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Driving behavior of patients with mild Alzheimer's Disease (AD) or amnestic Mild Cognitive Impairment (aMCI) carriers of the apolipoprotein e4 allele (*APOE4*)

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BACKGROUND

- Although patients with AD maintain the ability to operate a vehicle, driving behavior is impaired and their driving profile is described as conservative (Papageorgiou et al., 2016).
- Previous research suggests that patients with MCI have also driving performance deficits, although generally considered safe drivers (Devlin et al., 2012)
- However, literature regarding the severity of driving impairments in MCI and mild AD has not yet reached a consensus.
- According to a recent meta-analysis, severity of cognitive decline appears to have important predictive utility over driving ability in patients with AD and patients with MCI (Hird et al., 2016).
- *APOE e4* allele –a well documented genetic risk factor for AD- carriers have more severe cognitive impairments than non-carriers in MCI and AD.

AIM

Comparison of the driving behavior of patients with aMCI and mild AD carriers of the *APOE4* with non-carriers.

METHODS

Participants

Table 1
Descriptive measures of the two groups and comparison between them

	APOE4 carriers (N = 18)	*APOE4* non-carriers (N=18)		
	M (*SD*)	*M* (*SD*)	*t*	*p*
Age	71.6 (9.2)	73.9 (8.1)	0.79	0.438
Education	11.8 (3.9)	11.6 (4.7)	-0.15	0.878
Driving Experience	42.9 (11.7)	45.7 (8.6)	0.65	0.521
MMSE Score	25.8 (5.5)	25.6 (3.3)	-0.12	0.909

Note : *p < 0,05, **p < 0,001

Statistical Analysis

Independent samples t-test indicated **no significant differences** regarding demographic characteristics, which allows performing comparisons between the two groups.

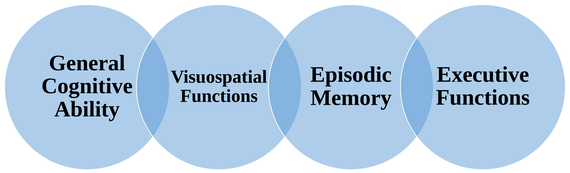
Inclusion Criteria:
1. Diagnosis:
a. aMCI based on Petersen and Morris criteria (2005) and CDR ≤ 0,5
b. AD based on McKhann et al. (2011) criteria and CDR ≤ 1
2. Valid Driving License
3. Active drivers
a. driving ≥ 1/week, b.10km/week, c.≥2500km/year.
4. Sufficient driving experience: >3 years of driving after getting a license.

Exclusion Criteria:
1. History of psychosis
2. Evidence of alcohol or drug addiction
3. Significant motor or visual disorder
4. Dizziness or nausea while in a moving vehicle
5. Record of traffic accidents (last two years)

Multidisciplinary experimental design

A. Detailed Medical - Neurological - Ophthalmological Assessment
B. Neuropsychological Assessment
C. Driving Simulation in rural environment:
Condition 1: low traffic volume Q=300 vehicles/h
Condition 2: high traffic volume Q=600 vehicles/h
D. DNA isolation with the High Pure PCR Template Kit by Roche and APOE genotyping was performed with a real time PCR method in the Light Cycler platform by Roche.

Figure 1. Cognitive Domains assessed through Neuropsychological Assessment



Driving Indexes

1. **Average Speed**
2. **Speed Variation**
3. **Distance from Heading Vehicle**
4. **Distance from Heading Vehicle Variation**
5. **Lateral Position**
6. **Lateral Position Variation**
7. **Reaction Time**
8. **Accident Probability**

RESULTS

Table 2
Comparison between APOE4 carriers and non-carriers on ***driving indexes*** *in Condition 1 and 2*

Driving Indexes	*APOE4* carriers (N = 18) *M (SD)*	*APOE4* non-carriers N=18) *M (SD)*	*t*	*p*	*d*
		Low Traffic			
Average Speed	36.6 (7.4)	39.6 (6.3)	1.19	0.246	-
Speed Variation	9.9 (2.5)	11.7 (2.8)	1.91	**0.066**	-
Lateral Position	1.5 (0.2)	1.5 (0.1)	-0.84	0.204	-
Lateral Position Variation	0.3 (0.04)	0.3 (0.04)	0.81	0.424	-
Heading Distance	548.0 (155.6)	542.8 (131.7)	0.10	0.924	-
Heading Distance Variation	244.9 (72.7)	227.9(56.2)	-0.70	0.490	-
Reaction Time	2083.8 (757.5)	1997.7 (333.0)	-0.40	0.690	-
Accident Probability	0.3 (0.6)	0.3 (0.5)	0.34	0.739	-
		High Traffic			
Average Speed	32.6 (7.1)	38.2 (6.1)	2.40	**0.023***	**0.85**
Speed Variation	7.7 (1.5)	11.2 (2.8)	4.36	**0.000****	**0.70**
Lateral Position	1.6 (0.1)	1.6 (0.1)	-0.55	0.586	-
Lateral Position Variation	0.3 (0.04)	0.3 (0.05)	0.84	0.407	-
Heading Distance	401.6 (214.1)	302.3 (106.5)	-1.66	0.107	-
Heading Distance Variation	204.8 (80.4)	157.4 (52.1)	-1.99	**0.057**	
Reaction Time	2438.4 (706.0)	2184.8 (643.1)	-1.08	0.290	-
Accident Probability	0.2 (0.5)	0.3 (0.6)	0.69	0.495	-

Note: *p < 0,05, **p < 0,001

Statistical Analysis

- **Independent samples t-test** indicated significant differences regarding **driving behavior**. After the Bonferroni application for multiple comparisons in low traffic volume no differences were depicted, however in high traffic volume: ***APOE4* carriers indicated lower Speed Variation.**
- **Independent samples t-test** indicated significant differences regarding **cognitive functions** only in episodic memory. No other significant differences were depicted between performances in neuropsychological measures. This result did not survive after the application of Bonferroni corrections.

CONCLUSION

- To our knowledge, this is the first study to investigate the possible effect of *APOE4* to driving behavior.
- *APOE4* carriers demonstrated lower speed variation in higher traffic volume, however, no differences were depicted in low traffic volume. ***APOE4* seems to challenge carriers in cognitively demanding conditions.**
- Lower speed variation might be a compensatory mechanism utilized by carriers in order to avoid driving errors. More specifically, it is an indication of serialization of behavior in a multicomponent task which demands switching attention among various tasks.
- **In conclusion, the driving simulator reported a difference which was not depicted through the thorough neuropsychological assessment.**
- Future studies, should consider investigating the driving behavior of *APOE4* carriers in preclinical stages.

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