COGNITIVE DEFICITS AND DRIVING ABILITY IN PATIENTS WITH PARKINSON'S DISEASE

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ABSTRACT

Background: The multimodal symptomatology of Parkinson disease (PD) appears to influence in a negative way aspects of cognition, behavior and motor control that are interwoven with the capacity of an individual to maintain adequate driving skills. Objective of the present review was to explore the link between cognition and driving fitness in patients with PD.

Methods: A systematic review of the literature was carried out for identifying relevant studies.

Results: Although it has not been sufficiently documented that drivers with PD have an increased rate of car accidents, according to multiple studies they face more difficulties than controls both on on-road and driving simulator evaluations. Notably, cognitive and not motor measures appear to be stronger predictors of driving performance in this clinical group. In particular, neuropsychological tests that engage executive, visuospatial and attentional resources are among the most sensitive predictors of the pass/fail outcome on driving evaluations.

Conclusions: Prospective studies by combining information from on-road and simulator driving could improve the validity properties of simulator assessments and expand our insight by exploring the unique contribution of broader sets of predictors. Also, an objective of future research should be the development of a wider array of cutoff scores with the use of larger and more representative samples that have the capacity to improve the accuracy of recommendations about future driving practices as well as of decisions about the restriction or total loss of driving privileges.

Keywords: Parkinson's disease; driving; on-road driving; driving simulator; cognition; attention; executive functions; visuospatial functions

INTRODUCTION

Parkinson's disease (PD) is a slowly progressive, degenerative disease of the basal ganglia with motor dysfunction as a cardinal feature, manifesting with bradykinesia, rigidity, resting tremor, flexed posture, shuffling gait and postural instability *(1, 2)*. In addition to motor dysfunction, PD causes cognitive (memory, visuo-spatial and executive dysfunction), emotional (e.g. depression, apathy) and behavioral-neuropsychiatric symptoms (e.g. agitation, hallucinations, delusions) *(3, 4, 5)*. These non-motor symptoms are usually unresponsive to dopaminergic treatment *(6)*. Other issues than can influence the functioning of individuals with PD are related to dosage regulation ("wearing-off syndrome", "on-off phenomenon", "peak dose dyskinesias"), and possible side effects of dopaminergic treatment such as excessive daytime sleepiness *(6)*. Hence, the multimodal clinical picture of PD appears to influence in a negative fashion various aspects of cognition, behavior and motor control that are closely linked to the capacity of an individual to maintain adequate driving skills.

OBJECTIVES AND METHODS

Objective of the current review was to present and discuss findings from previous research that has explored the link between cognition and fitness to drive in patients with PD. We searched the following databases for detecting relevant studies: (a) Pubmed, (b) Medline, (c) PsycINFO, (d) Google Scholar, and (e) Ageline. The search process was based on the combination of the following terms: Parkinson's disease, neurological disorders, cognitive impairment, attention, executive functions, visuospatial functions, driving, accidents, driving performance, fitness to drive, road test, road evaluation, driving simulator and driving predictors. Also, relevant work was identified by thoroughly studying the sources provided by the studies that the original search revealed. Based on the aforementioned process, 62 primary studies were initially identified. Subsequently, we reviewed this set of studies for excluding research papers that were not focusing on cognitive-related aspects of driving in patients with PD. Hence, 22 primary studies were recognized as relevant and included in the current review.

EPIDEMIOLOGIC DATA AND CRASH RATES OF PD

A retrospective study published in the early 90s that included 150 PD patients and 100 controls found that PD patients with more severe motor impairment as assessed by the Hoehn & Yahr (H&Y) scale experience an increased risk for car accidents *(7)*. In particular during the 3-year period prior to the conduction of the study, PD patients with H&Y stages 2 & 3 were involved in more motor vehicle accidents (MVAs) when compared either to patients with H&Y stage 1 or to normal controls. Also, epidemiological information from Germany suggests that 15% of the patients with PD holding an active driving license were engaged in car accidents during a period that covered the past five years *(8)*. Notably, the presence of sleeping disturbances while driving appeared to significantly increase the risk for car accidents in the specific clinical group. Limitations of the aforementioned study are the lack of a control group as well as the low participation rate that could induce selection bias, thus masking the actual frequency of car accidents in patients with PD.

However, findings from a recent prospective cohort study did not reveal differences in crash risk between patients with PD and controls even after adjusting for age, education, gender, and miles driven per week at baseline *(9)*. Nonetheless, the specific study revealed significantly greater rates of driving cessation in drivers with PD as compared to those of the control group. Hence, a possible reason for not detecting an increase crass risk in patients with PD could be explained by the decision of those individuals that were more impaired to stop driving before their

actual engagement in a car accident. Increased rates of driving cessation in patients with PD were also found in a retrospective study that took place in France *(10)*. Moreover, the specific study also showed absence of a significant association between PD and car crashes. However, a noticeable limitation of this work is the self-reported nature of the information about the number of crashes. In addition, the small number of cases with PD in the analyzed sample could reduce in a critical way the power of study.

Future longitudinal studies by studying large cohorts of drivers with PD could add to our knowledge about the presence or not of an increased crash risk in drivers with PD as well as about the parameters that play a role on the levels of driving cessation in the specific clinical group. Notably, in a recent study it was found that only subjective feelings of a decline in driving performance and not objective measures of cognitive functioning and simulated driving performance played a role on the driving cessation of patients with PD *(11)*.

INDICATIVE PREDICTORS OF DRIVING CAPACITY

Considerable effort has been directed toward the identification of neuropsychological measures that can serve as predictors of fitness to drive in individuals with PD. An indicative neuropsychological test that has been identified in several studies as predictor of driving skills in patients with PD is the Trail Making Test (TMT), especially part B of the specific test *(12, 13, 14)*. Abilities such as visual search, motor speed, and spatial skills are examined in both parts of the test *(15, 16)*. In addition part B assesses aspects of executive control, such as mental flexibility and task shifting *(17, 18, 19)*. In the study of Amick et al. *(12)* a significant association was found between a greater number of driving errors and a poorer performance on the parts A and parts B of the TMT in drivers with PD that underwent an on-road driving evaluation. Similarly, drivers with PD that were characterized as unsafe according to their on-road driving performance had important difficulties on the part B of the TMT *(14)*. Along the same vein, the study of Classen et al. *(13)* found in patients with PD that the part B of the TMT was significantly associated with the overall driving performance and the number of driving errors during an on-road assessment.

One more neuropsychological test that previous research has associated with driving skills of individuals with PD is the Useful Field of View (UFV) *(13, 20, 21)*. The UFV is a computerized test that assesses various aspects of visual perception and attention, namely central vision and processing speed, divided attention, and selective attention *(22)*. In the study of Classen et al. *(13)* a strong correlation between UFOV risk index and the divided attention subtest with both the global rating score and the number of errors made during an on-road driving test was observed in patients with PD. In the same group of patients the correlations with other cognitive tests ranged from weak to moderate. A more recent study by the same research group also revealed the capacity of UFV to serve as a central predictor of driving fitness in patients with PD *(20)*. Participants underwent an on-road driving evaluation and a number of visual, cognitive, and motor tests. In PD patients the divided attention subtest of the UFV showed the highest correlation with the pass/fail driving outcome and the number of maneuver errors.

The identification of UFV as a strong predictor of driving ability in patients with PD indicates the central involvement of impaired visual perception and visual attention in the driving difficulties commonly observed in the specific clinical group. Nonetheless, UFV is a computerized test that could be sensitive to various subject variables. Also, when using tests like the UFV, it is important to take under consideration the influence of primary aspects of visual functioning that could be impaired because of the neuropathology of PD. This is especially the case for contrast sensitivity (CS) that appears to commonly deteriorate in cases of PD because of the use of dopamine as neurotransmitter by cells within the retina *(23, 24, 25)*. Therefore, a good

recommendation when using the UFV or other similar tasks related to visual attention is to include in the same analysis CS measures, in order to study the unique contribution of each predictor after controlling for their shared variance.

Another test that research findings support its capacity to serve as predictor of driving fitness in individuals with PD is the Rey-Osterreith Complex Figure (ROCF) *(12, 14, 21)*. Notably, the aforementioned studies found associations between the ROCF test and driving performance during on-road testing procedures. This classical neuropsychological test assesses multiple cognitive domains, such as visual perception, visual spatial organization, motor functioning, executive skills, and non-verbal memory *(26)*. As in the case of the TMT, the ROCF puts a substantial load on multiple cognitive domains that are required in order to achieve adequate driving functioning.

ATYPICAL DRIVING CONDITIONS THAT INVOLVE INCREASED COGNITIVE LOAD

Two reports investigated safety errors in PD patients during on-road driving that required visual search and identification of targets *(27)*, and auditory-verbal distraction *(28)*. Of the participants, 79 PD patients and 151 controls underwent a landmark and traffic sign identification task (LTIT) during on-road driving *(27)*. The UFV and the copy condition of the Complex Figure Test were identified as independent predictors of landmark identification, but not of at-fault safety errors in drivers with PD. The strongest predictor for at-fault safety errors was the difference between the two conditions of the TMT, a measure of executive functioning that controls for the influence of psychomotor speed and visual search.

The influence of distraction in 71 PD patients and 147 controls was explored during daytime driving on a four-lane freeway under a driving condition that required the performance of the Paced Auditory Serial Addition Task (PASAT) which is considered to engage executive, attentional and working memory resources *(28)*. This aimed to mimic actual conditions of distraction, such as chatting while driving. The analysis showed that patients with PD made more driving errors in both the baseline and the distraction condition, without however the presence of a significant interaction effect. Nonetheless, PD patients had a more heterogeneous pattern of performance due to the distraction condition compared with controls, reflecting a greater possibility for increased amount of errors (28.2% vs. 15.8%) as well as a greater possibility for decreased amount of errors (16.9% vs. 3.4%). Variables that had the capacity to predict an increase in the number of at-fault safety errors due to the distraction effect were the following: (a) the general cognitive state as assessed by the MMSE; (b) the difference between Part B and Part A of the TMT; and (c) visual memory, as assessed by the Benton Visual Retention Test (BVRT).

In the aforementioned research, the investigators concluded that distraction did not have a stronger effect on PD patients than on controls. However, the greater fluctuation of driving errors due to distraction that was observed in the clinical group is a sign that this topic needs further investigation. Future studies could explore the impact of distraction on PD patients under more demanding driving conditions than those applied in the current study. Also, instead of the PASAT, more ecologically valid distractors could be tested, such as actual chatting or use of the mobile phone. An important limitation, acknowledged by the researchers, is the dissimilar performance of the two groups on the PASAT. Hence, a possibility that cannot be ruled out is that the level of distraction was not the same between controls and PD patients because the two groups did not engage a similar amount of cognitive resources for performing the specific task. Prospective works should take this issue under consideration and aim at developing distraction conditions that require from all participants to put in a similar level of cognitive effort.

The same research group *(29)* studied the driving ability of 77 patients with PD and 152 controls on on-road driving conditions that included a route-following task. Patients with PD made a greater number of navigation and safety errors. Also, a significant association between various neuropsychological measures and number of driving errors was observed. Visuo-spatial memory and familiarity with the driving region were the strongest predictors of incorrect turns, while visual processing speed and attention were the strongest predictors of at-fault safety errors.

Hence, it appears that patients with PD have increased difficulty to reach to their destination by using a set of verbal instructions that describes the route that should be followed *(29)*. Moreover, the increased number of incorrect turns and of at-fault safety errors indicates that this kind of driving practice should be avoided by individuals with PD.

OUTCOMES OF DRIVING SIMULATOR PROCEDURES

The link between cognitive functioning and driving performance in PD patients was investigated by studying the association between the ability of driving on a simulator and performance on a battery of neurological and neuropsychological tests *(30)*. The TMT-B, the Brixton test and the Symbol Digit Modalities test (SDMT), which engage executive functions or assess information processing speed, correlated with the majority of the driving measures in the driving simulator test in the group of PD. The driving measures included traffic signal approach speed, traffic signal deceleration point, mean curve speed, and curve direction effect on mean lateral position. The analysis revealed a limited number of significant correlations between the driving measures and measures of basic mobility speed, simple and choice reaction time, and the motor symptoms of the disease, as measured by the motor-UPDRS.

Another driving simulator study that was conducted by the same research group explored the role of internal and external cueing on the driving performance of patients with PD *(31)*. During the internal cueing condition the participants memorized a road sequence before starting to drive, whereas during the external cueing condition the presence of external cues informed the drivers about approaching obstacles. The analysis showed that drivers with PD as compared to controls had difficulty to adjust their driving behavior by using internal cues. Moreover, drivers with PD preferred to use external cues instead of internal cues when both options were available, whereas the opposite pattern was observed in the drivers of the control group. Drivers with PD needed also more time to initiate deceleration, had greater difficulty to stop at the proper position when approaching traffic signals, had lower speeds during driving around curves and showed greater variation in vehicle lateral position when driving around curves.

The impact of performing a concurrent task while driving has been investigated in a driving simulator experiment that included two groups of drivers, namely patients with PD and normal controls *(32)*. During the performance of the concurrent task both groups were affected at a similar level on various driving measures. However, patients with PD were disproportionally affected in their capacity to initiate deceleration when they approached a traffic signal. A parameter that should be considered is that controls outperformed the patients with PD on concurrent task performance, and, therefore, it could be assumed that patients with PD used only a small amount of resources for performing the parallel task in order to maintain adequate driving performance. Hence future studies should explore the impact of dual tasking on driving performance under concurrent tasks that require the engagement of a similar amount of resources from all drivers independently of whether they belong to the clinical or the control group.

The influence of low-contrast environmental conditions in driving performance of patients with PD was the objective of a driving simulator study performed by Uc et al. *(33)*. According to this research the impact of low-contrast visibility conditions had a greater impact on the driving

performance of individuals with PD than that of controls as assessed by the level of variation in lateral position and the counts of lane violation. The application of multivariate analysis showed that the UFV as well as measures of visuospatial skills and of motion perception were the strongest predictors of fitness to drive under low contrast conditions. The authors of the study conclude that the risk for unsafe driving could increase disproportionally for an important amount of drivers with PD when driving during twilight or under foggy conditions.

According to another driving simulator study, patients with PD appear to have increased difficulty as compared to controls in recalling road signs *(34)*. In terms of predicting the ability of drivers with PD to recall previously presented road signs, the difference between parts B and A of the TMT was identified as the best predictor, thus supporting the view that this capacity is executive-related at least in patients with PD.

A very recent research by applying a driving simulator system explored the influence of deep brain stimulation (DBS) of the subthalamic nucleus on the driving competence of patients with PD *(35)*. According to the findings of this work DBS appears to improve the driving skills of patients with PD. Nonetheless, future studies are warranted for assessing the external validity of the aforementioned research under on-road driving conditions. Also, because DBS may have a negative impact on cognitive functioning *(36, 37)*, the driving performance should be assessed as well under more demanding driving conditions that engage an increased amount of cognitive resources.

USE OF CUTOFF SCORES

Information about cutoff scores could improve the accuracy of the recommendations about future driving practices and help clinicians in their effort to identify individuals that are under increased risk to be involved in car accidents. However, in the literature only few studies have defined cutoff scores on certain neuropsychological measures for predicting the pass/fail outcomes on driving evaluations according to the best combination of sensitivity and specificity. In a study that applied the UFV *(13)* the optimal combination of sensitivity (87%) and specificity (82%) for passing the on-road driving test was achieved by a cutoff score of 3 (range 1-5) in the UFV risk index. Another attempt that included the subtest 2 of the UFV and the Rapid Paced Walk in a logistic model accurately classified 81% of the drivers (83% sensitivity and 78% specificity) in reference to the pass/fail outcome of an on-road evaluation *(20)*. Also, in the work of Worringham et al. *(38)* a combined set of predictors achieved sensitivity of 91% and specificity of 71% as concern the pass/fail outcome, without however providing information about specific cutoff values.

Prospective studies could replicate the existing cutoff scores by studying larger and more representative samples. Moreover, they could provide cutoff scores for additional neuropsychological and neurological measures either independently or in a combined way if this latter option improves the sensitivity and specificity properties.

COMPARISON OF COGNITIVE AND MOTOR MEASURES

In studies that have applied multivariate models, cognitive measures appear to be stronger predictors than motor indexes of driving fitness in patients with PD. For example, the study of Uc et al. *(33)* found that certain cognitive measures, such visual attention, constructional skills and visual memory could predict total driving errors, whereas this was not the case for motor dysfunction. Also, no significant associations between measures of motor function (UPDRS-motor, Tapping speed, Walking Speed) and driving errors were observed in another study of the same research group. On the contrary, the reduced driving performance of patients with PD was linked to the functioning of various cognitive domains *(29)*. Driving simulator research has also revealed

a similar pattern of results. Executive-related measures and measures of information processing speed were associated with the majority of the driving measures, while a limited number of significant correlations between the driving measures and motor symptoms of the disease, as measured by the motor-UPDRS were observed *(30)*.

A study that utilized a univariate statistical approach showed significant associations between driving fitness and specific items of the motor component of the Unified Parkinson Disease Rating Scale (UPDRS-motor) scale, namely postural stability, facial expression and neck rigidity *(14)*. Also, the severity of the disease, as determined by the Hoehn and Yahr scale, was significantly linked to unsafe driving in PD patients. Nonetheless, the findings of the specific work are limited because of the absence of a multivariate model that would have the capacity to assess the unique contribution of each predictor.

According to simulator data, motor measures and not only cognitive variables could have a central role as predictors of driving fitness under low visibility conditions that require sufficient response speed in order to avoid a crash *(33)*. Prospective research could add to the existing knowledge by studying the role of cognitive and motor measures as well as their interaction under various demanding driving conditions. Finally, a parameter that may explain why motor measures do no generally show a strong connection with driving performance in patients with PD could be the positive association that exists between motor dysfunction and driving cessation in the specific clinical group *(39)*.

CONCLUSIONS AND FUTURE DIRECTIONS

Several lines of previous research indicate that driving capacity in patients with PD is mainly compromised due to cognitive deficits that accompany this clinical condition. Notably, measures that engage executive, attentional and visuospatial resources show strong associations with driving fitness in individuals with PD. These three domains have been found to be crucial for safe driving in numerous studies *(40, 41, 42)*, as they affect primary driving tasks such as journey planning and route choice / way-finding, positioning and maneuvering the vehicle (e.g. left-turns, merging etc.), judging distances and predicting the development of driving situations, estimating risk and adapting driving behavior (e.g. speed).

Moreover, pronounced difficulties in indexes of driving performance seem to appear in drivers with PD under demanding driving conditions that involve increased cognitive load (e.g. dual-tasking, distraction, way-finding etc.). However, care should be taken the dual tasking or distraction conditions that are applied to require a similar amount of resources from all drivers independently of whether they belong to a clinical or the control group in order to compare their driving performance under balanced conditions.

The current knowledge about the driving performance of patients with PD is based both on on-road and simulator studies, two different methodological approaches with different advantages and limitations. For example, an important advantage of driving simulator experiments is that they provide the opportunity to test the driving performance of patients with PD under demanding driving conditions, whose assessment is very difficult or even unethical during on-road driving evaluations. Moreover, driving simulator procedures provide a detailed analysis of driving behavior that increases our insight about the underlying reasons that lead to driving errors or even to crashes. However, a limitation of driving simulator testing compared to on-road testing is that its validity has not been established yet in samples that include older individuals with an underlying neurological disorder.

Prospective studies by combining information from on-road evaluations and simulator designs could reach to more solid conclusions about the role and the effect size of various

predictors on driving performance measures. Also, an objective of future research should be the development of a wider array of cutoff scores with the use of larger and more representative samples of patients with PD. This kind of information can facilitate decisions about the restriction or total loss of driving privileges.

For improving our insight, the use of multiple measures that assess various domains appears to be essential, because this approach permits the extraction of the unique effect of each predictor as well as the estimation of its relative importance. Moreover, the combination of cognitive measures with brain imaging data could refine the methods currently used for assessing the driving ability of patients with PD *(43)*. Other issues that should be considered is the matching of the control group and the group of PD patients for age, gender and driving experience, as well as the sample size to be large enough for conducting the statistical procedures with sufficient power. 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 as well as during the time of the neurological/ neuropsychological assessment. Inclusion criteria for the selection of patients with PD should include the presence of a valid driver's license, regular and not occasional car driving, a score equal to or less than 1 on the CDR *(44)*, and a score between 1 and 3 in the scale of Hoehn & Yahr. On the other hand, exclusion criteria that should be considered are alcohol or illicit substance use, and the presence of significant neuropsychiatric symptoms related to PD (i.e. agitation, delusions, hallucinations).

Based on the findings of the previous studies it appears that various cognitive 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 in isolation, because this practice could lead to imprecise decisions that can have dangerous consequences. Future studies by expanding the existing bounds of knowledge can further our theoretical and practical insight about the link that exists between cognitive dysfunction due to PD and driving fitness under various driving conditions and environments.

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