., 2008; Lesikanet al., 2002; Paccalin et al., 2000; Uc et al., 2005), som estudies suggest a consistent relation ship between the two (Lesikar et al., 2002; Uc et al., 2005).

Holl is et al. (2003) examined the comparison between MMSE and sugglested that the MoCA was a useful screening test for identifying individ

Driving Indexes	Rural Area				Urban Area				
	MM SE		MeCA		M MSE		MeCA		
		p-value		p-value		p-v alue		p-value	
Av erage speed	.01	.94	05	.77	01	.96	.09	.61	
Lateral position	-10	.55	-33	.055	.22	.22	.18	.52	
Head way distance	.0 Z	.91	.0.4	.8.5	16	.58	.01	.94	
Reaction time	-33	.045*	-42	~01*	~.78	.00 0**	~ 47	.02*	
Accident probability	-34	.041*	046	.006*	~.56	.0.03*	~.47	.02	
Speed limit violations	- 2.3	.15	-39	.0.2*	.20	.27	.34	.059	

RESULTS

MoCA in order to predict driving performance. The study's findings Table 2. Correlations between MMSE, MoCA and Driving Indexes in mild AD patients

individuals with cognitive impairment who are at driving risk.		Driving Indexes		Rural Area				Urban Area			
AIM			1	MM 38		MeCA		MM SE		Me CA	
				p-value		p-value		p-value		p-value	
The present study compared the capacity MMS	3 and	Av erac e speed	.41	.09	.48	.044 *	.2.9	.28	.34	.21	
MoCA to predict specific driving indexes in patients	with	Lateral position	.22	.37	.06	.79	.21	.43	04	.55	
a MCL mild AD and healt hy individuals.		He ad way distance	- 53	.024*	~ 37	.014*	-28	.2.9	-26	.32	
METHODE		Reaction time	.07	.77	- 09	.62	-16	.5.2	.1.5	.65	
		Accident probability	.21	.39	.13	.61	-34	.03*	-53	.037*	
Participants:		Speed Limit violations.	-		-		-		-		
 44 patients with aMCI 		Specco in the second									
 23 patients with mild AD 		*p05. **p<.001									
 44 healthy individuals 		• In the AD group, no sp	ee d lim	it violations	were re	corded					
The diagnosis of aMCI was made by the Petersen et al. (2005		> In the healthy individu		MAKEred	-			inted with a		he driving	
The diagnosis of mild AD was made by the Petersen et al. (2003) The diagnosis of mild AD was made by the Mickhanni et al. (2		indexes					01.0 3500	acco with a	ii yor i	ine of white	
criteria											
				CON	CLUS	ON					
Inclusion & Exclusion Criteria:											
 have a valid driving ficense 		 Our findings indicated that both MMSE and MoCA as sociated with various driving indexes could be useful screening measures in order to as sets driving fitness briefly. 									
regular drivers		be useful screening m	02092	in order to	a ses d	siving Stop	ss brief	by:			
 CDR: MCI ≤ 0.5 , AD ≤ 1 		 Both routine cognitive screening tests were correlated with the critical driving indexes of reaction 									
 not have significant psychia tric history of psychosis not have any significant motor disorder 		time and accident or obability in the groups of driver with MCI and AD									
 not nave any significant motor disorder not have any significant visual disorder 		,						-			
		 In the mild AD group 									
Procedure		in terms of driving behavior. Thus, the aforementioned screening tools could be alternatively utilized in order to obtain an indication of the driving fitness in patients with mild AD.									
(a) All the participants underwent a completeneurological,	_	utilized in order to ob	tain an	indication o	ftheda	ving fitness	sin patie	im diay atao	16 AD.		
ne urops ychol ogica I and othal mological a ssessment. Gene cognitive ability was measured by the administration of N		 However, in the case 		T. M-C A		بم بالتربية المديد ا			-		
MoCA		- 110 wever, in the case	or allife	a, mouse w	- 0000	2000 - 2000 51	1000 005	ving variable		ure man an.	
(b) The participants went through a driving simulator experi	ment:	 Thus, MoCA seems to 									
		driving ability. This fi							be ab	e tter	
	Phase 1: Practice session (5-10 min.)		ction of	patients wit	h MCI	(Dong, et al	(2012)	L .			
 Phase 2: Two driving sessions (about 20 min. each) on urt streets with multiple lanes, and on a two-lane rural road. 			REF	ERENCES/	ACKN	DWLEDGI		TS			
streets with multiple lanes, and on a two-lane rural road. unexpected in cident occurs in each of the two sessions (s)		 Adler G., Kuskowski, M. 									
appearance of pedestrian or child on the road, sudden		 Adler G., Kuskowski, M. and Associated Disorde 			seconi	noicermen		e ment lä. Av	00000	LAS 0050	
appearance of an animal on the rura (road)		 Dong, et al. (2012). The 			e Assies	mentis suo	eriorto	theMini-M	ental 9	tate	
 Driving was assessed with a Foerst FPF driving simulator, 		Examination in detection									
different conditions		24(11):1749-55.		-				~~~~	~~~~	~~~	
		 Holl is, A. M, et al. (2015 									
		Assessment in the Pred	ict ion o	T Driving Te	Cutor	me Journal	of the	A meri con G	oriatr ic	s Society	

Driving Indexes:

- Average sipeed
- Lateral position
- Head way distance
- Reaction time
- Accident probability
- Speed limit violations



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Control vs. AD Group on Driving Indexes

Rural Area - Condition Without Distraction

	AD group		Contro	l group	t-test		
	Mean	SD	Mean	ean SD		р	
Average Speed	32.8	7.8	40.3	7.6	3.11	.004**	
Average Speed Variation	9.7	3.8	10.7	2.8	.94	.352	
Lateral Position	1.5	.17	1.5	.09	632	.531	
Lateral Positon Variation	.29	.05	.27	.06	-1.42	,164	
Headway Average	610.8	181.2	503.5	111.5	-2.28	,028*	
Headway Average Variation	273.8	100.8	222.1	54.9	-2.04	.048*	
Wheel Average	-1.3	1.5	-1.7	0.5	-1.31	.196	
Wheel Average Variation	16.9	2.5	16.7	2.2	26	.796	
Reaction Time	2457.6	967.8	1511.9	442.6	-4.04	.000**	
Number of Crashes	.53	.77	.09	.31	-2.37	.023*	
Speed Limit Violation	.05	.23	.09	.31	.50	.620	



Control vs. AD Group on Driving Indexes

Urban Area - Condition Without Distraction

	AD group		Contro	l group	t-test		
	Mean	SD	Mean	SD	Т	р	
Average Speed	24.7	6.7	27.9	5.3	1.45	.158	
Average Speed Variation	9.2	2.4	11.5	2.9	2.31	.028*	
Lateral Position	3.2	.63	2.9	.74	-1.32	.165	
Lateral Positon Variation	1.7	.54	1.5	.65	-1.07	,292	
Headway Average	125.3	26.1	129.2	36.1	.35	,732	
Headway Average Variation	56.9	8.4	54.2	11.6	770	.448	
Wheel Average	7.6	1.4	6.3	1.6	-2.28	.030*	
Wheel Average Variation	24.6	11.1	27.3	11.4	.67	.508	
Reaction Time	1683.6	460.5	1196.8	427.9	-2.85	.008**	
Number of Crashes	.62	.81	.00	.00	-2.67	.013*	

Percentage of AD drivers that exhibited similar driving performance to the Control group

Average Speed

• 47% of AD patients were on the range (±1SD) of normal performance

	AD (normal performance) N=8		AD (imperforman	t-test		
	Mean	SD	Mean	SD	Т	р
MMSE	24.6	3.2	21.6	3.7	1.80	.090
CTMT1	103.8	29.6	176.9	77.8	-2.46	.029*
CTMT2	106.5	43.2	214.3	55.2	-4.24	.001**
СТМТ3	122.1	41.4	229.5	72.4	-3.59	,003**
CTMT4	134.7	61.7	246.4	48.9	-3.84	,002**
CTMT5	246.6	52.1	315.7	38.9	-2.87	.013*
Incidental memory	4.7	1.1	6.0	1.1	-2.09	.060

Conclusions



REVIEW

Does the diagnosis of Alzheimer's Disease imply immediate revocation of a driving license?

Sokratis G. Papageorgiou¹, Ion N. Beratis¹, Dionysia Kontaxopoulou¹, Stella Fragkiadaki¹, Dimosthenis Pavlou², and George Yannis²

Special Issue on Controversies in Neurology. From the 10th World Congress on Controversies in Neurology (CONy), Lisbon, Portugal. 17–20 March 2016.

Abstract

Driving competence is strongly related to the autonomy and the feelings of self-worth of advanced agers. At present, older drivers appear to retain their driving license for longer periods of time as well as to drive more commonly and to cover longer distances as compared to the past. Nonetheless according to epidemiological data, older individuals appear to be a vulnerable driving group that manifests increased rates of road fatalities. Along this vein, several lines of previous research have focused on exploring the driving behavior of individuals with two common cognitive disorders, namely Alzheimer-dementia (AD) and Mild Cognitive Impairment (MCI). Based on previous findings, patients with AD commonly present increased driving difficulties at a level that clearly supports the discontinuation of driving. Nonetheless, some patients with AD, especially in the mild stages, retain adequate driving skills that are similar to those of cognitively intact individuals of similar age. As concern the group of drivers with MCI, it seems that there is an accentuated risk to develop driving difficulties, but their performance is not consistently worse than that of healthy control drivers. Nonetheless, additional studies are warranted for detecting useful predictors of driving behavior in the specific clinical group. Under this perspective and by integrating the previous findings, we suggest the need for implementing a personalized approach when taking decisions about the driving competence of drivers with AD and MCI that is based on the effective synthesis of multimodal driving-related indexes by the specialties of neurology, neuropsychology and transportation engineering.

Keywords: Driving, Dementia, Alzheimer disease, Mild Cognitive Impairment, Driving behavior.

To drive or not to drive?

Driving History (accidents, complaints from the patient of the informant)

Combined use of neurological,neuropsychological and driving measures that have predictive value of driving competence according to the clinical diagnosis (MCI, AD)

 Synthesis and possessing of relevant information by specialized neurologists and neuropsychologists

3



Also, definition of specific restrictions (speed, traffic conditions, driving at night) based on specific characteristics of each driver (disease, stage of the disease, age, performance on neuropsychological tests)

Figure 1. Proposed evaluation of drivers with AD or MCI.

AD = Alzheimer's disease; MCI = Mild Cognitive Impairment



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Thank you for your attention!

