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Which are the critical parameters assessing the driving performance of drivers with cerebral diseases? A literature review

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Abstract

The objective of this study is to examine and present the most critical parameters that can assess and predict the driving performance of individuals having some kind of cerebral disease. The cerebral diseases that have been studied are: Mild Cognitive Impairment (MCI), Alzheimer's disease (AD) and Parkinson's disease (PD). For that purpose an extended literature review was extracted in order to investigate the critical parameters which are examined in the scientific field of driving performance of drivers with brain pathologies. Methods of assessing driving, including on-road driving experiments, driving simulator experiments, neurological and neuropsychological tests etc., and related results of the literature are presented and assessed. Initially, the role of neurological and neuropsychological tests in assessing driving behaviour of patients with cerebral diseases is examined. Then, the role of on-road assessments and the role of driving simulator experiments, in evaluating the driving performance are thoroughly investigated. Twenty-eight studies examining driving parameters that could predict and assess the driving performance of patients suffering a brain pathology (MCI, AD and PD) are reviewed. All these studies concern recent research and report quantitative results. In this framework, the respective driving performance measures are recorded with the aim to investigate which ones are the most promising and in which way they are analyzed. Overall, the critical driving performance measures in which the group of patients with cerebral diseases had significant differences from the control group, were: driving errors, speed, lateral position, reaction time, accident risk, headway distance, left turns, and time to collision. However, the diversity in the measures used, in combination with the diversity in the design of the experiments (i.e. road/traffic factors examined, number/duration of trials) often complicates the synthesis of the results. In conclusion, the analysis of the driving performance of drivers with cerebral diseases may allow the identification of measures that can improve driving safety, such as restrictive measures, training and licensing, information campaigns, medical and neuropsychological monitoring.

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1. Introduction

1.1. Mild Cognitive Impairment (MCI)

Petersen et al., (1995) has described the concept of Mild Cognitive Impairment (MCI) as a cognitive state that lies between normal aging and dementia. Persons with MCI exhibit cognitive decline beyond what is expected to be normal for age, but they are overall functioning well and do not meet criteria for dementia. This condition has been studied intensively for over 30 years. The term MCI was first employed in 1988 and subsequently has been linked with a lot of possible etiologies and several terms (Reisberg et al., 2008). A typical MCI patient is one who has a memory impairment beyond what is felt to be normal for age, but is relatively intact in other cognitive domains. Accordingly, the criteria proposed for MCI by Petersen et al. (2001) refer to: a) memory complaint, corroborated by an informant, b) objective memory impairment, c) normal general cognitive function, d) normal activities of daily living, and e) absence of dementia.

Because the concept of MCI has been derived from clinical settings, MCI definitions are continually being revised. Therefore, at present we can distinguish the following clinical subtypes for the MCI concept, according to Petersen (2004): a) amnestic MCI, b) multiple domain (with a memory deficit) MCI, c) multiple domain (without a memory deficit) MCI, and d) single nonmemory domain (i.e. with executive functioning deficits) MCI. Along with multiple definitions, different etiologies have been proposed for MCI. More specifically, MCI can evolve as a result of a neurodegenerative process, such as Alzheimer's disease (AD); most of the subjects with memory loss will progress to AD at a rate of 10%-15% per year (Petersen et al., 2001). Another possible cause for the appearance of MCI is vascular dementia, secondary to small vessel disease (Petersen et al., 2001). The two MCI subtypes induced from this medical condition are the multiple domain MCI and the single domain MCI (nonmemory domain, i.e. with executive functioning deficits). Other etiologies or causes reported for the MCI condition are brain trauma and metabolic disturbance (Petersen, 2004; Winblad et al., 2004). The relationship between MCI and driving ability is not clearly established.

1.2. Alzheimer's disease (AD)

Alzheimer's disease (AD) is considered to be the most frequent type of dementia. The National Institute of Neurological and Communication Disorders and Stroke - AD and Related Disorders (1984) has outlined the criteria for the diagnosis of AD based on clinical and neurological examination. In 2011, the National Institute on Aging and the Alzheimer's Association revised the pre-existing criteria for AD dementia (McKhan et al., 2011). According to the authors, the criteria for dementia are clear impairment in daily functioning not in the context of delirium or major psychiatric disorder, which is due to cognitive or behavioral impairment on at least two areas including: episodic memory, executive functions, visuospatial abilities, language and changes in personality and behavior. AD leads progressively to a variety of symptoms, with the most commonly observed being the radial progression of episodic memory impairment. Driving capability is, on a great extent, relied on an accurate self-assessment of potential driving difficulties which would result in compensatory strategies and maintain an adequate level of safety. However, patients with AD are considered to have impaired awareness on their driving difficulties (O'Connor et al., 2013; Uc et al., 2005) and continue to drive even after having crossed the threshold of safe driving (Ernst et al. 2010).

1.3. Parkinson's disease (PD)

Parkinson's disease (PD) is a degenerative disease of central nervous system that have an impact mainly on motor function. Symptoms of PD may vary from person to person and include: tremor, slowness of movement (bradykinesia), rigidity, flexed posture, shuffling gait or postural instability, impaired posture and balance and loss of automatic movements. The main pathological finding in PD is the death of cells that secrete dopamine in the pars compacta region of the substantia nigra[†](Fritsch et al., 2012; Gazewood et al., 2013). Levodopa (L-Dopa), an amino acid precursor of dopamine, and a number of dopamine agonists, are at present the basic therapy for the motor symptoms of PD. Moreover, cognitive decline may be apparent to patients with PD. Attentional difficulties, executive dysfunction, impairment of visuospatial abilities and decline in episodic memory are considered to be the most frequently reported deficits (Dubois & Pillon, 1996; Muslimović et al., 2005). The aforementioned motor and cognitive symptoms may have an impact on driving performance in a variety of ways.

1.4. Driving performance of drivers with cerebral diseases

Driving performance can be affected by a wide variety of medical conditions, such as dementia (Ott & Daiello, 2010). MCI constitutes a medical condition that, as previously noted, mildly affects cognitive functions. In a similar manner, according to the most recent literature, MCI patients may experience an increased level of driving difficulties in comparison to their healthy counterparts without, however, being characterized as unsafe drivers (Fritteli et al., 2009; Kawano, et al., 2012; Olsen et al., 2014). So far, the literature investigating driving performance in the MCI population is relatively sparse (O' Connor et al, 2010).

Researchers suggest that individuals with AD are more than three times more likely to get involved in a car accident than age-matched drivers without primary degenerative dementia (Massie & Campbell, 1993; Tuokko et al., 1995). However, it is generally accepted that the accident probability in patients with dementia rises above acceptable rates beyond the third year of the disease (Drachman et al., 1993). Moreover, severity of cognitive and functional impairment has been correlated with worse driving performance as measured by the Clinical Dementia Rating (CDR) (see Appendix for definition) (Dubinsky et al, 2001).

In their review, Man-Son-Hing et al. (2007) indicated that, in comparison to healthy controls, AD patients have an impaired driving ability when tested with on-road driving experiments and driving simulator assessments. On the other hand, there are some studies which argue that not all patients with AD are unable to drive, especially in the earlier-mild stages of the disease (Carr et al., 2000; Perkinson et al., 2005). Due to the variance in the progression of symptoms in AD, most neurologists, neuropsychologists or transportation practitioners are faced with the critical question in everyday practice regarding the proper time for dissuading patients from driving, as ability to drive is an important factor of daily life that is of critical importance for preserving mobility, independence and self-confidence in the elderly (Gardezi et al., 2006; Johnson et al., 2013).

Several studies have investigated the driving capacity of patients with PD and have attempted to detect significant predictors, in many cases successfully, of driving competence or incompetence in the specific clinical group. Because driving is a multi-domain task that engages various aspects of cognition and motor functioning, studies investigating fitness to drive in patients with PD have used a large variety of measures for predicting driving capacity. The multimodal clinical picture of PD appears to influence in a negative fashion the performance of various activities of everyday life, including driving, as indicated by research that shows that PD patients have an increased risk to be engaged in car accidents (Uc & Rizzo, 2008; Uitti 2009). Dubinsky et al., 1991 conducted a retrospective study that included patients with PD and found PD patients to have increased accident probability, which indicates that the association between the level of motor functioning in patients with PD and car accident engagement is an area that warrants further investigation.

[†] A brain structure located in the mesencephalon (midbrain) that plays an important role in reward, addiction, and movement

2. Objectives - Methodology

The objective of this review is to identify which are the critical parameters that can assess and predict the driving performance of individuals with cerebral diseases, such as MCI, AD and PD. For the purpose of this review, the authors conducted a literature review on driving performance of persons with cerebral diseases searching: (a) PubMed, (b) Medline, (c) Cochrane, (d) Science Direct and (e) Google Scholar for relevant articles at any time. Keywords used individually or in various combinations included: "Mild cognitive impairment", "Alzheimer's disease", "Parkinson's disease", "driving", "simulator", "on-road assessment", "traffic", "car", "crash", "accident", "mobility", "behavior", "assessment", "performance", "cerebral diseases", "brain pathologies", "critical", "measures", "parameters", "neurological tests" and "neuropsychological tests". Studies which examined the relationship between cerebral diseases and driving performance, either as a main topic, or as included under the broad term of functional status, were included in this review. Reports were excluded if they were theses or non-English publications.

Initially, the role of neurological and neuropsychological tests in assessing driving behaviour of patients with cerebral diseases is analyzed. Then, the advantages and disadvantages of on-road assessments and the role of driving simulator experiments, in evaluating the driving performance are thoroughly reviewed. In sections 4, 5 and 6, twenty-eight studies examining driving parameters that could predict and assess the driving performance of MCI, AD and PD patients are analyzed. All these studies concern recent research and report quantitative results.

3. Assessing driving performance

3.1. The role of neurological measures and neuropsychological tests on the driving performance of drivers with cerebral diseases

The significance of administrating neuropsychological tests (for all tests definitions see Appendix) in order to evaluate the driving performance of those in the early stages of dementia and those who are cognitively intact concerns the international literature:

The Mini Mental State Examination (MMSE) is considered to be the most commonly used index for the evaluation of general cognitive ability and a lot of studies suggest a consistent relationship between driving performance and MMSE (Brown et al., 2004; Lesikar et al., 2002; Uc et al., 2005). Useful Field of View (UFOV) is a computerized test examining visual attention and more specifically processing speed, divided attention, and selective attention. A lot of studies examined and confirmed the predictive validity of UFOV regarding driving performance (Brown et al., 2005; De Raedt et al., 2001; Owsley et al., 1991; Paccalin et al., 2005; Uc et al., 2004; Whelihan et al, 2005). The Driving Scenes Test of the Neuropsychological Assessment Battery (Stern et al., 2003; Brown et al., 2005) was developed as a measurement of visuospatial attention skills considered to be important in driving ability. Finally, tests that appear to be efficient predictors of driving performance evaluating executive functions are: Porteus Maze Test (Grace et al., 2005; Ott et al., 2003), Trail Making Test - Trails A and B (Dawson et al., 2009; Ott et al., 2008; Paccalin et al., 2005; Reger et al., 2004; Szlyk et al., 2002) and Clock Drowning Test (De Raedt et al., 2001; Freund et al., 2002; Ott et al., 2000).

3.2. The role of on-road and driving simulator assessments

In on-road experiments studies, an instrumented vehicle is equipped with instrumentation to take recordings of a variety of aspects of driving (Rizzo et al., 2002). These technologies include GPS, video-cameras, sensors, accelerometers, computers, and radar and video lane tracking systems. On-road experiments attempt to gain greater insights into the factors that contribute to road user accident risk and the associated accidents factors at specific conditions. These investigations are conducted by trained experts from multiple disciplines to collect as much useful information as possible, to be of maximum benefit in answering current research questions and any that may arise in the future (Wadley et al., 2009; Bowers et al., 2013; Okonkwo, 2009). On road driving evaluations are generally considered to be the gold standard method for determining driving fitness (Odenheimer et al., 1994) as a large degree of control over the variables that affect driving behaviour occurs. On-road testing, also provides the

opportunity to examine driver competency, as drivers perform actual driving activities and includes aspects of driving that may not be easily replicable by other testing means (Ball & Ackerman, 2011).

Driving simulators allow the examination of a range of driving performance measures in a controlled, relatively realistic and safe driving environment. Driving simulators, however, vary substantially in their characteristics, and this can affect their realism and the validity of the results obtained. More specifically, driving simulators have a number of advantages over on-road studies: a) they provide a safe environment for the examination of various issues using multiple-vehicle scenarios, where the driver can negotiate very demanding roadway situations, b) greater experimental control can be applied in driving simulators compared with on-road studies, as they allow for the type and difficulty of driving tasks to be precisely specified and any potentially confounding variables, such as weather, to be eliminated or controlled for, and c) the cost of modifying the cockpit of a simulator to allow for the evaluation of new in-vehicle systems may be significantly less than modifying an actual vehicle. Finally, a large range of test conditions (e.g., night and day, different weather conditions, or road environments) can be implemented in the simulator with relative ease, and these conditions can include hazardous or risky driving situations that would be too difficult or dangerous to generate under real driving conditions (Papantoniou et al., 2013).

The use of driving simulators as research tools does, however, have a number of disadvantages (Blana & Golias, 1999). Firstly, data collected from a driving simulator generally include learning effects and may also include the effects of being directly monitored by the experimenter. Then, simulator sickness is another problem encountered with simulators and is particularly pronounced in older drivers (Papantoniou et al., 2013). Finally, there are certain objections regarding the validity of assessments on driving simulators and whether they objectively represent the participant's true driving abilities (Brown et al, 2004). However, Freund et al. (2002) suggest otherwise, because they found a significant correlation between on-road and driving simulator performance in healthy controls and patients with dementia, suggesting that lower driving simulator scores (with fewer errors) were strongly related to better on-road driving performance. Moreover, committing hazardous or fatal errors on the driving simulator was strongly related to failing the on-road test. The results of this research suggest that driving simulators are a valid estimator of on-road abilities.

4. Critical driving performance measures of drivers with MCI

In this chapter, eight studies that examine the driving performance of patients with MCI (4 through on-road assessment and 4 through driving simulator experiment) are presented and the critical parameters assessing the driving performance of this group of patients are extracted. In Table 1, all following studies and their basic results are presented.

Snellgrove, (2005) evaluated the driving behavior of patients with MCI through an on-road driving experiment. Results indicated that 50% of patients with MCI failed the driving test because of a series of driving errors: left and right turn errors, general driving errors and late braking related to poor planning and observation skills, difficulty to control the vehicle's speed, poor car positioning in the lane, pedal confusion and lack of defensive driving. More driving errors were made also by MCI participants in another study (Bowers et al. 2013).The authors examined the highway and non-highway driving skills of 11 patients with MCI. Results suggested that 8 MCI patients were rated as "at risk" committing driving errors such as, highway, observation, planning, speed control and indication errors.

Wadley et al. (2009) investigated the driving performance of 46 adults with MCI and 59 cognitively intact older adults using an on road driving experiment. All participants went through a neurological and neuropsychological examination and a visual screening. The on-road assessment was carried out using a standardized route with clear weather conditions, with a duration of 45 minutes, under the supervision of a certified driving rehabilitation specialist blind to the participants' group status. Participants' driving behavior was rated on a 5 point Likert scale and included several driving indexes, such as lateral position, gap judgment, turning, maintaining proper speed, stopping distance, signaling, obeying traffic signs, pre-turn and post-turn position, headway, steer steadiness, pre-crossing and post-crossing position and proper scanning of driving space. The results indicated significant differences between the MCI and the control group regarding lateral position and left-hand turns.

Frittelli et al. (2009) investigated the driving performance of 20 patients with mild AD, 20 patients with MCI and 20 controls, of similar demographic characteristics, using a driving simulator experiment[‡]. All participants were administered the Stanford Sleepiness Scale, the MMSE and a simple visual reaction time test. The driving simulation task included a two-lane urban road about 6km long with good visibility conditions, and a variety of events. Results indicated significant performance differences between AD patients, MCI participants and normal controls in mean time to collision and number of off-road events. The authors concluded that mild AD significantly affects driving behavior, whereas MCI has a limited impact on driving skills, and proposed that studies should target the investigation of accident risk.

A study that indicated no statistically significant differences between MCI drivers and healthy controls is that of Devlin et al. (2012). They investigated the brake patterns of older drivers with MCI when approaching junctions, as compared to their age-matched healthy counterparts, through a portable driving simulator. Fourteen drivers with MCI and 14 healthy controls with similar demographics and self-reported collisions experienced in the past 2 years, participated in the study. Researchers designed a brief driving scenario incorporating a number of intersections and monitored driver foot movements. All participants went through cognitive, vision and physical assessments. Screening included the administration of the MMSE, the Rapid Pace Walk test (see Appendix for definition), the Trail Making Test-part B (TMT-B), a reaction time task and a test for visual acuity. Overall, driving performance of MCI patients was worse than that of cognitively intact individuals but there was no statistically significant difference in any of the driving indexes, or in any of the neuropsychological and motor measures between the two groups.

Kawano et al. (2012) focused on identifying the specific cognitive characteristics of MCI patients that may predict safe driving performance. They designed a case control study and compared the driving performance of 12 patients with MCI, 26 elderly controls, and 19 young healthy adults using a simulated driving test. The driving evaluation task included a road tracking task, a car-following task, and a harsh braking task. The MCI group performed significantly worse than the normal older adults on the car-following task and significantly worse than the normal young adults on the car-following task and the road-tracking tasks. The authors suggested that differences in driving performance between MCI drivers and their age-matched counterparts may be due to poor flexibility and impaired visual attention, warranting the close supervision of the MCI driving population.

Griffith et al. (2013) indicated that drivers with amnestic MCI made more driving errors than cognitively intact individuals, in an on-road task. Driving variables that were examined included crossing intersections, merging, turning at junctions, exiting the interstate, changing lanes, driving on straight stretches and taking turns. The authors indicated difficulties in lateral position of patients with MCI, suggesting a link between the MCI and difficulties in positioning the vehicle in the lane.

Finally, in a study conducted by our research team (Pavlou et al., 2015a) we investigated the driving behavior of drivers with cerebral diseases through a driving simulator experiment. More specifically, the objective of this research was the analysis of the driving performance of drivers with (AD) and (MCI)[§], on the basis of a driving simulator experiment, in which healthy "control" drivers and drivers with cerebral diseases drove in different driving scenarios, following a thorough neurological and neuropsychological assessment. The driving scenarios included driving in rural and urban areas in low and high traffic volumes. The driving performance of drivers impaired by the examined pathologies (AD and MCI) was compared to that of healthy controls by means of Repeated Measures General Linear Modeling techniques. In this paper, a sample of 75 participants (38 healthy controls, 14 AD patients and 23 MCI patients was analyzed and various driving performance measures were investigated, including speed, lateral position, steering angle, headway, reaction time at unexpected events etc., some in terms of their mean values and some in both their mean values and their variability. The results suggested that patients with cerebral diseases performed significantly worse than the cognitively intact individuals, and there were common driving patterns for both cerebral diseases. More specifically, drivers with the above cerebral diseases

[‡] This study could be considered in the next section as well, because AD patients were also examined
[§] This study could be considered in the next section as well, because AD patients were also examined

had significantly lower speeds, kept larger headways compared to healthy drivers, appeared to have difficulties in positioning the vehicle on the lane, and had longer reaction times.

5. Critical driving performance measures of drivers with AD

In this chapter, thirteen studies that examine the driving performance of patients with AD (5 through on-road assessment and 8 through driving simulator experiment) are presented are presented and the critical parameters assessing the driving performance of this group of patients are extracted. In Table 1, all following studies and their basic results are presented.

Hunt et al. (1997) evaluated the reliability of a standardized road test and found that failure rate on the road test for the group of controls was 3%, for patients with very mild AD was 6 times higher, and for patients with mild AD was 14 times higher. They concluded that dementia adversely affects driving performance even in its mild stages, although some AD patients drive safely for some time after the start of the disease. A traffic-interactive, performance-based road test that examines cognitive behaviors, provides an accurate and reliable functional assessment of driving behaviour. Likewise, Fitten (1995) showed that individuals with mild AD perform significantly worse on an on-road assessment than control subjects, with the demented group driving at slower speeds and making more driving errors.

More driving errors were made also by AD participants in another study (Bieliauskas et al., 1998). They investigated the performance of 9 individuals with AD and 9 age-matched controls on neuropsychological testing on an on-the-road driving test. Patients with AD differed significantly from controls on all neuropsychological tests, measures of driving error and reaction times. Although certain general cognitive measures appeared to predict some driving errors for those with AD, neuropsychological tests showed relatively weak overall power in predicting measured driving errors, consistent with most of the literature.

Uc et al. (2004), aimed to assess navigation and safety errors during a route-following task in drivers with AD. Thirty-two subjects with probable AD of mild severity and 136 neurologically normal older adults were tested on a battery of visual and cognitive tests of abilities that are critical to safe automobile driving. Each driver also performed a route-finding task administered on the road in an instrumented vehicle. Main outcome variables were number of a) incorrect turns, b) times lost, and c) at-fault safety errors. The drivers with mild AD made significantly more incorrect turns, got lost more often, and made more at-fault safety errors than control subjects, although their basic vehicular control abilities were normal. The navigational and safety errors were predicted using scores on standardized tests sensitive to visual and cognitive decline in early AD. The authors concluded that drivers with AD made more errors than neurologically normal drivers on a route-following task that placed demands on driver memory, attention, and perception.

Ott et al. (2008) examined the driving impairment of patients with dementia, in order to focus on the driving abilities primarily impaired in this kind of cerebral disease. For that purpose, they examined 84 individuals with clinically diagnosed AD and 44 cognitively intact individuals of similar demographic characteristics. They assessed the participants over a period of 3 years during which they went through cognitive, neurologic, visual and physical evaluations, and the participants' family informants provided the experimenters with information regarding accident history and traffic violations history. All subjects also participated in an on-road driving evaluation two weeks after the medical assessment. The results indicated that, overall, individuals with AD had worse driving performance than the control group, they had more accidents and presented a more significant deterioration of their driving performance over the years. However, the level of driving impairment depends on the stage of the disease and the demographic characteristics.

Dawson et al. (2009) aimed to measure the association of cognition, visual perception, and motor function with driving safety in AD. For that purpose, 40 drivers with probable early AD and 115 elderly drivers without neurologic disease underwent a battery of cognitive, visual, and motor tests, and a driving simulator experiment. A composite cognitive score (COGSTAT) was calculated for each subject based on eight neuropsychological tests. Drivers with AD committed an average 10 more safety errors/drive compared to drivers without AD; the most common errors were lane violations.

Eby et al. (2012) compared the driving performance of drivers with mild dementia to that of healthy controls without any cerebral disorder, on an on-road experiment. The objective of this project was to use in-vehicle

technology to describe a set of driving behaviors that may be common in individuals with early stage dementia and compare these behaviors to a group of drivers without cognitive impairment. Seventeen drivers with a diagnosis of early stage dementia, who had completed a comprehensive driving assessment and were cleared to drive, participated in the study. Participants had their vehicles instrumented with a suite of sensors and a data acquisition system, and drove 1-2 months as they would under normal circumstances. Data from the early stage dementia group were compared to similar data from an existing dataset of 26 older drivers without dementia. In general, the driving performance of the two groups was not significantly different. However, the group of mild AD was found to have lower driving speed, was more unlikely to use their seat-belt and had disorientation issues. More specifically, the early stage dementia group was found to have significantly restricted driving space relative to the comparison group. At the same time, the early stage AD group drove as safely as the comparison group. Few safety-related behavioral errors were found for either group. Wayfinding problems were rare among both groups, but the early stage dementia group was significantly more likely to get lost.

Cox et al. (1998) indicated that AD patients when operating a driving simulator are more likely to have difficulty comprehending and operating the vehicle, drove outside the road lines, drove at significantly slower speed than the permitted limit, hit the brakes with little pressure when it is necessary, had difficulties with left turns and had a worse driving performance overall.

Frittelli et al. (2009) compared 20 patients with mild AD and 20 patients with MCI (as clustered by the CDR scores) with a group without any cognitive decline on a driving simulation task. Participants with mild AD had worse performance on two simulated driving indexes: a) mean time to collision and b) number of off-road events. Visual reaction times were worse in the mild AD group and had a marginal correlation with their performance on the simulator.

Rizzo et al. (2001) studied the response of 18 drivers with AD and 12 healthy controls of similar age to a vehicle incursion at an intersection in a high-fidelity simulator (Iowa Driving Simulator). The results indicated increased crashes for the AD group, inappropriate or too slow control responses, and inattention 5 sec preceding a crash event. Measures of lateral control and longitudinal vehicle control on the uneventful segments before the intersection varied within restricted ranges and did not differ significantly between the two groups. Interestingly, the authors suggest in their discussion that by manipulating task demands in a simulated environment, that is by increasing "exposure" of cognitively impaired drivers and posing sufficient challenge, it is possible to observe safety errors of different types and infer crash risk through these observations.

Uc et al. (2006) tested avoidance of rear-end collisions in 61 drivers with AD and 115 elderly controls, all holding valid driving licenses, using a high fidelity driving simulator. Indexes of driving performance used were the standard deviations of mean steering wheel position, mean speed change, mean number of large steering adjustments (>6) per minute. The response of the AD subjects in collision avoidance situations was less effective than that of the control group. Although the likelihood of rear-end collisions in AD drivers was not significantly higher, they were less quick to react and were more likely to respond in an unsafe manner, by suddenly slowing down or stopping before reaching the intersection. Drivers with AD had poorer vehicle control than cognitively intact drivers, based on significantly increased variability and a tendency for increased speed variability in baseline driving circumstances under low traffic conditions on an uneventful segment of two-lane highway. Poorer vehicle control at baseline predicted unsafe outcomes in the complex driving condition at the intersection, suggesting that basic driving performance measures in the driving simulator can predict outcomes in high risk situations.

Finally, Vaux et al. (2010) studied how the ability of participants with neurodegenerative disease (AD or PD)[**] to detect impending collisions differed from that of cognitively intact subjects of comparable age in a low-fidelity simulator (6 AD patients, 8 PD patients and 18 healthy controls). Performance on a battery of standardized neuropsychological tests suggested early cognitive decline in the AD and PD group. The dependent variables were the collision detection sensitivity, indicating the ability to detect collision, and independent variables were the number of obstacles and time to collision. The results suggest that drivers with AD and PD required additional time to detect impending collisions, which likely impairs their ability to avoid collision events measured by the current

[**] This paper could be considered in the next section as well, because PD patients were also examined

simulation task. Impairments on the collision detection tasks in the neurodegenerative disease group reflected a variety of combined disturbances of visual-sensory processing, motion processing, attention, visuospatial skills and executive functions, as implied by the association between poor collision sensitivity and poor performance on tests of cognition and visual attention.

6. Critical driving performance measures of drivers with PD

In this chapter, ten studies that examine the driving performance of patients with PD (7 through on-road assessment and 3 through driving simulator experiment) are presented are presented and the critical parameters assessing the driving performance of this group of patients are extracted. In Table 1, all following studies and their basic results are presented.

Heikkilä et al. (1998) evaluated the driving ability of 20 patients with PD and 20 age-matched and sex-matched healthy controls by a structured on-road driving test. All participants were also assessed by the test package of the Austrian Road Safety Board (see Appendix for definition). Patients with PD showed significantly worse driving performance than control subjects in all neuropsychological tests. The number of driving errors correlated with performance on tests of all the cognitive domains investigated by the test package in both groups (except for the visual memory test). Slowness of visual processing, errors in perception, and slowness in recalling visual material, explained 62% of the variance in driving errors in the group of PD.

Grace et al. (2005) evaluated 18 patients with PD and 21 healthy elderly controls with a standardized on-road driving test and a battery of neuropsychological tests that measure visuospatial skills, psychomotor speed, memory, and executive functioning. Based on their performance on the road test, the patients were classified as either safe (n=11) or unsafe drivers (n=7). Unsafe drivers with PD differed significantly from safe drivers with PD on the delayed recall condition of the Hopkins Verbal Learning Test-Revised (see Appendix for definition), on the Rey-Osterrieth Complex Figure (see Appendix for definition) (ROCF), on TMT-B. Also, the severity of the disease, as determined by the Hoehn and Yahr scale (see Appendix for definition), was significantly linked to unsafe driving in PD patients.

Uc et al., (2006) aimed to assess the ability for visual search and recognition of roadside targets and safety errors during a landmark and traffic sign identification task in drivers with PD. Seventy-nine drivers with PD and 151 neurologically normal older adults went through a battery of visual, cognitive, and motor tests. The drivers were asked to report sightings of specific landmarks and traffic signs along a four-lane commercial strip during an experimental drive in an instrumented vehicle. The PD drivers identified significantly fewer landmarks and traffic signs, and they committed more safety errors than control subjects, even after adjusting for baseline errors. The cognitive and visual deficits associated with PD resulted in impaired visual search while driving, and the increased cognitive load during this task worsened their driving safety. The strongest predictor for safety errors was the difference between the two conditions of the TMT that is considered to be a measure of executive functioning that controls for the influence of psychomotor speed and visual search.

Singh et al. (2007) aimed to explore the driving problems associated with PD and to ascertain whether any clinical features or tests predict driver safety. The driving ability of 154 individuals with PD referred to a driving assessment center was determined by a combination of clinical tests, reaction times on a test rig and an in car driving test. The majority of cases were able to continue driving although 46 individuals required an automatic transmission and 10 others needed car modifications. Ability to drive was predicted by the severity of physical disease, age, presence of other associated medical conditions, particularly dementia, duration of disease, brake reaction, time on a test rig and score on a driving test. Overall, most individuals with PD were safe to drive, although many benefited from car modifications or from using an automatic transmission.

Lee and al. (2007) explored the validity of driving simulator technology in assessing drivers with PD. Fifty PD patients and 150 healthy controls of similar demographics participated in the study. The criteria for assessing the simulator and on-road tests were combined by principal component analysis (PCA), while an overall simulated driving index and a road assessment index were developed for the PD group and the control group. The indices were significantly different in the experimental and control groups. In the simulated driving test, the drivers with PD performed significantly less safely than the controls. Participants with PD tended to drive slower in response to road

hazards, and were unable to control speed and movement of the steering wheel, to apply the brakes smoothly, to address two tasks simultaneously, and to make quick decisions and judgments.

Uc et al. (2009) studied the driving performance of 84 patients with PD and 182 elderly controls. Participants went through an on-road drive test with an instrumented vehicle and were subjected to visual, motor, and cognitive tests similar to those used in their previous studies (Uc et al., 2006a; Uc et al., 2006b). The findings indicated that in addition to age and global cognitive function, decline in visual attention (UFOV), motion perception, far visual acuity, constructional skills (CFT-copy), and visual memory (CFT-recall) predicted total driving errors. There was no significant association with motor dysfunction. However, although driving errors were more frequent in the drivers with PD, approximately 25% of them had error counts similar to the median errors of the control drivers.

Classen et al. (2011) used screening tests administered by a certified driving rehabilitation specialist and by PD specialty neurologists to develop a model to predict on-road outcomes for patients with PD. The authors administered a battery of screening tests to 41 patients with PD and 41 age-matched control participants before on-road testing. They used statistical models to predict actual on-road performance. The PD group had a higher failure rate, indicating more on-road errors. For the PD participants, the UFOV Subtest 2 and Rapid Pace Walk were responsible for most of the variance in the on-road test. The model accurately categorized pass-fail outcomes for 81% of PD patients. Clinical screening batteries may be predictive of driving performance in PD. The identification of UFOV in individuals with PD as a strong predictor of on-road driving ability indicates the central involvement of impaired visual perception and visual attention in the declined driving ability of PD patients.

Ranchet et al. (2013) aimed to determine the role of cognitive impairments in specific executive functions on driving performance of patients with PD. For this purpose, 19 patients with mild to moderate PD and 21 healthy controls matched for age, education, and driving experience were tested using a neuropsychological battery assessing global cognitive abilities, updating, flexibility, and inhibition. Participants also underwent a 45-minute road test in which they were scored by a driving instructor and a second experimenter. To separate "at-risk" drivers from safe drivers, a composite driving indicator was calculated from the Test Ride for Investigating Practical Fitness to Drive score, the penalty score from the observation grid, and the number of safety interventions made by the driving instructor. The authors found out that 8 out of 40 participants (all PD patients) were rated as “at risk”.

Finally, a study carried out by our research team (Pavlou et al., 2015b) aimed in investigating the driving performance of drivers with PD in a driving simulator experiment, in which healthy participants and PD patients drove in different driving scenarios. Sixty-two participants participated, 21 PD patients and 41 demographically matched control drivers. The driving scenarios included driving in rural area in low and high traffic volumes and driving on a motorway. The driving performance of PD was compared to that of healthy controls by means of a generalized linear model (GLM) which was developed in order to estimate the effect of the examined disease in driving behaviour. Various driving performance measures were examined, including speed, lateral position, steering angle, headway distance, reaction time at unexpected events, accident probability, some in terms of their mean values and some in both their mean values and their variability. Moreover, another factor indicating driving behaviour was examined: maneuvers through work-zone segments in motorway. The results showed that PD patients performed significantly worse than the control group. More specifically, they drove at significantly lower speeds and with larger headway compared to healthy drivers, had higher reaction times, were more likely to have an accident in the work-zone segment of the motorway, had difficulties in positioning the vehicle in the lane and had difficulties in dealing with demanding tasks, such that of maneuvering inside a work-zone segment.

7. Discussion - conclusions

The objective of this review was to identify the critical parameters that can assess and predict the driving performance of individuals with cerebral diseases. Firstly, we investigated the role of neurological and neuropsychological tests in predicting the driving performance of drivers with cerebral diseases. The literature indicated that the most useful neurological/neuropsychological tests that can predict the driving performance of drivers with brain pathologies are the following: MMSE, UFOV, Trail Making Test, NAB Driving Scenes Test, Porteus Maze Test and Clock Drowning Test. Then, the significant role and the validity of driving assessments (on-road and driving simulator experiments) in assessing the driving behaviour of drivers suffering a brain disease was highlighted.

The main part of this paper included the review of 28 studies (with average sample size: 90 participants of older age (>55 years old)), which allowed the drawing of conclusions about the driving deficits of drivers suffering from cerebral diseases, such as MCI, AD and PD, in their mild stages and the critical parameters assessing the driving performance of these group of patients were extracted.

Table 1 presents the results of the review in a summary format.

Table 1 Overview of the literature

			Diagnosis				**Sample Scheme**			**Type of assessments**				**Driving Performance Measures with Significant differences**											
	Authors	year	MCI	AD	PD	Controls	sample size	age <55	age >55	on road	driving simulator	neurological /neuropsychological examination	questionnaire	driving errors	speed (+variability)	lateral position (+variability)	reaction time	accident risk	headway	left turns	time to collision	confusion or disorientation	seat-belt use	significant differences only in neuropsychological tests	**overall worse driving performance**	
1	*Wadley et al.*	2009	●	-	-	●	105 (46+59)	-	●	●	-	●	●			●				●					●	
2	*Snellgrove*	2005	●	-	-	-	115	-	●	●	-	●	-	●	●	●									●	
3	*Griffith et al.*	2013	●	-	-	●	49 (15+34)	-	●	●	-	●	●	●		●									●	
4	*Bowers*	2013	●	-	-	-	47	-	●	●	-	●	-	●	●										●	
5	*Devlin et al.*	2012	●	-	-	●	28 (14+14)	-	●	-	●	●	●	-	-	-	-		-	-	-				-	
6	*Kawano et al.*	2012	●	-	-	●	57 (12+45)	●	●	-	●	●	●				-		●						○	
7	*Fritteli et al.*	2009	●	●	-	●	60 (20+20+20)	-	●	-	●	●	●	●			●				●				●*	*MCI: 5/8*
8	*Pavlou et al.*	2015	●	●	-	●	75 (23+14+38)	-	●	-	●	●	●		●	●	●		●						●	
9	*Hunt et al.*	1997	-	●	-	●	123 (65+58)	-	●	●	-	●	-	●											●	
10	*Fitten*	1995	-	●	-	●	69 (27+42)	●	●	●	-	●	-	●											●	
11	*Bieliauskas et al.*	1998	-	●	-	●	18 (9+9)	-	●	●	-	●	-	●			●								●	
12	*Uc et al.*	2004	-	●	-	●	168 (32+134)	-	●	-	●	●	-	●						●		●			●	
13	*Ott et al.*	2008	-	●	-	●	128 (84+44)	-	●	●	-	●	●					●							●	
14	*Dawson et al.*	2009	-	●	-	●	165 (40+115)	-	●	-	●	●	●	●											●	
15	*Eby et al.*	2012	-	●	-	●	43 (17+26)	-	●	●	-	●	●		●							●	●		-	*AD: 12/13*
16	*Cox et al.*	1998	-	●	-	●	50 (29+21)	-	●	-	●	●	●	●	●					●		●			●	
17	*Rizzo et al.*	2001	-	●	-	●	30 (18+12)	-	●	-	●	●	-				●	●							●	
18	*Uc et al.*	2006	-	●	-	●	176 (61+115)	-	●	-	●	●	-		●	●	●	●			●				●	
19	*Vaux et al.*	2010	-	●	●	●	32 (6+8+18)	-	●	-	●	●	-								●				●	
20	*Ranchet et al.*	2013	-	-	●	●	40 (19+21)	-	●	●	-	●	●		●	●		●	●						●	
21	*Heikkila et al.*	1998	-	-	●	●	40 (20+20)	-	●	●	-	●	●	●											●	
22	*Grace et al.*	2005	-	-	●	●	39 (18+21)	-	●	●	-	●	●											●	-	*PD: 8/10*
23	*Uc et al.*	2006	-	-	●	●	230 (79+151)	-	●	●	-	●	●	●										●	●	
24	*Uc et al.*	2009	-	-	●	●	168 (84+182)	-	●	●	-	●	●	●											●	
25	*Singh et al.*	2007	-	-	●	-	154	-	●	●	-	●	●				○								○	
26	*Lee et al.*	2007	-	-	●	●	200 (50+150)	-	●	●	●	●	●	●	●	●		●							●	
27	*Classen et al.*	2011	-	-	●	●	82 (41+41)	-	●	●	-	●	●	●											●	
28	*Pavlou et al.*	2015	-	-	●	●	62 (21+41)	-	●	-	●	●	●	●	●	●	●	●	●						●	
*only for the AD group		Total	8	13	10					17	12			16	9	8	6	6	4	3	3	3	1	2		

More specifically, regarding drivers with MCI, the 8 studies that were reviewed indicate that the MCI population seems to be at risk for driving difficulties, although their performance on on-road or on simulator testing is not consistently significantly worse than that of their healthy counterparts. One study showed no significant difference in driving performance of patients with MCI and healthy controls, two studies indicated worse driving performance but not at a significant level, and 5 studies resulted in significant differences in several driving performance measures between the two examined groups of drivers.

Patients with MCI show greater decline in driving frequency and greater difficulty as compared to cognitively intact persons, and are reported to show situational avoidance similar to that of people with dementia, although to a lesser degree. Given the small number of existing studies and the concomitant methodological variability, it is not

safe to draw conclusions, except for the need for systematic monitoring of the MCI population. Issues of public safety and quality of life warrant the designing of studies that explore the relationship of MCI and driving performance. A strong limitation of the review regarding the MCI group is the fact that the methodological design of the experiments show considerable variability, in terms of the driving performance measures used (i.e. speed and lateral position for the simulators, number of errors for the on-road assessments, self-reported driving frequency in the questionnaires, the duration of the assessment, the confounding factors controlled for etc.), making it difficult to compare the results. It has also been highlighted that there is notable variability in the neuropsychological tools used to complement the assessment, with unclear selection criteria for forming the batteries, making it hard to validate the association of each tool with driving ability.

In summary, the driving performance measures in which drivers with MCI have difficulties and have significant differences from demographically matched healthy controls are: driving errors, lateral position of the vehicle, reaction time, speed, headway, left turns and time to collision. A level of driving impairment is generally reported for the MCI group, which means that they still constitute a population at risk that warrants close supervision. Thus, detection of deficient MCI drivers is critical for road safety. The prediction of driving fitness seems to be possible by neuropsychological tests and neurological or psychiatric measures.

Regarding drivers with AD, the 13 studies that were reviewed indicate that the AD population is at a high risk for driving difficulties, and their driving performance on on-road or on simulator assessments is consistently worse than that of their healthy counterparts. More specifically, only one study showed no significant difference in the driving performance of patients with AD compared to healthy controls. In summary, the driving performance measures in which drivers with AD have difficulties and differ significantly from demographically matched healthy controls are: reaction time, driving errors, speed, accident probability, lateral position of the vehicle, headway, left turns, time to collision, confusion or disorientation and use of seat-belt.

Several studies clearly demonstrated driving performance decline in on-road, as well as simulation experiments in patients with AD. However, as subgroups of these patients have been found to be capable of driving, an accurate prediction of fitness to drive is crucial for patients with AD. The neuropsychological literature suggests that performance on tests measuring selective attention, visuospatial abilities, and, to a lesser extent executive functioning and memory, may predict the ability to drive safely in AD. It is worth mentioning that attention, visuospatial skills and executive functions have been noted as the most critical functions for safe driving in several studies, as they appear to affect important driving tasks, such as journey planning, finding one's way, positioning and maneuvering the vehicle, judging distances and predicting the development of driving situations, estimating risk and adapting speed, etc. The above patient groups' awareness of the effect of the disease on their driving ability may also be a key aspect of further research. It has been demonstrated that early AD patients may attempt to compensate for their reduced driving skills by limiting the number and length of their driving trips, by avoiding demanding driving situations (e.g. nighttime, adverse weather, unfamiliar road network, etc.) and by driving at reduced speeds. However, it is possible that their reduced exposure and the avoidance of certain situations may further compromise their driving performance. Moreover, the driving at reduced speed may, under certain conditions, have either a positive or a negative effect on the traffic safety of these drivers.

Concerning drivers with PD, the 10 studies that were reviewed indicate that the PD patients are at a high risk for driving difficulties, and their driving performance on on-road or on simulator assessments was consistently worse than that of cognitively intact individuals. Eight studies showed significant differences in several driving performance measures between the two examined groups. In summary, the driving performance measures in which drivers with PD have difficulties and have significant differences compared to demographically matched healthy controls are: driving errors, speed, accident probability, lateral position of the vehicle, reaction time, headway, and time to collision.

Drivers with PD are at risk of driving impairment because of deterioration of the cognitive functions associated with driving during the course of the disease. Unsafe drivers differ from safe drivers in memory, visuoconstructional, and planning measures, but not on fine motor tasks. Their driving impairment results from a combination of cognitive, visual-perceptual and motor dysfunction. As with the other disease categories, few studies have examined the effect of distraction on the driving performance of patients with PD, and the distraction task employed in one study was not ecologically valid. The stage of the disease, medication, and other disease

parameters need to be carefully documented in order to draw conclusions about the parameters of the disease that are associated with driving impairment.

Generally, the use of multiple measures that assess various domains should be the choice of preference in research projects that investigate the driving capacity of PD patients, because it permits the extraction of the unique effect of each predictor as well as the estimation of its relative importance. Also, the disease stage of the PD patients should be defined together with the enclosure of sufficient information about the medication regime and medication status during the driving process and the neurological/neuropsychological assessment. Based on the findings of the previous studies it appears that various measures could be helpful in detecting individuals with PD that have impaired driving skills. However, neurological and neuropsychological testing should be viewed as one part of the screening process that could help the evaluation of the driving capacity of patients with PD and should not be used alone, because this could lead to imprecise and dangerous consequences. Future studies that take into account the above recommendations can further our knowledge about the driving capacity of patients with PD under classical driving conditions as well as under driving conditions with distraction.

Overall, after examining the 28 studies, the critical driving performance measures in which the group of patients with cerebral diseases had significant differences with the control group, which indicate driving deficits, were: driving errors in 16 studies, speed (or its variability) in 9 studies, lateral position (or its variability) in 8 studies, reaction time in 6 studies, accident risk in 6 studies, headway in 4 studies, left turns in 3 studies, time to collision in 3 studies, confusion or disorientation in 3 studies, seat-belt use in 1 study. It is important to mention that not all driving performance measures presented above were examined in all 31 studies.

Driving simulators can be used in order to further test the driving abilities of the patient groups in different driving conditions, compared with age- and driving experience-matched controls. Results from experiments using driving simulators indicate that different driving tasks involve different driving abilities and cognitive constructs. Driving simulators are ideally suited for testing the effects of distraction in the above groups, which has not been done in the literature.

After evaluating the results that were extracted from the present paper, some restrictive countermeasures regarding driving behaviour of drivers with cerebral diseases in mild stages could be proposed:

(a) Assessment of critical driving indexes (driving errors, left turns, time to collision, confusion or disorientation, seat-belt use, reaction time, accident probability, driving speed, lateral position variation, headway distance, steering angle) with the use of a driving simulator, after the initial diagnosis of the cerebral disease.

(b) On-road assessment evaluating the driving performance of the drivers with cerebral diseases on a regular basis (that may not exceed the period of one year).

(c) Application of a driving related neurological/neuropsychological assessment that assesses the following domains: general cognitive state and dementia severity, functionality assessment, sleeping abnormalities, motor fitness, along with tests that evaluate psychomotor speed, visual attention, executive functions, and visuospatial working memory.

The aforementioned neurological/neuropsychological measures could be helpful in detecting individuals with questionable or problematic driving ability. Nonetheless, neurological and neuropsychological testing should be viewed as one part of the screening process that is accompanied when necessary by on-road or simulated driving evaluation. Finally, when the stage of the cerebral disease is going deeper and their driving ability is assessed as poor and deteriorated, people with a cognitive disability could be pushed to alternative forms of mobility by their relatives or by their therapist.

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More information available at: http://www.nrso.ntua.gr/driverbrain and at: http://www.nrso.ntua.gr/distract.

Appendix

The definition - brief explanation of the neurological and neuropsychological terminology of this paper is the following:

- Clinical Dementia Rating (CDR): a numeric scale used to quantify the severity of symptoms of dementia.
- Trail Making Test (TMT): has two subtasks, Part A (TMT-A) and Part B (TMT-B) (Reitan, 1979). Each subtask is shown on a white paper (A4 dimensions) and the participants are asked to connect randomly located circles, as fast as possible. Part A includes circles with numbers only (1-25) that have to be connected in numerical order, while Part B includes circles with both numbers (1-13) and letters (A-M) that have to be connected alternately. Abilities, such as visual search, motor speed, and spatial skills are examined in both parts of the test. In addition, part B is considered to assess aspects of executive control, such as mental flexibility and task shifting (Strauss et al., 2006)
- Mini Mental State Examination (MMSE): a test of general cognitive functioning (Folstein, & McHugh, 1975). Components that are assessed are: a) attention, b) time and space orientation, c) memory, d) language, and e) visuospatial skills
- Porteus Maze Test: a psychological test, designed to measure psychological planning capacity and foresight in children, adolescents, and adults
- Clock Drowning Test: used for screening for cognitive impairment and dementia and as a measure of spatial dysfunction and neglect
- Stanford Sleepiness Scale: the most commonly used subjective measure of alertness
- Rapid Pace Walk test: a measure of lower limb mobility
- Digit Span test: a test which exercises the verbal working memory
- Clock Drawing Test: a test used for screening for cognitive impairment and dementia and as a measure of spatial dysfunction and neglect
- Austrian Road Safety Board: comprises sections of visual short term memory, perceptual flexibility and decision making, continuous vigilance, complex choice reaction time, and information processing capacity
- Hopkins Verbal Learning Test-Revised: a brief verbal learning and memory instrument (Benedict et al., 1998). It consists of a 12-item word list presented in three consecutive trials. Also, the test includes a delayed free recall and a recognition trial.
- Rey-Osterrieth Complex Figure: a neuropsychological assessment in which examinees are asked to reproduce a complicated line drawing, first by copying it freehand (recognition), and then drawing from memory (recall)
- Hoehn and Yahr scale: a commonly used system for describing how the symptoms of Parkinson's disease progress

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