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Short communication

Motor dual-tasking deficits predict falls in Parkinson's disease: A prospective study

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ABSTRACT

Introduction: Falls severely affect lives of Parkinson's disease (PD) patients. Cognitive impairment including dual-tasking deficits contribute to fall risk in PD. However, types of dual-tasking deficits preceding falls in PD are still unclear.
Methods: Walking velocities during box-checking and subtracting serial 7s were assessed twice a year in 40 PD patients over 2.8 ± 1.0 years. Fourteen patients reported a fall within this period (4 excluded fallers already reported falls at baseline). Their dual-task costs (DTC; mean ± standard deviation) 4.2 ± 2.2 months before the first fall were compared with 22 patients never reporting falls. ROC analyses and logistic regressions accounting for DTC, UPDRS-III and disease duration were used for faller classification and prediction.
Results: Only walking/box-checking predicted fallers. Fallers showed higher DTC for walking while box-checking, $p = 0.029$, but not for box-checking while walking, $p = 0.178$ (combined motor DTC, $p = 0.022$), than non-fallers. Combined motor DTC classified fallers and non-fallers (area under curve: 0.75; 95% confidence interval, CI: 0.60–0.91) with 71.4% sensitivity (95%CI: 41.9%–91.6%) and 77.3% specificity (54.6%–92.2%), and significantly predicted future fallers ($p = 0.023$). Here, 20.4%-points higher combined motor DTC (i.e. the mean difference between fallers and non-fallers) was associated with a 2.6 (1.1–6.0) times higher odds to be a future faller.
Conclusion: Motor dual-tasking is a potentially valuable predictor of falls in PD, suggesting that avoiding dual task situations as well as specific motor dual-task training might help to prevent falls in PD. These findings and their therapeutic relevance need to be further validated in PD patients without fall history, in early PD stages, and with various motor-motor dual-task challenges.

1. Introduction

Falls entail very severe health-related consequences in patients with Parkinson's disease (PD). Predictors of future falls which can be quantified, modified and used to inform therapeutic fall prevention strategies are therefore urgently needed.

Recently, an expert consensus [1] on potential risk factors of falls in PD suggested 16 generic (e.g. age, sex, alcohol consumption) and 15 PD-specific risk factors (e.g. disease severity, fall history, shuffling/small scaled gait, postural instability). Multifactorial analyses of prospective studies in PD [2–9] showed that for many of these factors effect sizes of fall prediction are small to intermediate, vary between studies, may be confounded with other predictors, suggesting that further, yet unidentified risk factors exist.

Increasing evidence suggests cognitive impairment, with frontal deficits in particular [4], as a predictor of falls in PD. However, specific cognitive deficits in PD, and their relation to falls are scarcely investigated. Available literature points to a moderate association of attention (relative risk, RR: 1.8) [2], and a weak association of orientation deficits (RR: 1.3) [8] with future falls in PD when accounting for PD motor symptoms. Moreover, dual-tasking deficits have been recognized as an important risk factor of falls in PD in cross-sectional studies [esupp ref1&2]. Still, evidence from prospective longitudinal studies is limited. The only study focusing

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on this aspect showed no association of future falls with auditory Stroop performance (a cognitive test engaging executive functions, specifically response inhibition) during gait [10]. We therefore hypothesized that specific dual-tasking deficits are predictive of future falls in PD, and investigated two different dual-tasking paradigms performed in a longitudinally assessed PD cohort, to evaluate their predictive value for future falls.

2. Methods

2.1. Participants and basic clinical assessment

Forty PD patients fulfilling the UKPDS-BB criteria were recruited from the outpatient clinic, Department of Neurodegeneration, University of Tübingen, Germany, and assessed every six months for 2.8 (±1.0, SD) years (up to 8 visits) in the prospective, observational MODEP study (MODeling Epidemiological data to study Parkinson's disease progression). Only clinical and experimental data assessed in OFF-medication state were considered. PD symptoms were assessed using the revised Unified Parkinson Disease Rating Scale part-III (UPDRS-III), Hoehn and Yahr score (H&Y), Trail-Making-Test (TMT), Montreal Cognitive Assessment (MoCA) and Beck Depression Inventory (BDI-II). The study was approved by the local ethical committee (Medical Faculty, University of Tübingen; Nr 46/2010). All participants gave written informed consent.

2.2. Dual-tasking assessment

Three different single tasks were performed as fast as possible: **(1) Walking:** 20-m obstacle-free straight walking. **(2) Box-checking:** marking 32 boxes with a cross on a clipboard using the dominant hand. **(3) Subtracting:** ten serial subtractions of 7s from a 3-digit number and verbally indicating resulting numbers. Then, the motor-motor dual-task **(1 + 2)** and the motor-cognitive dual-task **(1 + 3)** were performed, with the instructions to perform both tasks as fast as possible. These task conditions are sensitive to subtle deficits [esupp ref3] which may be challenging in everyday situations with increased risk of complications. No hint for task prioritization was given. Performances were measured as speed of walking [m/s], checked boxes [boxes/s] and correct subtractions [subtractions/s]. Dual-task costs (DTC) were calculated [11] as: DTC=(1-dual-task speed/single task speed)*100. Positive DTC values indicate the percentage of decreased performance in dual-tasks relative to single tasks. As participants might show task prioritization [11] or even positive DTC in both tasks, we calculated the sum of both DTC, i.e. combined DTC = DTC (walking while performing secondary task) + DTC (secondary task while walking).

2.3. Definition of fallers and non-fallers

At each visit, falls were retrospectively assessed by asking each participant whether a fall occurred during the last week/month/six months/year. A fall was defined as inadvertently coming to rest on the ground without overwhelming external force or major internal event (e.g. paralysis or loss of consciousness due to stroke) [esupp ref4]. Fourteen PD patients reported at least one fall during the observation period, and were therefore defined as fallers. Data of fallers assessed during the last visit before the first fall occurred were included in the analysis. Twenty-two non-fallers, i.e. PD patients who never reported falls in the MODEP study, were compared with the faller group. Non-fallers did not have a defining event (i.e., a first fall within the observation period) that allowed us to specify a visit out of all visits performed during the course of the longitudinal MODEP study. Therefore, we had to define a selection criterion for the visit to be included in the analysis. We decided to use the mean age of the faller group, i.e., 64.6 years. The visit where the individual non-faller's age was closest to the mean age of the faller group was selected. Additionally, 4 fallers already reported falls at the baseline assessment of the MODEP study and were excluded from the present analyses as no assessment data prior the first reported fall was available.

2.4. Statistical analysis

Significances of demographic and clinical variables were tested using Whitney-Mann U-tests and chi-square tests. Single- and dual-tasking differences between fallers and non-fallers were tested using univariate analyses of covariance (ANCOVAs) accounting for disease duration and UPDRS-III as covariates. Logistic regressions were conducted with fallers/non-fallers as dependent variable and single task performance, DTC or combined DTC, respectively, as well as disease duration and UPDRS-III as predictors. The resulting odds ratio (OR) relates to a 1-unit change of the predictor of interest, e.g. 1%-point of DTC, which is a relatively small change. In order to scale the unit of the predictor by a given factor, the variable value (of combined DTC) can be divided by the same factor (i.e. the number value of the variable is smaller but the unit is proportionally larger). This “rescaling” of the unit of combined DTC was performed for different factors ranging from 1 to 50 (0.1 increments). For each rescaled combined DTC variable a logistic regression was performed. The resulting ORs (of being a faller) were plotted against their corresponding 1%-point, 1.1%-point, …, or 50%-point change in combined DTC. Receiver Operating Characteristic (ROC) analyses were used for evaluation of predictors based on sensitivity, specificity and area under the curve (with 95% confidence intervals). We used the minimum value of Youden's index to yield an optimum cutoff of the ROC-curve variable without prioritization of sensitivity or specificity. Threshold of significance was set to $\alpha = 5\%$. Statistical analyses were performed using IBM SPSS Statistics, Version 22.0. (Armonk, NY, IBM Corp., USA), for logistic regressions MATLAB version R2015b (Natick, MA, The MathWorks Inc., USA), and for computation of sensitivity/specificity confidence intervals MedCalc, version 15.11.4 (MedCalc Software, Ostend, Belgium) were used.

3. Results

3.1. Descriptive statistics

Fallers and non-fallers did not differ significantly in demographic or clinical parameters except for the UPDRS-III score (Table 1). Here, compared with non-fallers (mean ± standard deviation (SD); UPDRS-III: 28.4 ± 12.7) fallers (36.8 ± 16.0) showed significantly higher motor symptom severity scores of the UPDRS-III ($p = 0.035$). In fallers, all analyzed data were assessed 4.2 ± 2.2 months (range: 3–11 months) before the first reported fall.

3.2. Single and dual-task performance

Fallers and non-fallers did not differ significantly in walking and box-checking speed under single task condition ($p > 0.1$, Table 1; ANCOVA with UPDRS-III and disease duration as covariates). However, during dual-tasking, fallers showed significantly slower walking speed while box-checking ($p = 0.031$) but no significant difference in the speed of box-checking while walking ($p = 0.502$) compared with non-fallers (Fig. 1a and b). Similarly, DTC of walking while box-checking were significantly higher in fallers compared with non-fallers ($p = 0.029$), and DTC of box-checking while walking showed no significant difference ($p = 0.179$). Combined motor DTC also showed a significant performance difference