Exploring the Association between Working Memory and Driving Performance in Parkinson's disease

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Abstract

Objective: The aim of this studywas to explore whether varying levels of operational and tactical driving task demand differentially affect drivers with Parkinson's disease (PD) and control drivers in their sign recall. *Methods*: Study participants aged between 50 and 70 years included a group of drivers with PD (n = 10) and a group of age- and sex-matched control drivers(n = 10). Their performance in a sign recall task was measured using a driving simulator. *Results*: Drivers of the control group performed better than drivers with PD in a sign recall task, but this trend was not statistically significant (p = 0.43). Also, regardless of group membership, subjects' performance differed according to varying levels of task demand. Performance in the sign recall task was more likely to drop with increasing task demand (p = 0.03). This difference was significant when the variation in task demand was associated with a cognitive task, i.e., when drivers were required to apply the instructions from working memory. *Conclusions*: Although the conclusions drawn from this study are tentative, the evidence presented here is encouraging with regard to the use of a driving simulator to examine isolated cognitive functions underlying driving performance in PD. With an understanding of its limitations, such driving simulation in combination with functional assessment batteries measuring physical, visual and cognitive abilities could comprise one component of a multi-tiered system to evaluate medical fitness to drive.

Keywords: driving simulator; Parkinson's disease, working memory, sign recall, fitness to drive

INTRODUCTION

The ability to drive can be affected by various motor, visual, cognitive and perceptual deficits related to normal ageing or caused by age-related neurological disorders such as Alzheimer's disease (AD),Parkinson's disease(PD), or stroke (Akinwuntan, 2012). Most countries in the industrialized world have therefore established legislative criteria and procedures to determine fitness to drive in these at-risk populations since age and medical diagnosis alone are poor predictors of driver safety and crash incidence (Staplin, 2012; Uc and Rizzo, 2011; Staplin et al., 2003).

The evaluation of fitness to drive in individuals with PD is of particular interest due to the heterogeneity of motor and non-motor visual and cognitive symptoms that may adversely affect safe driving. Drivers with PD suffer from physical symptoms such as reduced speed of movement, slower reaction times, and a diminished ability to turn their head to check mirrors. The majority of drivers with PD are aware of their physical limitations and will self-regulate their driving behaviors as the disease further progresses (Davies et al. 2011); Crizzle et al (2013) found that PD drivers who perceive their health more poorly have greater symptomatology (UPDRS motor scores, contrast sensitivity, depression, brake response time) and had more restricted driving patterns. However, many patients with PD, even in the early stages of the disease, have cognitive impairments that compromise their driving performance (Uc and Rizzo, 2011; Davies et al. 2011). Importantly, people with cognitive impairment may lack awareness of their dysfunctions and, consequently, may not self-regulate to compensate their functional deficits (Davies et al., 2011). In an evidence-based review of studies on driving performance, Crizzle et al. (2012) propose a framework of risk factors to help clinicians determine when drivers with PD are at risk of failing a driving evaluation. These authors found that cognitive deficits, rather than motor and visual deficits, are the main risk factors of impaired on-road driving. Although on-road tests are acclaimed to be the gold standard of fitness to drive, they can be very risky, expensive, and lack the opportunity to offer standardized traffic situations needed to evaluate isolated driving skills such as risk avoidance, hazard perception, and vigilance (Ball and Ackerman, 2011; Mullen et al., 2008).

Driving simulators have the unique capability of interactively engaging the visual, motor, and cognitive skills needed for driving in an immersive setting without jeopardizing the safety of the driver. Driving simulators vary in their characteristics, i.e. motion base vs. fixed base, interactivity, resolution and field of view, which makesthe exact replication of reality impossible (Uc and Rizzo, 2011, Rizzo 2011; Staplin 2010; Vardaki, Yannis et al. 2013). Yet, they have enabled a better understanding of driving errors and their relationships with the type and degree of a driver's functional impairments, allowing researchers to distinguish between controls and people with PD (Uc and Rizzo, 2011). Simulator studies have shown that drivers with PD exhibit substantial difficulties while driving under low visibility conditions, which is likely the result of deficits in contrast sensitivity (Uc et al., 2009, Crizzle et al. 2012). In a validation study (Devos et al. 2013a; Devos et al. 2007) of a screening battery to predict fitness to drive decisions in individuals with PD, the inclusion of driving simulation increased the accuracy of the clinical model, suggesting an association between driving simulation measures and real-world driving performance in PD.

Lee et al. (2007) explored the validity of an interactive PC-based STISIM driving simulator against on-road driving in 50 PD patients and 150 healthy controls of comparable age (aged between 60 and 80). The critical item scores on

the simulator and road tests were identified via principal component analysis to create an overall Simulated Driving Index and a Road Assessment Index. Drivers with PD performed less safely than controls both in the simulator and road tests. Forty percent of the variability in the Road Assessment Index of drivers with PD could be explained by the Simulator Driving Index, after adjusting for age, gender and average miles per year. The corresponding percentage of the control group was 68 percent. These findings suggest that driving simulators can provide valuable information on driving ability in PD and can be developed into a cost-effective screening tool.

Another advantage of driving simulators is that the complex activity of driving can be deconstructed into isolated cognitive skills necessary for safe driving. One of the key cognitive functions for safe driving is working memory. Working memory allows a driver to remember—and apply when needed—navigational directions and rules for traffic operations, even asthe driver is processing and responding to the real-time demands of steering, anticipating and avoiding conflicts, and performing other moment-to-moment vehicle control tasks (Staplin, 2012; Staplin et al., 2003). Executive functions including decision-making, impulse control, judgment, task switching and planning, strongly interact with working memory (Rizzo, 2011). The ability to recall directions and information from signs and other traffic control devices is an important element in avoiding the confusion that can lead to accidents. Drivers with working memory problems were more likely to get lost in trafficand respond inappropriately to unusual or unexpected traffic situations (Ball et al., 2006; Staplin et al., 2003). Moreover, working memory was found to be associated with crash occurrence in a sample of older drivers (Lee et al. 2003). Performance in driving tasks involving working memory was measured with a recall task. According to the results of a logistic regression analysis, after adjusting for age, each added point on recall task was associated with a 45% decrease in risk of a crash (Lee et al., 2003).

Several studies have investigated the impact of isolated executive impairments on driving performance in PD. Devos et al. (2013b) found that driving skills that lead to failure on a road test are lateral position on the road at low speed, speed adaptations at high speed, and left turn maneuvers. Independently of age and gender, motor subtype, motor symptom severity, binocular acuity, executive dysfunction, divided attention, and visual scanning predicted failure on a road test in PD and poor performance on these critical road skill items. Ranchet et al. (2011b) found that when compared to controls, drivers with mild to moderate PD exhibited significant impairments with updating of information, as indicated by worse performance in the n-back test and a simulated test of sign recall (Ranchet et al, 2011b). Preliminary results of a two-year follow-up showed statistically significant changes over time in the n-back updating task, but only for controls. This result suggests a decline in updating ability as a result of normal ageing. In the updating task on the simulator, there were no changes over time in either group (Ranchet et al, 2011a). In a later study (Ranchet et al., 2013), two cognitive tests measuring updating (the n-back task) and mental flexibility (the plus-minus task) were found to predict driving safety even after adjustment for group membership, i.e. patients with PD and healthy controls, explaining 53% of the total variance. These tests discriminated between safe and "at-risk" drivers scored during an on-road test. Davies et al. (2011) found that drivers with PD exhibited poorer decision making skills in baseline simulated driving scenarios as well as while driving under time pressure. Notably PD drivers were not found to be dangerous or unsafe drivers (Davies et al. 2011).

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The association of PD with working memory impairments has been supported by numerous studies (e.g. Channon, 1997) that used cognitive tasks developed to examine capacities related to working memory, e.g recall precision (Zokaei et al., 2014) or inhibition tasks (Kensinger et al., 2003).However, the relationship between working memory and driving in PD has been poorly investigated. In a pilot study using a fixed-base driving simulator, Vardaki, et al.(2014) found that a group of medically at-risk subjects with mild cognitive impairment (MCI) or PD performed worse in a sign recall task than controls; and that a longer versus shorter delay before message recall had no significant effect on either group. Increasing the level of driving task demand between message presentation and recall (while holding delay roughly equal) had an inverse impact on recall performance across both PD and MCI drivers. However, in the study, the MCI and PD were, on average, over a decade older than the controls. The present investigation builds upon the tentative conclusions from this pilot study, using an improved experimental methodology (i.e. by controlling the time the drivers are exposed to the message) to examine how varying levels of operational and tactical driving task demands might differentially affect message recall for older drivers with PD versus a group of comparably aged control drivers with no medical condition.

METHODS

Participants

This driving simulation study was conducted at the Department of Transportation Planning and Engineering of the School of Civil Engineering at the National Technical University of Athens (NTUA) in Athens, Greece. This study was part of a larger driving simulator experiment described in Yannis et al. (2013), from which current participants were drawn. All participants in this research held a valid driving license, and had to meet certain inclusions criteria: (1) more than three years of driving experience; (2) driving at least 2500km during the last year; (3) driving at least once a week during the last year; (4) driving at least 10km/week during the last year; and (5) a Clinical Dementia Rating (CDR) score <1. Exclusion criteria were (1) history of psychiatric conditions;(2) kinetic disorders that prevents them from basic driving movements; (3) dizziness or nausea while driving, either as a driver or as a passenger, (according to self-reports);(4) pregnancy; (5) history of alcohol or drug abuse; (6) eye disorder that prevents them from driving safely; and (7) any disease of the central nervous system, other than the ones that are investigated in thedriving simulator experiment.

The PD subjects were recruited from the Movement Disorder Clinic at the Attikon University General Hospital. Two groups of drivers participated in the present study, a group of drivers diagnosed with idiopathic Parkinson's disease (PD) and a group of controls. The PD group included 10 male subjects with a mean age of 62.2 years (s.d.=8.4). The control group consisted of 10 subjects (7 men), who were free of any medical condition that may impact safe driving, with a mean age of 57.6 years (s.d.=5.1).

All subjects completed a series of neuropsychological tests at the ATTIKON University General Hospital. At a later date (within a period ranging from one week to 10 days) they participated in the driving simulation experiment. The drivers with PD were tested during periods of optimal symptom control ("on"-medication).

Procedure

Neuropsychological tests: We used the following tests: Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) to test general cognitive functioning; Frontal Assessment Battery (FAB; Dubois, Slachevsky, Litvan, &Pillon 2000) as an indicator of the presence and severity of executive dysfunction; Letter Number Sequencing (LNS; Wechsler, 1997a) to test working memory (executive component); Spatial Span Task (Wechsler, 1997b) as a measure of visuospatial working memory; Symbol Digit Modalities Test (Smith, 1991) as a measure speed of information processing; Useful Field of View (UFOV; Ball & Owsley, 1993) that includes three subtests of speed of information processing, divided attention, and selective attention; Hopkins Verbal Learning Test-Revised (HVLT-R; Benedict, Schretlen, Groninger, & Brandt, 1998) to test verbal learning and memory; Spatial Addition Test (Wechsler, 2009) to measure visuospatial working memory. Trail Making Tests (TMT; Reitan, 1979 Part A (TMT-A) and Part B (TMT-B) to measure visuomotor tracking and aspects of executive control, such as mental flexibility and task shifting (Strauss et al., 2006); and finally the Driving Scenes Test-Neuropsychological Assessment Battery (NAB; White & Stern, 2003) to measure working memory, visual scanning, attention to detail, and selective attention.

Driving simulator experiment: The driving simulation was conducted using a FOERST Driving Simulator FPF, manufactured by the FOERST company (Figure A1). The driving simulator consists of a mock-up car, fixed support base and 3 LCD wide 40"screens which provided a 170 degree field of view. Drivers viewed the LCD displays from a distance of 125 cm. Display resolution for the LCD screens was full HD (1920x1080pixels). The full dimensions are 230x180cm, with a base width of 78cm. The driving simulator features an adjustable driver seat, steering wheel of 27 cm diameter, pedals (throttle, brake, clutch), dashboard and two side view mirrors and one rear view mirror. Performance data were extracted directly from the simulator at 30 Hz.

Experimenters were blind to the results of the neuropsychological tests. All subjects gained a degree of familiarity with the simulator through participation in a prior experiment that lasted approximately 45 minutes and involved simulated scenarios of urban and rural driving (Yannis et al, 2013). Subjects were allowed a rest period of at least 15 minutes between their experience in the prior experiment and their participation in the present study. This prior experience allowed participants to practice all their driving skills (distance judgment, pedal and steering control) and also served as a screen for susceptibility to simulator adaptation syndrome (SAS) for the study sample. According to the experiment protocol, any subject who reported any of the symptoms of SAS would be disqualified from participation in the study. None were so affected.

The study aim noted above was addressed in an experiment completed in a single laboratory session. The experiment included three conditions, TC1 and TC2 and TC3, and used repeated measures for the PD and control subjects during simulator drives of approximately two minutes duration. The experiment measured the effect of different levels of intervening driving task demands on the recall of the sign information by the PD and control subjects, while the amount of time between the presentation and recall of the safety message was roughly equivalent across conditions.

In order to have precise control over the time the message was displayed to the subjects, before each of the three drives in the simulator a safety message on a sign was presented for a fixed interval (~8 sec) on the screen that was constant across study participants (Campbell et al., 2012).

Before each of the three drives in the simulator, subjects were instructed to respond to traffic control information and always maintain safe gaps with other vehicles just as they would when actually driving. They were also instructed to maintain a constant speed at the posted speed limit unless they encountered the road section where barriers were present. Specifically, they were told to try to "maintain a constant speed at the maximum posted speed limit for the roadway throughout the entire drive, unless you encounter road conditions where you must reduce speed to avoid hazards. In this situation, drive at what you feel is the maximum safe speed." They were also told by the experimenter, "If a vehicle ahead of your vehicle apply its brakes immediately after changing lanes, you should follow it and change lanes, too. If not, stay in your own lane. This rule applies throughout the entire drive." The last instruction was: "Finally, I am going to show you a picture of a highway message sign now. Please read it aloud. I will ask you to recall this information at the end of your drive. As soon as you read the message to me, your drive will begin".

Alternate messages were constructed for use in each test condition, each with three items of information, indicating the *type of situation ahead*, *distance* and a *driver action* that is required (Campbell et al., 2012) using standard wording (HMTI, 2010). (The information items conveyed in the example in Figure A2 indicate a *Border crossing*, 6 *km*, where the driver must *stop for inspection*; the other messages presented were: *Tunnel*, 5 *km*, *reduce speed* and *Ice on the road*, 4 *km*, use chains).

All driving scenarios involved driving along straight sections and gentle curves on a limited access, divided roadway. Scenarios avoided sharp curves or frequent stops (Trick et al. 2011) to reduce the likelihood of SAS. Across all test conditions, the driving scenario began with a period of low-demand driving, requiring minimal steering input and with the only other traffic being two vehicles ahead with the lead vehicle in a safe distance ahead of the driver. A speed limit sign of 60km/h was posted very early in the drive and remained throughout TC1, where the driver experienced only a low level of demand for intervening, operational-level driving tasks. In test conditions TC2 and TC3, however, after the initial period of low-demand driving, the level of demand was varied by imposing different types of operational and tactical driving tasks on subjects. In TC2, subjects were required to make a double lane change that involved driving through a road work section, containing large blocks (barriers) on each side of the road, causing the road to progressively narrow (1:20 taper ratio; lane width 3m). The posted speed limit changed at the beginning of the work area to 50km/h and changed again to 60km/h at the end of the work area. In TC3, drivers met the same steering requirements as in TC2, but the demand on working memory was different from the other test conditions, i.e., after the forced lane changes along the road works section, they were required to execute an additional lane change in response to a discriminative stimulus which was the activation of the brake lights on a lead vehicle. This decision rule was included in the pre-drive instructions. The research design required subjects to remember and apply rules for car following and lane changes throughout the drives. Lane changes of lead vehicles

without brake light activation were also present in all three test conditions. The presentation order of conditions was randomized.

Immediately after the end of each drive (after 100sec), subjects were asked to recall the safety message presented on the corresponding sign. The experimenter then assigned a score 0-3, indicating that none, 1, 2 or all 3 information units were recalled. With the exception of the distance unit, the accuracy of recall was assessed on the basis of the meaning of the message information, rather than the exact wording.

RESULTS

Analysis of the Demographic Variables

PD and control subjects were compared on various demographics using the Wilcoxon Rank Sum Test. The groups were not significantly different in terms of age (p=0.247) and gender (p=0.280) at the 0.05 level. No differences were found in terms of driving experience, frequency of driving (number of days they drive per week), years of education, CDR, and number of (self-reported)motor vehicle accidents within the last two years (Table1).Significant differences were found in the number of kilometers driven per week (p=0.035) and in the total number of self-reported accidents (p=0.029) (Table 1). None of the drivers in both groups reported an accident within the last two years. CDR scores indicated no dementia (CDR=0) for the control group subjects and for nine subjects in the PD group; one PD driver had CDR score =0.5, indicating very mild dementia. Drivers reported the number of kilometers driven per week using a five point scale (Table 1). The drivers with PD had mild to moderate disease severity, as indicated by their Unified Parkinson's Disease Rating (UPDRS) score and the Hoehn&Yahr (H&Y) stage (Table 1).UPDRS and H&Y were administered in 'on' phase by a neurologist.

Neuropsychological test

In Table 2 the between-group comparisons in performance measures in neuropsychological tests are presented. Significantly worse performance was found in the PD group in measures assessing executive functioning(FAB), recall of verbal material(HVLT-Total), visuospatial working memory(Spatial Addition), information processing speed(SDMT), and selective attention(UFOV part 3). Hence, the overall pattern of performance indicates that the group of patients with PD as compared to the control group had more difficulties on neuropsychological tests engaging in episodic memory operations as well as in executive, attentional and working memory resources.

Speed Choice

For the present analysis, data were analyzed from participants that had performed the cognitive task in TC3 according to the instructions, executing a lane change in response to the discriminative stimulus. As a manipulation check, to confirm that the demand of the driving task varied across test conditions as revealed through drivers 'speed reductions to negotiate the road works section, a two-way mixed ANOVA (using SPSS) tested for main effects of medical status (PD), a between-subjects variable, and the level of demand for intervening driving tasks, a within-subjects variable, on drivers' speed; and also for a possible two-way interaction between these variables.

Table 3 provides descriptive statistics for the two levels of each independent variable. For the total group (n = 20), the mean speed mean in Level 1 of intervening task was higher than the mean speed in Levels 2 and 3. In addition, the mean speed of the PD group was lower than the mean speed of the control group across all levels of task demand.

The ANOVA results indicated a significant effect of group membership on speed (F (1, 18)=9.07, p=0.008). Analysis of the main effect of level of intervening task demand on speed violated the assumption of sphericity. Using Greenhouse-Geisser corrected degrees of freedom the corresponding F was significant, i.e., the differences in speed associated with the level of intervening task demand were significantly different (F (1.32, 36)=57.22, p<0.001). In other words, regardless of group membership, subjects reduced speed across driving test conditions. Bonferroni corrected post hoc test showed that the mean speed in level 1 was significantly higher than in both levels 2 and level 3 (both p<0.001). Speeds at level 3 were not significantly different than speeds at level 2 (p>0.05). These results suggest that only the change in demand at the operational level had an impact on speed choice.

The interaction graph (Figure 1) illustrates these differences as well as the nature of the interaction between group membership (medical status) and intervening task demand which is not statistically significant (F (1.32, 36)=1.42, p>0.05). The "whiskers" (bars) denote one standard error around the mean of speeds for each group with varying levels of task demand.

Recall Scores

Table 4 provides descriptive analyses of the sign message recall data. The PD group performed more poorly in the sign recall task, demonstrating higher percentages of low recall scores (0 and 1) than the control group.

A General Estimating Equation (GEE) model was specified to examine the relationship between participant group and performance in the sign recall task, adjusting for potential intercorrelations among sign recall task for each participant at the three test conditions. The number of clusters -the sample size- is small (below 40) for the GEE model (Teerenstra et al., 2010). An independent working correlation structure (which is simple analytically) was used to analyse the data set, i.e., assuming that within cluster observations are independent. Convergence was achieved. The ordinal logistic GEE (cumulative logit link function) showed that controls were more likely to perform better than PD drivers in the sign recall task; this trend however was not statistically significant (B(SE)=.53(.68), Exp(B)=1.70, 95% CI=0.45 - 6.41, p>0.05) (Table 5). This analysis revealed that, regardless of group membership, subjects performed better in the recall of safety information in TC1 versus TC3 (B(SE)=.72(.48), Exp(B)=2.05, 95% CI=0.79 - 5.29, p>0.05) (Table 5), although this difference was not significant. Performance in the sign recall task was more likely to be higher in TC2 (lower level of driving task demand) than TC3 (higher level of driving task demand) and this difference was statistically significant (B(SE)=.89(.42), Exp(B)=2.44, CI=1.07- 5.60, p<0.05). While age was not included in the final model specification, it was considered during the model building process, but not retained as it was not significant in any reasonable significance level.

CONCLUSIONS AND DISCUSSION

The goals of this exploratory study were to determine whether varying levels of operational and tactical driving task demands would differentially affect highway sign message recall between drivers with Parkinson's disease (PD) and control drivers with no medical condition. An experiment was carried out using a fixed-base driving simulator, in a single laboratory session. Both groups of study participants were "young-old" drivers (Knoblauch et al. 1997)of similar age (between 50 and 70 years). The two groups of participants were matched in terms of individual

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characteristics associated with driving competence such as age, driving experience and driving exposure. They were also matched in terms of (self-reported) number of accidents within the last two years. Results showed that performance in the sign recall task was more likely to drop with increasing task demand; this difference was statistically significant, when the variation in task demand was associated with a cognitive task, i.e., when drivers were required to apply the instructions from working memory (to change lane in response to discriminative stimulus). The application of neuropsychological tests focusing on various domains of cognition showed that the drivers with PD had difficulties on recalling verbal material as well as on performing executive, attentional and working memory operations.

The results of our study suggest that when new information is presented (e.g., on a variable message sign or in-car visual display) that must be retained in working memory and applied after some period of driving, performance of older drivers will worsen as driving task demand increases. The results also showed that controls were more likely to perform better than PD drivers in the sign recall task, however, the absence of statistical difference in performance between groups might be explained by the small sample (limited power). Also, this analysis revealed no statistically different performance in recall between TC1 (Demand Level 1) and TC3 (Demand Level 3); while subjects performed better in TC2 (Demand Level 2) than in TC3. There are at least two possibilities for this result: It would be hypothesized that the highest recall would occur when the demands on working memory are lowest, i.e., in TC1. TC1 generally showed this effect, but not at a statistically significant level. This may simply reflect another limitation of the small sample size. Another possibility is that there was not a sufficient increment in the working memory demands of TC2 versus TC1; only in TC3 did subjects have to apply the instructions concerning the discriminative stimulus, and this is where recall scores were consistently the lowest.

Our results are in line with the results of Ranchet et al.(2011b) who found that drivers with PD when compared to controls performed worse in the n-back test and a simulated test of sign recall. Furthermore, studies have shown that measures of specific executive functions should be included in assessment batteries evaluating drivers with PD (Ranchet et al., 2013). Our combined findings, although preliminary, suggest that updating and mental flexibility are critical for safe driving in PD.

Although analysis revealed significant differences in measures in neuropsychological tests between the control and PD groups, we did not find between-groups differences in sign recall. It may be probable that the small size of our sample did not allow us to observe meaningful performance differences related to PD. In effect the conclusions that can be drawn from this study are tentative; studies with larger sample sizes are needed to confirm our pilot findings. Referring to other limitations of the study we note that the study was limited in power to analyze individual characteristics such as driving experience, motor severity, or cognitive status, with performance on the simulated tasks. Finally, it must be acknowledged that, when using a simulator to assess driving skills in older adults, their performance is more likely (than younger drivers) to be affected by simulator sickness, even if they do not demonstrate overt symptoms (Brooks et al., 2010). In our study none of the participants reported any of the symptoms of SAS.

Further analysis may allow us to identify performance differences associated with PD. Notwithstanding the above mentioned concerns, the evidence presented here is encouraging with regard to the potential use of a (fixed-base) driving simulator that can reliably discriminate (older) individuals with medical conditions that often cause loss of functions needed to drive safely from healthy drivers in the same age cohort. With an understanding of its limitations, such driving simulation in combination with measures of physical, visual and cognitive abilities shown to be significant predictors of older driver crash risk could comprise one component of a multi-tiered system to evaluate medical fitness to drive.

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REFERENCES

- Akinwuntan AE, Wachtel J, Rosen PN. Driving simulation for evaluation and rehabilitation of driving after stroke. Journal of Stroke and Cerebrovascular Diseases. 2011;21(6):478-486.
- Ball K, Owsley C. The useful field of view test: a new technique for evaluating age-related declines in visual function. Journal of the American Optometric Association. 1993;64:71-79.
- Ball KK, Roenker DL, Wadley VG, Edwards JD, Roth DL, McGwinJrG, Raleigh R, Joyce JJ, Cissell GM, Dube T. Can High-Risk Older Drivers Be Identified Through Performance-Based Measures in a Department of Motor Vehicles Setting? Journal of the American Geriatric Society. 2006; 54(1):77-84.
- Benedict RHB, Schretlen D, Groninger L, Brandt J. Hopkins Verbal Leaning Test-Revised: Normative data and analysis of inter-form and test-retest reliability. The Clinical Neuropsychologist. 1998;12(1):43–55.
- Brooks JO, Goodenough RR, Crisler MC, Klein ND, Alley RL, Koon BL, Logan WC, Ogle JH, Tyrrell RA, Wills RF. Simulator sickness during driving simulation studies. Accident Analysis & Prevention. 2010;42(3):788-796.
- Campbell JL, Lichty MG, Brown JL, Richard CM, Graving JS, Graham J, O' Laughlin M, Torbic D, Harwood D. Human Factors Guidelines for Road Systems. Washington D.C: Transportation Research Board of the National Academies; 2012. NCHRP Report 600 (Second Edition).
- Channon S. Impairments in deductive reasoning and working memory in Parkinson's disease. Behavioural Neurology. 1997;10:1-8
- Crizzle AM, Classen S, Uc EY. Parkinson disease and driving. An evidence-based review. Neurology. 2012;79:2067–2074.

- Crizzle AM, Myers AM, Roy EA, Almeida QJ. Drivers with Parkinson's disease: are the symptoms of PD associated with restricted driving practices? J Neurol. 2013 Oct;260(10):2562-8. doi: 10.1007/s00415-013-7017-9. Epub 2013 Jul 3.
- Davies J, Lee H, FalkmerT. An Investigation into the Impact of Parkinson's Disease upon Decision Making Ability and Driving Performance, Diagnostics and Rehabilitation of Parkinson's Disease, Dr. Juliana Dushanova (Ed.); (2011), ISBN: 978-953-307-791-8, InTech, DOI: 10.5772/20188. Available from: http://www.intechopen.com/books/diagnostics-and-rehabilitation-of-parkinson-s-disease/an-investigation-into-the-impact-of-parkinson-s-disease-upon-decision-making-ability-and-driving-per
- Devos H, Vandenberghe W, Nieuwboer A, Tant M, Baten G, De Weerdt W. Predictor of fitness to drive in people with Parkinson's disease. Neurology. 2007;69:1434-1441.
- Devos H, Vandenberghe W, Nieuwboer A, Tant M, De Weerdt W, Dawson JD, Uc EY. Validation of a Screening Battery to Predict Driving Fitness in People With Parkinson's Disease. Movement Disorders. 2013(a);28(5):671-674.
- Devos H, Vandenberghe W, Tant M, Akinwuntan AE, De Weerdt W, Nieuwboer A, Uc EY. Driving and off-road impairments underlying failure on road testing in Parkinson's disease. MovDisord. 2013(b);28(14):1949-56.

- Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research. 1975;12:189–98.
- Hakamies-Blomqvist L, Peters B. Recent European research on older drivers. Accident Analysis & Prevention. 2000;32:601-607.
- Hellenic Ministry of Transport and Infrastructure (HMTI), Freeway Signing Guidelines., Athens 2010.
- Kensinger E, Shearer DK, Locascio JJ, Growdon JH, Corkin S. Working memory in mild Alzheimer's disease and early Parkinson's disease. Neuropsychology. 2003;17(2):230-239. Available at: <u>http://dx.doi.org/10.1037/0894-4105.17.2.23</u>
- Mullen NW, Chattha HK, Weaver B, Bedard M. Older driver performance on a simulator: associations between simulated tasks and cognition. Advances in Transportation Studies. 2008;Spec. Iss:31-42.
- Ranchet M, Broussolle E, Poisson A, Paire-Ficout L. Relationships between cognitive functions and driving behavior in Parkinson's disease. European Neurology. 2012;68(2):98-107. DOI:10.1159/000338264
- Ranchet M, Paire-Ficout L, Broussolle E. Longitudinal two-year follow-up of updating and flexibility functions in drivers with Parkinson's Disease: preliminary results. Proceedings of the Sixth International Driving Symposium on Human Factors in Driver Assessment, Training and Vehicle Design, in Olympic Valley - Lake Tahoe, California, USA, June 27-30, 2011. DA 2011; 255-262.
- Ranchet M, Paire-Ficout L, Marin-Lamellet C, Laurent B, Broussolle E. Impaired updating ability in drivers with Parkinson's disease. Journal Neurology Neurosurgery Psychiatry. 2011;82(2):218-23. doi: 10.1136/ jnnp.2009.203166. Accessed August 27, 2010.

Dubois, R, Slachevsky A, Litvan I, Pillon, B. The FAB: A frontal assessment battery at bedside. Neurology. 2000;55:1621–1628.

- Ranchet M, Paire-Ficout L, Uc EY, Bonnard A, Sornette D, Broussolle E. Impact of specific executive functions on driving performance in people with Parkinson's disease. MovDisord. 2013;14:1941-8. doi: 10.1002/mds.25660. Accessed October 1, 2013.
- Reitan R. Trail-making test. Arizona: Reitan Neuropsychology Laboratory. 1979.
- Rizzo M. Medical Disorders. Handbook of Driving Simulation for Engineering, Medicine and Psychology. CRC Press; 2011.
- Singh H, Barbour BM, Cox DJ. Driving Rehabilitation as Delivered by Driving Simulation. Handbook of Driving Simulation for Engineering, Medicine and Psychology, CRC Press; 2011.
- Smith A. Symbol Digit Modalities Test. 1991. Los Angeles, CA: Western Psychological Services.
- Staplin L, Lococo K, Byington S. Older driver highway design handbook. Mc Lean, VA: Federal Highway Administration; 1998.
- Staplin L, Lococo KH, Gish KW, Decina LE. Model Driver Screening and Evaluation Program. Final Technical Report. Volume 2: Maryland Pilot Older Driver Study. Washington, D.C.: National Highway and Traffic Safety Administration; 2003. Available at: http://www.nhtsa.dot.gov/people/injury/olddrive/modeldriver/
- Staplin L, Lococo KH, Martell C, Stutts J. Taxonomy of Older driver behaviors and Crash Risk. National Highway and Traffic Safety Administration; 2012. Final Report, DOT HS 811 468A.
- Staplin L. Choosing Among Measures of Driver Cognitive Status that Predict Crash Risk. Maryland Older Driver Safety Symposium, May 16, 2012.
- Staplin L. Safe Driving Tactics: What Role for Low Cost Simulation? Proceedings of the 89thAnnual Meeting of the Transportation Research Board (TRB), January 10-14, 2010, Washington, D.C., USA.
- Strauss E, Sherman EMS, Spreen O. A compendium of neuropsychological tests. 2006. New York: Oxford University Press.
- Teerenstra S, Lu B, Preisser JS, van Achterberg T, Borm GF. Sample size considerations for GEE analyses of threelevel cluster randomized trials. *Biometrics*. 2010;66(4):1230-1237. doi:10.1111/j.1541-0420.2009.01374.x.
- Uc EY, Rizzo M. Driving in Alzheimer's Disease, Parkinson's Disease, and Stroke. In: Fisher DL, Rizzo M, Caird J, Lee JD. Handbook of Driving Simulation for Engineering, Medicine and Psychology. CRC Press. 2011; 48: 1-12.
- Uc EY, Rizzo M, Anderson SW, Dastrup E, Sparks JD, Dawson JD. Driving under low-contrast visibility conditions in Parkinson disease. Neurology 2009;73:1103–1110.
- Vardaki S, Yannis G, Papageorgiou S. A Review of Driving Performance Assessment in Simulators, accepted for presentation at the Road Safety and Simulation RSS013 International Conference, October 22-23, 2013. Rome.
- Vardaki S, Yannis G, Pavlou D, Beratis I, Papageorgiou S. Sign recall in a fixed-base simulator as a measure of fitness-to-drive, Proceedings of the 93nd Annual Meeting of the Transportation Research Board (TRB); January 12-16, 2014; Washington, D.C., USA.
- Wechsler D. Manual for the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III). 1997a. San Antonio, TX: The Psychological Corporation.
- Wechsler D. Wechsler Memory Scale Third Edition. Manual. 1997b. San Antonio, TX: The Psychological Corporation.

Yannis G, Golias J, Antoniou C, Papadimitriou E, Vardaki S, Papantoniou P, Pavlou D, Papageorgiou S, Andronas N, Papatriantafyllou I, Liozidou A, Beratis I, Kontaxopoulou D, Fragiadaki S, Economou A. Design of a large driving simulator experiment on performance of drivers with cerebral diseases. Proceedings of the 4th International Conference on Road Safety and Simulation; October 23-25, 2013; Rome, Italy.

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- Zokaei N, Burnett Heyes S, Gorgoraptis N, Budhdeo S, Husain M. Working memory recall precision is a more sensitive index than span. Journal of Neuropsychology. DOI: 10.1111/jnp.12052. First published online: September 11, 2014.
- Wechsler D. Wechsler Memory Scale—Fourth Edition (WMS–IV) technical and interpretive manual.2009. San Antonio, TX: Pearson.
- White T, Stern RA. *Neuropsychological Assessment Battery (NAB): Demographically Corrected Norms Manual*.2003. Lutz, FL: Psychological AssessmentResources, Inc.

	PD group $N = 10$		Co	P-values	
	Median	Interquartile range	Median	Interquartile range	
Age	65.5	53.25-70	58	54-60.5	0.247
Driving experience (years)	37	31.75-43	34.5	30.25-38.25	0.218
Days/week	4	3-4.25	5	3.75-7	0.143
Kilometers driven ^b	3	2-3	3	3-5	0.035ª
Accidents (total)-self-reported	0.5	0-1.5	1.5	1-5	0.029 ^a
Accidents in the last two years(self-reported)	0	0	0	0	1.000
Education (years)	14	10.75-16.25	14.5	12-16.5	0.684
CDR ^c	0	0-0	0	0-0	1.000
Disease specific measures					
UPDRŜ ^đ	12.5	8.5-25.25			
H&Y ^e	2.0	2-2			
Levodopa equivalent dosage (mg/day)	575	325-762.5			
Epworth Sleepiness Scale score	4	4-11			

Table 1. Comparison of patients with PD and of a Controls on various demographics using the Wilcoxon Rank Sum Test.

^aStatistically significant between-group difference at the 0.05 level ^b1=1-20km; 2=21-50km; 3=50-100km; 4=100-150 and 5=>150

^cClinical Dementia Rating

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^dUnified Parkinson's disease Rating Scale – motor scores ^eHoehn&Yahr stage

Table 2. Comparison of patients with Parkinson's disease with the Control group on a broad array of neuropsychological tests using the Wilcoxon Rank Sum Test

	PD group		Control g	P- values	
	Median	Interquartile	Median	Interquartile	
		range		range	
MMSE	29	27.5-29.8	30	28.5-30	.163
Frontal Assessment Battery ^a	15	9.2-15	17	16-18	<.001
HVLT - total immediate recall	18	16.2-22	23	18.5-27	.037
HVLT – total delayed recall	6	4.2-6	6.0	5-7.5	.549
LNS ^b	9	4-10	10	9-11	.211
Spatial Addition Test ^a	7	5.3-8.8	14	10-18.5	.001
SDMT ^c ,a	30.5	22.8-39.8	46	43-53.5	.001
TMT-A ^{d a}	43.5	33.8-77.8	41	32-47.5	.191
TMT-B ^e	123.5	82.5-291.3	103.0	67-131	.141
UFOV1 ^f	317	183.8-533.8	167	167-400.5	.209
UFOV2 ^g	1899.5	367-2875.8	400	300-833.5	.099
UFOV3 ^{h a}	2884	2192-4583.5	1533	1033.5-2350	.023
Driving Scenes Test	39	32.7-49.2	44	42-49.5	.154

^aStatistically significant between-group difference at the 0.05 level

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^aStatistically significant betwee ^bLetter Number Sequencing ^cSymbol Digit Modalities Test ^dTrail Making Test Part A ^eTrail Making Test Part B ^fUseful Field of View part 1 ^gUseful Field of View part 2 ^hUseful Field of View part 3

Table 3. Descriptive Statistics of Speed

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	Group	Mean	Std. Deviation	Ν
Speed, Demand Level1	Control	68.10	11.27	10
	PD	51.80	14.31	10
	Total	59.95	15.07	20
Speed, Demand Level2 ^a	Control	39.09	10.87	10
	PD	30.54	8.72	10
	Total	34.81	10.55	20
	Control	39.31	8.82	10
Speed, Demand Level3 ^a	PD	30.97	9.56	10
	Total	35.14	9.92	20

^aAverage speed along the road works section

	DemandLevel1 (TC1)	Demand Level2 (TC2)	Demand Level3 (TC3)		
	Recall sco	ores of PD group			
percent of recall score "0"	20.0%	10.0%	10.0%		
percent of recall score "1"	10.0%	10.0%	20.0%		
percent of recall score "2"	0.0%	20.0%	20.0%		
percent of recall score "3"	70.0%	60.0%	50.0%		
Median	3.0	3.0	2.5		
Interquartile range	1.5-3	2-3	1.25-3		
	Recall sc	cores of Controls			
percent of recall score "0"	0.0%	0.0%	0.0%		
percent of recall score "1" 10.0%		0.0%	0.0%		
percent of recall score "2"	20.0%	20.0%	60.0%		
percent of recall score "3"	70.0%	80.0%	40.0%		
Median	3.0	3.0	2.0		
Interquartile range	2.25-3	3-3	2-3		

Table 4. Recall Scores in Varying Levels of Intervening Task Demand

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Parameter		В	Std. Error	Exp(B)	95% CI for Odds Ratio		Hypothesis Test		
					Lower	Upper	Wald	df	Sig.
							Chi-		
							Square		
Threshold	Recallscores=0	-1.93	0.94	0.14	0.02	0.91	4.26	1.00	0.04
	Recallscores=1	-1.00	0.70	0.37	0.09	1.45	2.04	1.00	0.15
	Recallscores=2	0.31	0.57	1.36	0.44	4.18	0.29	1.00	0.59
Controls		0.53	0.68	1.70	0.45	6.41	0.61	1.00	0.43
PD		0							
TC1-Demai	nd-Level1	0.72	0.48	2.05	0.79	5.29	2.19	1.00	0.14
TC2-Demand Level2		0.89	0.42	2.44	1.07	5.60	4.46	1.00	0.03
TC3-Dema	nd Level3	0							

Table 5.Multinomial regression predicting recall scores

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Fig 1.. Mean speed for each group with varying levels of task demand with error bars denoting one standard error around the mean