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Impaired navigation in drivers with Parkinson's disease

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Navigating a new route during automobile driving uses the driver's cognitive resources and has the potential to impair driving ability in people with Parkinson's disease (PD). Our aim was to assess navigation and safety errors during a route following task (RFT) in drivers with the illness. Seventy-seven subjects with mild-moderate PD (median Hoehn–Yahr stage = 2.0) and 152 neurologically normal elderly adults, all active and licensed drivers, were tested with a battery of visual, cognitive and motor tests of abilities. Each driver also performed a RFT administered on the road in an instrumented vehicle. Main outcome variables included: number of incorrect turns, times lost and at-fault safety errors. All group comparisons were adjusted for age, gender, education and familiarity with the region. Drivers with PD performed significantly worse on cognitive, visual and motor tests compared to controls, and took longer to finish the RFT. Higher proportions of these drivers made incorrect turns {53.9% in PD versus 21.1% in controls, Odds Ratio (OR) [95% Confidence Interval (CI)] = 2.8 [1.4, 5.7], $P = 0.006$}, got lost (15.8% versus 2.0%, OR [95%CI] = 4.7 [1.1, 20.0], $P = 0.037$), or committed at-fault safety errors (84.2% versus 46.7%, OR [95%CI] = 7.5 [3.3, 17.0], $P < 0.001$). Within the patient group, the navigational and safety errors were predicted by poor performances on cognitive and visual tests, but not by the severity of motor dysfunction. Drivers with PD made more navigation and safety errors than neurologically normal drivers on a RFT that placed demands on driver memory, attention, executive functions and visual perception. The PD group driver safety was degraded possibly due to an increase in the cognitive load in patients with limited reserves. Navigational errors and lower driver safety were associated more with impairments in cognitive and visual function than the motor severity of their disease in drivers with PD.

Keywords: Parkinson disease; driving; cognition; vision; accident; traffic; automobile; navigation

Abbreviations: AVLT = Auditory Verbal Learning Test; BVRT = Benton Visual Retention Test; CFT = Complex Figure Test; COWA = Controlled Oral Word Association; CS = contrast sensitivity; ESS = Epworth Sleepiness Scale; FVA = far visual acuity; GDS = Geriatric Depression Scale; FR = functional reach; JLO = judgment of line orientation; MMSE = Mini Mental Status Examination; NVA = near visual acuity; PD = Parkinson's disease; SE-ADL = Schwab-England Activities of Daily Living; SFM = structure from motion; TMT = Trail Making Test; UFOV = Useful Field of View; UPDRS = Unified Parkinson's Disease Rating Scale.

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Introduction

In addition to hallmark motor dysfunction, Parkinson's disease (PD) also causes variable impairments of cognition, vision, sleep, autonomic function and behaviour (Lang and Lozano 1998; Bodis-Wollner 2003; Uc *et al.*, 2005*a*). These widespread abnormalities impair driving safety (Madeley *et al.*, 1990; Dubinsky *et al.*, 1991; Lings and Dupont 1992; Heikkila *et al.*, 1998; Frucht *et al.*, 1999; Hobson *et al.*, 2002; Moller *et al.*, 2002; Zesiewicz *et al.*, 2002; Brodsky *et al.*, 2003; Radford *et al.*, 2004; Stolwyk *et al.*, 2005; Meindorfner *et al.*, 2005; Worringham *et al.*, 2005; Wood *et al.*, 2005; Uc *et al.*, 2006*a*, *b*), based on epidemiological studies, (Dubinsky *et al.*, 1991), road-tests (Heikkila *et al.*, 1998; Wood *et al.*, 2005; Worringham *et al.*, 2005; Uc *et al.*, 2006*a*, *b*) and driving simulator experiments (Madeley *et al.*, 1990; Moller *et al.*, 2002; Zesiewicz *et al.*, 2002; Stolwyk *et al.*, 2005). Safe automobile driving requires a driver to navigate a vehicle in familiar and unfamiliar territories. Getting lost can increase driver anxiety due to uncertainty of location, extended

searching for landmarks or attempts to read maps or signs, and divert cognitive resources from key driving tasks in drivers whose baseline cognitive resources are limited (Uc *et al.*, 2004). Drivers with PD may be at particular risk for navigation errors. The head of the caudate is part of the frontostriatal circuitry that gets affected by PD (Kish *et al.*, 1988; Alexander *et al.*, 1990) and is an important structure in route following (Maguire *et al.*, 1998; Hartley *et al.*, 2003). Mild PD can impair spatial working memory (Owen *et al.*, 1997; Postle *et al.*, 1997*a*, *b*; Hodgson *et al.*, 1999) and impair navigation during walking (Bowen *et al.*, 1972).

This study tested the hypothesis that patients with mild–moderate PD commit navigation errors on a route following task (RFT) that resembles the real-world situation in which a driver must follow verbal directions to a destination (Uc *et al.*, 2004). This RFT was implemented in an instrumented vehicle (IV) designed to record driver speed, steering, braking and acceleration and to assess driver errors (Uc *et al.*, 2004, 2005*b*, 2006*a*, *b*). IVs permit quantitative assessments of driver performance in the field under actual road conditions, and are not subject to the type of human bias that can affect inter-rater reliability between different evaluators. An additional goal was to establish if drivers with PD, under the influence of the cognitive load imposed by the RFT, commit more safety errors that could place them at greater risk for a potential crash. We also tested whether navigation and safety errors could be predicted by cognitive, visual and motor measures sensitive to decline in mild–moderate PD.

Methods

Subjects

The PD group consisted of 77 participants (65 men and 12 women) with mild–moderate disease severity [Hoehn–Yahr (HY) score = 2.2 ± 0.6, Table 1]. The PD patients from the Movement Disorders Clinics at the Department of Neurology, University of Iowa and Veterans Affairs Medical Center, both in Iowa City, were asked consecutively if they were still licensed and driving. Those who were still driving were offered the opportunity to participate in the study. Their mean ± SD (median) Mini Mental State Exam (MMSE) score was 28.3 ± 1.8 (29.0) with a range of 22–30 (two subjects scored 22, one scored 24). All subjects were community dwelling, independently living and licensed active drivers. The controls consisted of 152 neurologically normal elderly (75 men and 77 women), who were also licensed active drivers. Driving exposure as miles/week on all participants was obtained from the Driver Habits Questionnaire (Uc *et al.*, 2006*a*) and there was no significant difference between the groups.

Inclusion criteria

Subjects with idiopathic PD (PD group) or elderly without neurological disease (control group) who are currently active drivers with a valid State driver's license and driving experience of greater than 10 years.

Table 1 Characteristics of patients with Parkinson's disease ($n = 77$)

Characteristic	Value
Age (years)	65.9 ± 8.6 (66.0)
Disease duration (years)	5.7 ± 5.1 (4.0)
Hoehn-Yahr stage (↓)	2.2 ± 0.6 (2.0)
UPDRS-mental (↓)	2.7 ± 2.2 (2.0)
UPDRS-ADL (↓)	11.6 ± 5.5 (11.0)
UPDRS-motor (↓)	23.7 ± 8.7 (24.0)
UPDRS-total (↓)	40.1 ± 13.5 (37.5)
Tapping speed (↑)	35.6 ± 5.9 (35.2)
7m walk (↑)	14.4 ± 4.0 (14.0)
Schwab-England score (↑)	84.0 ± 9.4 (90.0)
Levodopa equivalent (mg/day)	588 ± 593 (403)
MMSE (↑)	28.4 ± 1.8 (29.0)
Epworth Sleepiness Scale (↓)	9.6 ± 4.2 (10.0)

Values represent mean ± SD (median).
Upward arrow = higher score better, Downward arrow = lower score better.
UPDRS = Unified Parkinson's Disease Rating Scale; ADL = Activities of Daily Living; MMSE = Mini Mental State Examination.

Exclusion criteria

Cessation of driving prior to encounter; acute illness or active confounding medical conditions such as vestibular disease, alcoholism or other forms of drug addiction (subjects with history of drug or alcohol dependency have to be in remission for at least 2 years); other neurologic disease leading to dementia (e.g. Alzheimer's disease, strokes) and motor dysfunction; secondary parkinsonism (e.g. drug-induced); Parkinson-plus syndromes (e.g. multiple system atrophy, progressive supranuclear palsy, corticobasal degeneration); concomitant treatment with centrally acting dopaminergic blockers within 180 days prior to baseline; treatment with any investigational drug within 60 days prior to baseline; major psychiatric disease not in remission and diseases of the optic nerve, retina or ocular media with corrected visual acuity less than 20/50.

In order to maintain ecological validity, we performed all testing during the times when the subject would normally feel ready to drive, i.e. during the 'on' times, and also allowed subjects to take rest periods as needed.

Informed consent was obtained according to the Declaration of Helsinki (*BMJ* 1991; 302: 1194) and institutional and federal guidelines for human subjects' safety and confidentiality.

Off-road testing battery

The battery methodology in explained in detail in our recent work (Uc *et al.*, 2005*a*). For all tests, raw scores were used for analysis. Tables 1 and 2 show the abilities tested by each measure and the direction of good performance. The Useful Field of View (UFOV) task (Visual Attention Analyzer Model 3000, Visual Resources Inc.), a predictor for crashes in elderly and patients with AD, measures speed (in ms) of visual processing, divided attention, and selective attention. We used the sum of subsets subtests of the UFOV task in our analyses (Uc *et al.*, 2005*a*). Contrast sensitivity (CS) was assessed using the Pelli–Robson chart. The best corrected visual acuity was measured using the ETDRS chart for far visual acuity (FVA) and reduced Snellen chart for near visual acuity

Table 2 Comparison of patients with Parkinson's disease ($n = 76$) and controls ($n = 152$) using Wilcoxon Rank Sum test

Off-Road Battery			Parkinson's Disease	Controls
Demographics		Age	65.9 ± 8.6 (66.0)	65.3 ± 11.5 (68.0)
		Education (years)	14.8 ± 2.9 (13.0)*	15.6 ± 2.6 (16.0)
		Gender	(62 Male, 15 Female)***	(75 Male, 77 Female)
		Familiarity	25 Familiar***	110 Familiar
Category	**Function**	**Measure**		
Basic visual Sensory functions	Near Visual Acuity	Snellen Chart- logMAR (↓)	0.069 ± 0.070 (0.073)***	0.021 ± 0.041 (0.000)
	Far Visual Acuity	ETDRS Chart- logMAR (↓)	−0.029 ± 0155 (0.000)***	−0.085 ± 0.124 (-0.080)
	Contrast Sensitivity	Pelli-Robson Chart (↑)	1.70 ± 0.15 (1.65)***	1.84 ± 0.15 (1.95)
Visual Perception	Motion Perception	SFM% (↓)	12.6 ± 5.3 (11.9)**	10.4 ± 2.8 (10.1)
	Attention	UFOV (↓)	881 ±371 (824)***	634 ± 247 (610)
	Spatial Perception	JLO (↑)	24.4 ± 4.3 (25.0)*	25.7 ± 3.9 (27.0)
Visual Cognition	Construction	BLOCKS (↑)	33.1 ±11.9 (30.0)***	39.9 ± 10.7 (40.0)
		CFT-COPY (↑)	26.9 ± 5.1 (28.0)***	31.8 ± 3.8 (33.0)
	Memory	CFT-RECALL (↑)	13.2 ± 5.4 (13.3)**	15.8 ± 5.9 (15.0)
		BVRT-error (↓)	7.4 ± 4.2 (7.0)***	4.6 ± 2.6 (4.0)
Executive Functions	Set Shifting	TMT(B-A) (↓)	83.8 ± 80.3 (59.6)***	46.4 ± 34.6 (37.5)
	Verbal Fluency	COWA (↑)	34.5 ± 11.3 (33.0)**	39.1 ± 11.1 (40.0)
Verbal Memory		AVLT-RECALL (↑)	7.3 ± 3.6 (7.0)***	10.2 ± 3.2 (11.0)
Depression		GDS (↓)	6.0 ± 5.5 (5.0)***	3.3 ± 3.6 (2.0)
Balance		FR (↑)	11.5 ± 3.2 (11.0)***	13.4 ± 2.7 (13.5)

Values represent mean ± SD (median)
Upward arrow = higher score better; downward arrow= lower score better.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
AVLT = Auditory Verbal Learning Test; BVRT = Benton Visual Retention Test; CFT = Complex Figure Test; COWA = Controlled Oral Word Association; GDS = Geriatric Depression Scale; FR = Functional Reach; JLO = Judgment of Line Orientation; SFM = Structure from Motion; TMT = Trail Making Test; UFOV = Useful Field of View.

(NVA), both expressed as LogMAR (logarithm of the minimum angle of resolution), with 0 representing 20/20 vision. Perception of 3D structure from motion (SFM) was tested using computer-generated animation sequences (Uc *et al.*, 2005*a*).

The Unified Parkinson's Disease Rating Scale (UPDRS) and timed motor tests such as tapping and walking speed were administered to all subjects with PD (Table 1) (Defer *et al.*, 1999). Total daily levodopa-equivalent amount (mg) of anti-parkinsonian medications was calculated using an established formula (Uc *et al.*, 2004). We also used Epworth Sleepiness Score (ESS) and Geriatric Depression Scale (GDS) to assess non-motor aspects of PD, and Schwab-England Activities of Daily Living (SE-ADL) scale as a measure of overall disability associated with PD (Uc *et al.*, 2005*a*).

The road test

The experimental drive was conducted aboard an instrumented vehicle known as ARGOS (the Automobile for Research in Ergonomics and Safety), a mid-sized 1995 Ford Taurus station wagon with an automatic transmission and with hidden instrumentation and sensors (Uc *et al.*, 2004, 2005*b*, 2006*a*, *b*). Experimental performance data such as steering wheel position and vehicle speed were digitized at 10 Hz and reduced to means, SDs or counts. Driver's lane tracking and driving behaviour were recorded by videotape at 30 frames per second using miniature lipstick-size cameras mounted unobtrusively within the vehicle. Digital driving data were superimposed on multiplex views using four channels of video. Control of speed and lane position are critical aspects of driving, and unplanned lane deviations occur with degradation of driving performance (Uc *et al.*, 2004, 2005*b*, 2006*a*, *b*].

The road test in ARGOS was administered within one week of cognitive and visual testing, sometimes on the same day. Order of testing (cognitive and visual versus ARGOS) was random. The subjects were seated comfortably in the driver's seat. The experimenter sat in the front passenger seat to score the on-road performance and operate the dual controls, if needed. The experimenter gave standard instructions to the drivers on operating ARGOS. The experimental drive lasted approximately 45 min and started after the driver acclimated to ARGOS on a short test drive. The subjects drove across residential city streets, suburban commercial strips, rural two-lane highways and a four-lane 65 mph speed limit freeway. Secondary tasks such as route following were interspersed across ~7 miles of the drive ('on-task' segments). Road testing was carried out only during the day (usually between 9:00 a.m. and 4:00 p.m.) on specific roads surrounding Iowa City and during the optimal motor response to anti-parkinsonian medications ('on' time). Drivers were not tested in inclement weather that might cause poor visibility or road conditions. The assessment incorporated several essential maneuvers such as turns, stopping at a stop sign and maintaining vehicle control.

Route-following task (Uc *et al.*, 2004)

Route following was tested as part a sequence of on-the-road tasks administered in ARGOS. Drivers were given verbal instructions to follow a route (Fig. 1) while the car was stopped and parked. The experimenter made sure that the driver was able to hear and understand the instructions. Hearing was screened before the drive using a standard audiogram and no subject was excluded due to hearing problems. The instructions: (i) From the main hospital entrance, turn left onto Hawkins Drive;

Fig. 1 The route following task depicted on a Google Earth image as an overlay. Used with permission from Google Earth™ mapping service/Digital Globe.

Table 3 Main and secondary outcome measures of the route following task expressed as means ± SD (median) in Parkinson's disease ($n = 76$) and controls ($n = 152$), compared using Wilcoxon Rank Sum. Regression techniques were used to adjust analyses for familiarity with the region, age, gender, and education. ('Δ' represents difference upon substraction of errors during 'baseline' from 'on task' error counts.)

	PD	Controls	Crude P	Adjusted-P
Main outcomes				
No of incorrect turns	0.68 ± 0.85 (1.00)	0.22 ± 0.45 (0.00)	<0.001	0.002
No of times lost	0.20 ± 0.57 (0.0)	0.02 ± 0.14 (0.0)	<0.001	0.019
No of at-fault safety errors (on task)	2.49 ± 1.85 (2.00)	0.78 ± 1.10 (0.0)	<0.001	<0.001
No of at-fault safety errors/mile (baseline)	0.28 ± 0.17 (0.25)	0.07 ± 0.08 (0.04)	<0.001	<0.001
No of at-fault safety errors (on task, adjusted for baseline)			0.001	0.002
Δ At-fault Safety errors (on task–baseline)	2.19 ± 1.85 (2.00)	0.72 ± 1.07 (0.0)	<0.001	<0.001
Secondary outcomes				
Learning to Criterion (No of recitations)	3.92 ± 1.76 (3.00)	2.75 ± 0.86 (3.00)	<0.001	0.001
Time to finish (s)	238 ± 111 (204)	177 ± 71 (154)	<0.001	0.003

(ii) Right onto Melrose Avenue; (iii) Left on Koser Avenue; (iv) Left on George Street were read to the subject just prior to beginning the experimental drive and the drive started only after the driver recited the instructions correctly twice in a row. Each segment was ~0.2 miles long. Driver familiarity with the section of town where the RFT was administered was assessed (as 'yes' or 'no' obtained by asking the driver about prior driving experience in and around Iowa City)(Uc *et al.*, 2006*a*) and incorporated into analyses. After a turn error, subjects were allowed to drive one additional block before the experimenter disclosed the error to the subject. After identification of an error, the subject was given the opportunity to correct the error. If the driver failed to correct the error, the experimenter redirected the driver to the proper route. The primary outcome measures were number of: (i) Incorrect turns defined as turning too soon, too late, or in the wrong direction (maximum 4), (ii) times lost defined as incorrect turns after which the driver did not recognize and correct the error and (iii) at-fault safety errors such as erratic steering, lane deviation, shoulder incursion, stopping or slowing in unsafe circumstances and unsafe intersection behaviour. The secondary outcome measures were the number of trials to learn to criterion and time to finish the task.

Statistical analysis

We used the Wilcoxon Rank Sum test to compare the results off-road battery (Table 2) and the outcome measures of the RFT (Table 3) between the groups. We used regression models to adjust the RFT main outcome comparisons for age, gender, education and for previous familiarity with the route. We adjusted

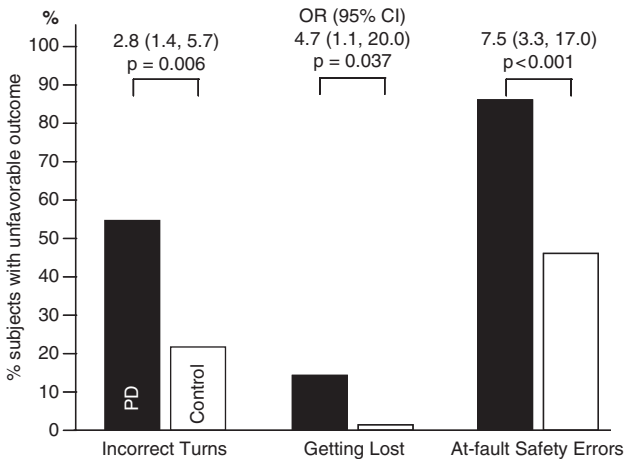

Fig. 2 Proportion of subjects with unfavorable outcomes and odds ratios (OR) with 95% confidence intervals (CI) on the route following task in PD and normal control group. The unfavourable outcomes are defined as making at least one incorrect turn, getting lost at least once, and making $\geqslant$1 at-fault safety errors, all significantly higher in the in the PD group (Logistic regression). The ORs and *P*-values are adjusted for age, familiarity with the region, gender and education.

Table 4 Vehicle control measures on a straightaway freeway segment with 65 mph speed limit expressed as means $\pm$ SD (median) in Parkinson's disease (PD) and normal control group compared using the Wilcoxon Rank Sum test for speed and linear regression for other variables

	PD	Controls	*P*-value
Mean vehicle speed (mph)	57.4 $\pm$ 6.0 (58.6)	60.9 $\pm$ 5.2 (61.6)	<0.001
Speed variability (mph) = mean SD of vehicle speed	2.00 $\pm$ 1.05 (1.88)	1.78 $\pm$ 0.88 (1.53)	0.790
Steering variability (degrees) = mean SD of steering wheel position	1.93 $\pm$ 0.51 (1.94)	2.03 $\pm$ 1.37 (1.94)	0.979

the at-fault safety errors during RFT also for errors during segments when no task was administered. We used Wilcoxon Rank Sum test to compare the within-group changes in error counts from baseline to RFT segment between groups. We used exact logistic regression compare the proportion of drivers in each group who at least one incorrect turn, at least one at-fault safety error or got lost at least once and calculating odds ratios (OR) based on group status, adjusted by age, gender, familiarity with the region and education (Fig. 2).

We compared groups on the basic vehicular control abilities as indexed by speed, speed variability (mean SD of speed) and steering variability (mean SD of steering wheel position) on a straightaway freeway segment with 65 mph speed limit and no secondary task load using the Wilcoxon Rank Sum test (for speed) and linear regression (to adjust for speed when examining the other measures—Table 4).

Based on the distribution of the number of incorrect turns and getting lost, we categorized these dependent variables into levels of 0 and $\geqslant$1 and used exact logistic regression to determine the significant univariate predictors within the PD group. To determine the univariate predictors of at-fault safety errors during RFT, we calculated Spearman correlations for continuous variables or performed linear regression for categorical variables such as gender and familiarity with the region. The independent variables consisted of all the demographic, motor, cognitive and visual measures in the off-road battery listed in the Tables 1 and 2. Within the PD group, we used backward elimination stepwise regression models to test multivariate significance of predictors of incorrect turns, getting lost and at-fault safety errors.

Results

The drivers with PD had mild–moderate disease severity (Table 1). The group of drivers with PD was less educated, had a larger proportion of males and was less familiar with the testing region than the comparison group (Table 2). The PD group also performed worse on neuropsychological and visual tests, showing mild cognitive and visual perceptual deficits (Table 2).

Higher proportions of drivers with PD compared to controls made incorrect turns {53.9% in PD versus 21.1% in controls, OR [95% Confidence Interval (CI)] = 2.8 [1.4, 5.7], $P = 0.006$}, got lost (15.8% versus 2.0%, OR [95%CI] = 4.7 [1.1, 20.0], $P = 0.037$) or committed at-fault safety errors (84.2% versus 46.7%, OR [95%CI] = 7.5 [3.3, 17.0], $P < 0.001$), adjusted for age, gender, education and familiarity with driving neighbourhood (Fig. 2). Also, drivers with PD made significantly more incorrect turns, got lost more often and committed more at-fault safety errors than the neurologically normal controls (Table 3). They also required more trials to learn the route correctly and took longer time to finish the route (Table 3). The difference between the RFT outcome measures in the PD patients and control groups persisted after adjusting for familiarity with the region, age, education and gender (Table 3).

In addition to the at-fault safety errors during RFT, PD patients committed more at-fault safety errors also during the baseline period when no secondary task was administered (Table 3). The number of at-fault safety errors increased from 0.28 $\pm$ 0.17 (mean $\pm$ SD) per mile at baseline to 2.49 $\pm$ 1.85 during RFT in the PD group, whereas the error count only increased from 0.07 $\pm$ 0.08 to 0.78 $\pm$ 1.10 in the control group, $P < 0.001$. The group difference in at-fault safety errors during RFT persisted after adjustment for at-fault safety errors at baseline (i.e. errors committed during segments of drive where no tasks were administered). These results suggest that the cognitive demands of the RFT task increased the likelihood of errors.

Drivers with PD drove slower than control drivers on a straight segment of the drive during which no secondary task such as RFT was administered (median 58.6 mph in PD versus 61.6 mph in controls, $P < 0.001$, Table 4). The were no significant differences between groups in other vehicular control measures such as speed and steering

variability (Table 4), suggesting that slower driving in PD is a compensatory behaviour to mitigate effects of reduced motor, visual and cognitive abilities.

Within the PD group, measures of verbal (AVLT-RECALL) and non-verbal memory (CFT-RECALL), cognitive flexibility (TMT[B-A]) and visual attention (UFOV), and cognitive screening with MMSE correlated significantly (Spearman coefficients) with the number of at-fault safety errors. Significant predictors of making at least one incorrect turn were non-verbal memory (CFT-RECALL and BVRT), executive functions (TMT[B-A] and COWA), visual perception and attention (FVA, JLO, UFOV), visuospatial construction abilities (CFT-COPY, BLOCKS), general cognitive function (MMSE), and familiarity with the region. CFT-RECALL and MMSE were the only predictors of getting lost. Multivariate regression analyses on these significant univariate predictors showed that non-verbal memory (CFT-RECALL) and familiarity were the most important predictors of incorrect turns, and that visual processing speed and attention (UFOV) were the most important predictors for at-fault safety errors. Note that MMSE was not included in the model because it is a global indicator of cognition.

We analysed the relationship of PD medication status on the RFT outcomes, and found no significant associations. Specifically, we found that there was no significant correlation between total daily levodopa equivalent and RFT outcomes. As a second approach, we classified the PD subjects as being on levodopa (LD, $n = 21$), dopamine agonist (DA, $n = 22$), on levodopa and dopamine agonist (LDDA, $n = 27$) or other/no treatment ($n = 6$), and made formal comparisons among these groups using chi-squared tests and Fisher's exact tests. We found that medication group status (LD versus DA versus LDDA; or LD+LDDA versus DA) did not predict the presence/absence of incorrect turns, getting lost or at-fault safety errors.

A *post hoc* analysis showed that 91 control drivers and only eight PD drivers had no impairments (Number of incorrect turns, getting lost or at-fault safety errors all zero) on the RFT task, $P < 0.001$, Fisher's exact test. Compared to the other drivers with PD, the eight with no RFT impairments scored better on TMT[B-A] (mean ± SD [median] 37.7 ± 17.3 [30.4] s in unimpaired PD versus 89.2 ± 83.1[64.1] s in others, $P = 0.009$, Wilcoxon rank Sum test), BLOCKS (40.4 ± 8.7 [42.0] versus 32.1 ± 12.0 [29.5], $P = 0.049$), and a higher level of education (17.1 ± 2.0 [18.0] years versus 14.5 ± 2.8 [13.0], $P = 0.017$).

Discussion

The findings in this study support our hypothesis that drivers with PD make more navigational errors (indexed by incorrect turns and getting lost in the RFT) than neurologically normal drivers on the road (Table 3). The RFT in this study resembles the real-world situation in which a driver must follow verbal directions to a destination and places demands on driver memory, attention, executive functions and perception. The cognitive demands of the RFT and inability to follow a route may further reduce driving safety in cognitively impaired drivers with PD (Uc *et al.*, 2004), who had a larger increase in at-fault safety errors from baseline segments to RFT and continued to show greater number of at-fault safety errors during the RFT (Table 3), even after adjusting for baseline errors. The group differences in RFT outcomes could not be explained by lower education, greater male gender proportion or less regional familiarity of the PD subjects, because significant differences between groups in RFT outcome measures persisted after adjusting for these independent variables.

Driving performance and safety in PD is an active research topic (Madeley *et al.*, 1990; Dubinsky *et al.*, 1991; Lings and Dupont 1992; Heikkila *et al.*, 1998; Frucht *et al.*, 1999; Hobson *et al.*, 2002; Moller *et al.*, 2002; Zesiewicz *et al.*, 2002; Brodsky *et al.*, 2003; Radford *et al.*, 2004; Meindorfner *et al.*, 2005; Stolwyk *et al.*, 2005; Wood *et al.*, 2005; Worringham *et al.*, 2005). This study focuses on navigation in drivers with PD. Impaired navigation or way-finding, i.e. topographical disorientation (Aguirre and D'Esposito, 1999), is likely to reflect cognitive deficits in PD (Bowen *et al.*, 1972). Navigational abilities in PD patients have been tested directly using a route-walking test (Bowen *et al.*, 1972), and indirectly by examining visuospatial abilities on a variety of neuropsychological tests (Bowen *et al.*, 1972; Heikkila *et al.*, 1998; Moller *et al.*, 2002; Radford *et al.*, 2004). To our knowledge, no study has tested route following in patients with PD during actual driving, as in this study.

Our navigation task is route based [rather than map based (Aguirre and D'Esposito, 1999)] and resembles the common situation, in which a driver receives verbal instructions that describe a sequence of steps to a destination. The RFT engages anterograde memory, visual perception and attention, recognition of landmarks such as street signs, and visuospatial abilities (such as right/left discrimination, and executing remembered turns in the correct direction). The RFT also requires drivers to monitor their navigation errors and correct them to resume the proper route. This self-monitoring and correction requires executive functions, mental rotation [which can be abnormal in PD (Amick *et al.*, 2006)] of imagined space, recognition of recently encountered landmarks from an altered perspective and comparison with the mental model developed from the initial sequence of verbal instructions. In line with these information procession demands of the RFT, measures of verbal and visual memory (AVLT, CFT-RECALL, BVRT), executive function (TMT[B-A], COWA), visual sensory abilities (FVA) and perception (JLO), visual attention (UFOV), visuoconstructional abilities (CFT-COPY, BLOCKS) and overall cognitive function (MMSE) correlated significantly with the RFT outcome measures.

Independent predictors of the RFT performance included CFT-RECALL and familiarity with testing region, CFT-RECALL for times lost (only significant univariate predictor besides MMSE, a general measure), and UFOV for at-fault safety errors, consistent with memory and attention demands of the RFT. UFOV, a predictor for crashes in elderly and patients with AD (Duchek *et al*., 1998; Owsley *et al*., 1998), can also contribute to the evaluation of drivers with PD, as in our previous work (Uc *et al*., 2006*a*, *b*).

Motor dysfunction (e.g. tremor during holding the steering wheel) has the potential to increase driving safety errors, yet we found no significant difference in vehicle control measures such as speed and steering variability or acceleration patterns between groups on a straightaway freeway segment, even after adjusting for slower speed of the drivers with PD (Table 4). In this vein, univariate and multivariate predictors of RFT outcomes within the PD group were cognitive and visual, rather than motor. These results are consistent with previous findings (Uc *et al*., 2006*a*, *b*) by us and other researchers (Heikkila *et al*., 1998; Stolwyk *et al*., 2005, 2006*a*, *b*; Wood *et al*., 2005; Worringham *et al*., 2005) that driving performance and safety depends primarily upon cognitive and visual aspects of PD, even though PD has been recognized primarily as a motor disorder (Lang and Lozano, 1998).

Our finding that cognitive and visual dysfunction, rather than motor impairments were associated with navigation and driver safety errors has important parallels with the growing literature on dual task interference in gait performance in PD patients with limited cognitive reserves. Executive dysfunction in PD may exacerbate the effects of dual tasking on gait, reducing walking speed, stride length and balance (Rochester *et al*., 2004; Galletly and Brauer 2005; Yogev *et al*., 2005). Cognitively, challenging situations increase the likelihood that freezing of gait occurs (Giladi and Hausdorff, 2006).

We cannot rule out that some drivers with PD might have given up their driving privileges due to motor dysfunction prior to being considered for this study. However, PD patients disabled due to motor dysfunction usually have severe postural instability and gait disorder (i.e. Hoehn–Yahr stages 4 or 5), which are associated with cognitive dysfunction and dementia (Uc *et al*., 2005a). Thus, even in those patients with severe motor disability who quit driving, cognitive dysfunction might have significantly contributed to the cessation of driving. Although the study was limited to PD patients who remained active drivers, there still was a range of motor impairments in this group, yet without correlation with RFT outcomes and driving performance.

Familiarity with the neighbourhood was a partial mitigating factor in this study. While familiarity did not affect driving safety errors it predicted fewer incorrect turns suggesting that the impaired individuals drive better in familiar neighbourhoods.

A small number of drivers with PD performed completely normally on the RFT. These drivers had a higher level of education, better non-verbal problem solving abilities (BLOCKS) and better set-shifting and cognitive flexibility as indexed by the TMT(B-A) test, an executive function test which is independent of motor speed (Jahanshahi *et al*., 2000). Driving while performing a task like RFT requires executive control over attention and contention scheduling to preserve driving safety despite the added demands of the RFT (e.g. recalling the route, attending to street signs and comparing the travelled route to the mental image created by the instructions). The effect of executive dysfunction on RFT performance in PD is consistent with the findings of our previous studies where patients with PD were asked to perform a secondary task while driving (Uc *et al*., 2006*a*, *b*). This suggests that presumed reduction of resources in the Supervisory Attentional System (Shallice and Burgess, 1996) or Central Executive (Baddeley *et al*., 1986) due to dopaminergic dysregulation of the frontostriatal circuits (Owen, 2004; Brown and Marsden, 1988) may contribute to decreased driving performance, while performing secondary tasks in drivers with mild-moderate PD.

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