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How to evaluate effects of occupational therapy – lessons learned from an exploratory randomized controlled trial

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ABSTRACT

Background: Although occupational therapy (OT) is frequently prescribed in clinical practice, there is still insufficient evidence regarding its efficacy to improve Parkinson's Disease (PD)-related activity limitations.
Objectives: To evaluate the efficacy of OT and the validity of different outcome-parameters to reflect efficacy, including gold-standard clinical rating scales and quantitative motor assessments.
Methods: 40 patients were included in an exploratory, randomized-controlled, single-blinded trial, receiving either (I) ten weeks of OT, with a main focus on motor aspects of activity limitations and a ten-week follow-up assessment or (II) no intervention. Inclusion criteria were diagnosis of PD and Hoehn & Yahr stage 2–3. Patients with major depression, other neurological or orthopedic diseases or OT beforehand were excluded from the study. To monitor treatment effects the MDS-UPDRS part II and III were used for patient- and clinician-based assessment. Objective Pegboard as well as Q-Motor "tremormotography" and "digitomotography" were applied.
Results: The interventional group reported a subjective amelioration of activity limitations, with a significant improvement of MDS-UPDRS part II at the end of the study ($p = 0.030$). However, clinician's rating and quantitative motor assessment failed to detect a significant improvement of motor impairment and fine motor control.
Conclusions: This study goes in line with previous trials, showing an individual improvement of activity limitations from the patients' point of view. The discrepancy between self-perception, focusing on activity limitation, and clinician-based rating, focusing on motor impairment, challenges the current gold standard assessments as valid outcome parameters for occupational therapy trials aiming for an individualized improvement of disease burden.

1. Introduction

The importance of non-pharmacological interventions as part of a comprehensive treatment for Parkinson's disease (PD) is increasingly recognized and advocated [1]. While the primary target of pharmacological treatment is an improvement of motor impairment (in particular the cardinal motors signs bradykinesia, rigor and tremor), the aim of many non-pharmacological interventions is an improvement of activity limitations and participation restrictions. This is especially true for Occupational therapy (OT), which focuses primarily on improvements of daily living tasks. Although OT is widely utilized by clinicians internationally and is part of PD treatment guidelines in many countries, the effectiveness of OT has not been sufficiently validated yet. While some studies showed an improvement of daily activity performance [2], other studies failed to prove effectiveness [3]. Several meta-analyses came to the conclusion that although most studies indicate treatment effects of OT, evidence is still insufficient and more randomized, controlled studies are needed [4–6]. To explain the dichotomy between the wide clinical reliance on OT and the low evidence base, study design issues and especially inadequate outcome measures have been discussed [7]. Taken together, previous research has shown that there is a need for more randomized-controlled studies on the one hand, and for the definition of clinically pertinent outcome measures on the other hand to prove the effect of OT in PD.

We performed a randomized-controlled, single-blinded study to evaluate (I) the efficacy of OT for the treatment of PD and (II) the

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validity of different outcome parameters to assess effects of OT training. Improvement of activity limitation and fine motor control were chosen as main targets for the OT training. Additionally, we hypothesized a direct improvement of motor impairment as secondary target of the OT intervention. Based on the defined goals of the OT training the following outcome parameters were chosen: MDS-UPDRS part II, reflecting the patients' self-perception of activity limitations in daily motor tasks, quantitative assessment tools (Pegboard, Q-Motor "digitomotography" and Q-Motor "tremoromotography"), to aim for an objective evaluation of motor performance in particular fine motor control, and the MDS-UPDRS part III as a clinician-based assessment of motor impairment. Additionally, all patients were asked to fill out a semi-structured evaluation form to assess the individual impression of therapeutic effects.

2. Methods

2.1. Subjects

Forty-one patients were recruited from the outpatient clinic of the department of Neurodegeneration at the University of Tübingen. Inclusion criteria were: (I) PD diagnosis according to the UK Brain Bank Criteria and (II) Hoehn & Yahr 2, 2.5 or 3. Exclusion criteria entailed: (I) signs or diagnosis of disorders other than PD affecting the central nervous system or motor function, (II) major depression, defined as > 18 points on the Beck Depression Inventory (BDI) and (III) occupational therapy beforehand. All patients gave their written informed consent. One patient was excluded from the study after visit one due to a long distance to the clinics, therefore data of 40 patients were used for data analysis. The study was approved by the local ethical committee.

2.2. Study design

The study was constructed using an exploratory, randomized-controlled design with two study groups: The OT group received occupational therapy for ten weeks, followed by a period of no exercise/training. The control group started with a ten week period of no training. To enable all patients the opportunity to test occupational therapy, patients of the control group received the same OT training after the first ten weeks of no intervention. All patients underwent all assessments at baseline and follow-up 1 (after ten weeks). For the evaluation of sustained treatment effects in the OT group all assessments were repeated after twenty weeks (follow-up 2). Patients were randomly assigned to one of the study groups (according to a computer-generated code) by a neurological resident.

2.3. Intervention

All patients received occupational therapy for ten weeks, with an intensity of 60 min (= 1 session) per week. The training took place at the rehabilitation centre of the University of Tuebingen and was performed by the same certified and experienced occupational therapist for all patients. The training comprised three main targets:

1) Activity limitations: The main focus of the training was the improvement of motor aspects of activity limitations. Before the start of the training limitations of each patient were inquired and individual strategies to improve task performance and daily functioning were defined. Perceived deficits of the patients included beyond others limitations in dressing, eating, cooking or writing.
2) Fine motor control: As secondary aim the OT intervention focused on the improvement of fine motor control. The therapeutic approach included general aspects as well as task specific approaches, adapted to the individually most bothersome activity limitations demanding fine motor control.
3) Motor impairment: Additionally, we hypothesized that, although the main focus of OT is on improvement of activity limitation as a consequence of motor impairment, motor impairment per se can also be addressed directly. While recent studies focused mainly on activity limitations, there is some evidence that OT might also improve specific aspects of motor impairment, e.g. bradykinesia or tremor [16–18]. The training was based on the observation that some patients tend to apply too much force, become more tense and agitated when they realize impairment, leading to a deterioration of bradykinesia, rigidity and tremor. Body sensation, awareness and relaxation were trained in order to voluntarily reduce and regulate the muscle tone and tremor.

Patients were encouraged to continue the learned exercises at home and transfer them into their everyday life. All patients were asked to keep their usually performed health interventions (e.g. physiotherapy) at the same intensity level as performed before the study intervention and to remain at their usual PD medication stable.

2.4. Assessments

Part II (Motor aspects of experiences of daily living) and III (Motor examination) of the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) were used as current clinical gold standard scale. As the sum scores of Part II and III combine many different aspects of motor impairment and daily functioning, sub-analyses were performed to evaluate more detailed improvements in specific areas. Therefore six factors of the MDS UPDRS factor structure, elaborated by Goetz et al. [8], were chosen, reflecting the main goals of the OT intervention. The chosen factors include three factors of Part II, reflecting activity limitations and fine motor control, and three factors of Part III, reflecting motor impairment.

(A) Self-perception: MDS-UPDRS part II (interview)
- •Factor 1: Speech, Saliva and drooling, Chewing and swallowing, Handwriting, Doing hobbies and other activities
- •Factor 2: Eating tasks, Tremor
- •Factor 3: Dressing, Hygiene, Turning in bed, Getting out of bed, Walking and balance, Freezing

(B) Clinician's rating: MDS UPDRS part III
- •Factor 2: Rest tremor amplitude (Right and left upper and lower extremity, lip/jaw), Constancy of rest tremor
- •Factor 3: Rigidity (neck, right and left upper and lower extremity)
- •Factor 4: Finger tapping, Hand movement, Pronation/Supination (right hand)

To objectively quantify fine motor control and tremor, patients were asked to perform.

1) *Pegboard test:* Patients were asked to place small metal sticks in a board with predrilled holes as fast as possible.
2) *Q-Motor Grip Lift Task ("tremormotography"):* Patients lifted a small weight using the precision grip. An included 3-D position sensor measured orientation (x-, y-, z-axis) and position (roll, pitch, yaw) of the patient's hand.
3) *Q-Motor Tapping Task ("digitomotography"):* Characteristics of Speeded and Metronome Tapping were detected by a force transducer.

The Grip Lift and Tapping Tasks were part of a specific quantitative motor ("Q-Motor") assessment, which has been validated for the assessment of motor performance in Huntington's Disease [9,10] as well as for fine motor control and dyskinesias in Parkinson's Disease [11,12]. For a more detailed description of the setup we refer to Ref. [13]. All tasks were performed in a standardized manner, starting with the right hand.

Moreover, all patients were asked to fill out a semi-structured evaluation form at the end of the study. The Montreal Cognitive Assessment (MOCA) was used to assess cognitive function as possible confounder for therapeutic effectiveness. The clinician performing the neurological examination was certified in performing the MDS-UPDRS and blinded to the group assignment. Assessments were performed in the "On"-phase of the patients.

2.5. Statistics and data processing

For statistical analyses SPSS 24.0 (SPSS Inc., IBM, USA) was used. Q-Motor data were processed blinded and semi-automated by the Q-Motor laboratory in Muenster (PI: Ralf Reilmann). Data of the body site more affected by the Parkinsonian symptoms (assessed with the MDS-UPDRS) were used for longitudinal analyses. As the established MDS-UPDRS factor structure is separated for movements of the right and left hand, correlations were performed using Q-Motor data of the right hand and factor 4 (movements of the right hand) of the MDS-UPDRS. For the assessment of fine motor skills six "digitomotography" parameters were included for analyses, as they had been validated in Parkinson's Disease by Maetzler et al. [9]: Mean and standard deviation (SD) of the inter-peak-interval (IPI mean, IPI SD) during the speeded tapping, as well as mean and coefficient of variation of tap force (TF mean, TF CoV) and mean and variability of tap deviation DEV (DEV mean, DEV SD) from the predefined metronome rhythm. For the assessment of tremor the two parameters "Orientation-Index" and "Position-Index" of the "tremormotography" were chosen, measuring position (x, y, z; 0,75 mm resolution) and orientation (roll, pitch, yaw; 0,025° resolution) of the hand.

Comparisons between the two groups were performed by the Fisher's exact, Mann-Whitney- U or student's t-test. ANCOVA with repeated measures was used to assess changes over time with and without training. Variables were tested for normal distribution using the Kruskal-Wallis-Test, not normally distributed parameters were decadic logarithmized for repeated measures. With regard to the exploratory study design, no correction was applied for multiple testing.

3. Results

3.1. Subject characteristics

Patients did not differ with regard to age, gender, disease duration and Hoehn & Yahr at baseline (Table 1). All individuals showed MOCA scores ≥ 20 points, without significant group differences (OT1 29.0, 23–30; OT2 28.0, 20–30; p = 0.49). Both groups showed slight changes in levodopa equivalent dosage (LED) during follow-ups (mainly due to on-demand medication), without significant group differences. Changes in LED between BL and FU1 were used as covariate (continuous variable) for the following longitudinal analyses.

Table 1
Characterization of study groups.

Subject characteristics	OT n = 21	Control n = 19	p value
Age (ys)[a]	61.4 (11.8)	64.7 (11.9)	0.39
Male Gender	47.6%	57.9%	0.55
Disease duration (ys)[b]	1.0 (1–7)	2.0 (1–12)	0.74
Hoehn & Yahr			
2–2.5	95.2%	100%	> 0.99
3	4.8%	0%	
MOCA[b]	29.0 (23–30)	28.0 (20–30)	0.49
BL LED (mg)[b]	300 (80–1037)	352 (100–1543)	0.67
FU1 LED (mg)[b]	330 (80–1037)	352 (120–1444)	0.90

[a] Values as mean (SD).
[b] Values as median (range); BL: Baseline; Control: no intervention; FU: Follow-up; LED: levodopa equivalent dose; MOCA: Montreal Cognitive Assessment; n: number; OT: occupational therapy during week 1–10; p: level of significance; y: years.

3.2. Response to intervention analyses

A group-dependent improvement of the MDS-UPDRS part II sum score was seen for the OT group after 10 weeks of OT (p intervention × group = 0.030), resulting in a significant lower sum score compared to the control group at FU1 (p = 0.003). A sustaining effect of the intervention for the OT group was seen at FU2. Looking at the established factors for the MDS-UPDRS part II, no group differences were seen at baseline. After the intervention the OT group scored significant lower in the point values of factor 1, 2 and 3, when compared to controls, however, the intervention × group analyses failed significance. No significant changes were seen for the MDS-UPDRS Part III sum score and the analyses of its individual factors after the intervention (Table 2).

Analyses of the quantitative motor assessments showed no group-specific differences after the intervention for all parameters. In all patients a significant improvement of the Pegboard testing at FU1 was seen. (Table 2).

3.3. Evaluation

The majority of patients (70%) reported an improvement of activity limitations after occupational therapy. 77.5% wanted to continue with the regular training instructed by an occupational therapist and 90% wanted to continue practicing the learned exercise. Individual statements on the improvement of activity limitations differed widely between the patients, including a variety of activities of daily living. One patient specifically reported an improvement of motor impairment (tremor)(Table 3).

4. Discussion

This study provides additional evidence for a subjective improvement of motor aspects of daily living tasks after occupational therapy as assessed by the MDS-UPDRS part II and confirmed by the subjective evaluation of patients, with a sustaining effect after 10 weeks. Our results go in line with a previous study by Sturkenboom et al. [2], showing an improvement of self-perceived performance of activities of daily living after occupational therapy. However, this study failed to show significant improvements of motor impairment from the clinician's point of view (assessed by the gold-standard rating scale MDS-UPDRS part III) and motor performance by using objective quantitative motor assessments.

The discrepancy between self-perception and objective/clinician-based assessment has raised the question whether occupational therapy is indeed an effective therapy in PD, independently from subjective improvement as a function of personal support and attention during the training. To answer this question it is essential to reevaluate the currently applied clinical assessments, including the gold standard MDS-UPDRS, as measurement tool to assess an improvement of activity limitations, as main objective of OT interventions. Although this scale has been previously recommended for OT trials [14], it comprises two main problems. First, having a closer look at the different parts of the MDS-UPDRS, it becomes evident, that the patient-based questions of the MDS-UPDRS part II focus on limitations in daily functioning, while the clinician-based items of the MDS-UPDRS part III assess motor impairment, regardless of its impact on activities of daily living. In consequence, when using the MDS-UPDRS as an outcome measure, interventions focusing on an improvement of activity limitation can only be evaluated from the patients' point of view (i.e. with Part II). Accordingly, an observation based scale assessing improvements of activity performance from the clinicians' point of view would have been an important additional outcome parameter. Moreover, part II of the MDS-UPDRS includes both activities of daily functioning (e.g. eating tasks

Table 2
Longitudinal analysis of clinical scores and quantitative motor assessment.

	OT n = 21	Control n = 19	p-value group	p-value intervention	p-value group×intervention
MDS-UPDRS					
Part II: Motor aspects of daily living (Sum score)					
BL	7.0 (3.9)	8.4 (3.6)	0.25		
FU1	5.1 (3.1)	8.1 (3.7)	0.003*	0.003*	0.030*
FU2	5.3 (2.6)				
Part III: Motor examination (Sum score)					
BL	24.5 (6.6)	23.2 (8.5)	0.57		
FU1	26.1 (8.8)	24.9 (9.9)	0.70	0.09	0.93
FU2	24.0 (8.0)				
Quantitative Motor Assessment					
Pegboard (s)					
BL	69.8 (9.9)	80.4 (22.2)	0.10		
FU1	66.3 (8.3)	75.0 (18.0)	0.21	0.010*	0.51
FU2	66.7 (10.4)				
Orientation Index (deg/s)					
BL	3.57 (0.80)	3.82 (2.77)	0.39		
FU1	6.64 (9.11)	3.41 (1.77)	0.61	0.78	0.14
FU2	6.41 (13.38)				
Position Index (deg/s)					
BL	0.82 (0.20)	0.83 (0.49)	0.27		
FU1	1.05 (0.89)	1.63 (3.82)	0.58	0.95	0.76
FU2	0.83 (0.43)				
IPI Mean (s)					
BL	0.22 (0.06)	0.31 (0.39)	0.15		
FU1	0.21 (0.04)	0.28 (0.18)	0.002*	0.37	0.67
FU2	0.21 (0.04)				
IPI SD (s)					
BL	0.04 (0.02)	0.06 (0.10)	0.36		
FU1	0.03 (0.02)	0.07 (0.15)	0.47	0.72	0.38
FU2	0.03 (0.01)				
TF Mean (N)					
BL	2.14 (1.90)	2.33 (2.07)	0.99		
FU1	2.01 (1.58)	1.96 (2.20)	0.17	0.07	0.81
FU2	1.97 (1.53)				
TF CoV					
BL	17.1 (7.0)	16.7 (7.4)	0.96		
FU1	15.3 (5.3)	15.6 (9.6)	0.58	0.41	0.31
FU2	15.7 (6.2)				
DEV Mean (s)					
BL	−0.02 (0.04)	−0.03 (0.08)	0.57		
FU1	0.18 (0.08)	0.18 (0.08)	0.31	0.07	0.15
FU2	0.17 (0.07)				
DEV SD (s)					
BL	0.18 (0.07)	0.20 (0.12)	0.99		
FU1	0.18 (0.08)	0.18 (0.08)	0.99	0.51	0.51
FU2	0.17 (0.07)				

Values are given as mean (SD) for better overview; p-value group: occupational therapy vs. control group at baseline (first line) and follow-up (second line); p-value intervention: change of both groups from baseline to follow-up; p-value group × intervention: group-specific change from baseline to follow-up; BL: Baseline; Control: no intervention; CoV: Coefficient of variation; DEV: Variability of tap deviation from the predefined metronome rhythm; FU1: Follow-up 1; FU2: Follow-up 2; IPI: Inter Peak Interval; LED: levodopa equivalent dose; MDS-UPDRS: Movement Disorder Society Unified Parkinson's Disease Rating Scale; n: number; OT: occupational therapy during week 1–10; p: level of significance; pts: points; SD: Standard deviation; TF: Tap Force; ys: years.

and handwriting) and aspects of motor impairment (e.g. tremor) in one sum score. It therefore combines two different constructs of limitations/impairment, which may not be addressed by the same training [6].

Another important aspect for the evaluation and interpretation of this and other OT studies becomes evident by having a closer look at the subjective evaluation of the training in our study. A majority of patients reported an improvement of activity limitations after OT, however, each patient referred to different targets of the training with a wide range of different motor and daily living tasks. This demonstrates the highly individual training approach of occupational therapy, which is intended to improve specifically the most burdensome activity limitations of an individual patient in order to maintain independence.

Table 3
Patient's evaluation of the training.

Evaluation	Yes	Indecisive	No
Did Occupational Therapy improve your symptoms of Parkinson's Disease?	70%	25%	5%
Would you like to continue with Occupational Therapy?	77.5%	0%	22.5%
Do you plan to continue practicing the learned exercises?	90%	0%	10%
What has been improved after Occupational Therapy?	Eating (2), Cooking (1), Drinking (1), Grabbing (1), Dressing (1), Handling with coins (2), Typing (1), Writing (6), Opening bottles (1), Hygiene (2), Making music (1), Painting (1), Handicraft (1), Walking (6), Posture (1), Tremor (1), Mobility/Fine motor skills in general (8)		

However, these individual training effects are not addressed by the outcome scales currently applied. In particular, using the sum scores of the different MDS-UPDRS parts means to include many different aspects of motor impairment activity limitations and participations restrictions in PD, although they may not be targeted by a specific treatment, nor may they reflect the individual disease burden of a patient. Thus, the MDS-UPDRS sum scores are not well-suited for the evaluation of individual treatment effects, which are the basis of most non-pharmacological treatment approaches, including occupational therapy. As an alternative, we used the clinimetrically established factors of the MDS-UPDRS, as they focus separately on specific constellations of motor impairment and activity limitations that have been addressed by the OT intervention. However, also these established factors provide combinations of different motor aspects, which are not always appropriate from a clinical point of view. As an example factor 3 of the MDS-UPDRS part II combines aspects of fine motor control (Dressing and Hygiene) with aspects of gait (Walking and Freezing), although these are highly different forms of motor function, which are addressed by different forms of training. More importantly, although these aspects were in general goals of the OT intervention, each patient defined the personal burden caused by limitations in these motor activities different, leading to individual different areas of focus of the training.

Apart from improvement of activity limitations, a secondary target of the performed OT intervention was an improvement of fine motor control, with the Pegboard assessment as corresponding outcome parameter. Again, no group-dependent improvement was seen after the OT intervention, with a similar improvement in both groups indicating only a general learning effect. In contrast, a previous study of Vanbellingen et al. showed a significant improvement of fine motor control in the Pegboard test after a specific dexterity training [15]. However, in this study a task specific training design was used, contrary to the individual training approach of our OT study. We therefore conclude that the Pegboard assessment might not be valid to reflect individual treatment effects of OT.

Finally, following the hypothesis that OT can also have an effect on motor impairment per se, we added the Q-motor assessment as an additional (quantitative) measurement of motor impairment to the MDS-UPDRS part III. Again, Q-motor tremor- and digitomotography showed no improvement after the OT intervention. These results leave the question open, whether motor impairment per se cannot be improved by an OT intervention, or whether the quantitative motor assessment tools are too uniform to reflect an individual improvement after an individual training approach.

This study faces several limitations, first of all the small sample size of the groups. Secondly, previous studies indicated point values from 2 to 3 in the MDS-UPDRS part II as minimally clinically important differences (MCID), which was not achieved in this study (1.9 points difference) [19]. However, Schrag et al. also indicated that the MCID depends on the stage and severity of the disease [20]. Considering all point values of the MDS-UPDRS and the disease duration in our study it is evident that the included patients were only mildly affected and in an early phase of the disease. This is due to the fact that the Department of Neurology at the University of Tuebingen recommends OT for nearly all patients, therefore patients with longer disease duration were already on OT and had to be excluded from the study. Higher MDS-UPDRS scores at baseline may have led to greater improvement after training. Additionally, as indicated above, similar to former studies a placebo effect in the interventional group cannot be ruled out. Moreover, although attempts were made to perform the assessments of each visit at the same time and in the “On” phase of the patient, slight divergences regarding the timing after medication intake are possible. Additionally, as patients were allowed to keep their usual health interventions, it cannot be excluded that the reported improvement of gait was associated with concomitant physiotherapy, although the patient felt it was an effect of OT. Finally, the evaluation questionnaires were performed for all individuals at the end of the study, resulting in a ten week time interval from training to evaluation for the interventional group.

In conclusion, the findings of this study challenge the validity of the currently used standardized assessment tools to reflect the effect of individual occupational therapy training approaches in PD. To overcome the recurrent problem of insufficient capturing of treatment response in non-pharmacological and in particular OT trials, several basic principles regarding the selection of outcome parameters might be taken into account for future trials:

First, a balanced evaluation of the patients' and clinicians'/therapists' point of view, including most importantly an assessment of activity limitations and only secondary an assessment of motor impairment. Secondly, a clear distinction of both concepts of disability, activity limitations/participation restrictions on the one hand and motor impairment on the other hand. Thirdly, an assessment of individual treatment responses allowing a weighting of important limitations and impairments, following the principle of individualized medicine. Examples for already in PD evaluated rating scales are besides others: the Canadian Occupational Performance Measure for patient's evaluation of daily living activities (subjective, individualized) [21] and the Continuous-Scale physical functional performance test (objective, not individualized) [22,23], the Perceive, Recall, Plan and Perform system (objective, individualized) [24], Performance Assessment of Self-Care Skills (objective, not individualized) [25] and the USCD Performance-Based Skills assessment (objective, not individualized) [26]. Finally, future studies should consider the emerging role of OT in the treatment of non-motor symptoms such as cognitive impairment and as a support for psychosocial concerns.

Declaration of interest

Stefan Streich, Isabel Wurster, Robert Schubert and Sybille Wolfram have nothing to disclose. Eva Schaeffer received intramural research funding for a research rotation position from the University of Kiel and speaker's honoraria from Bayer Vital GmbH and Novartis. Dr. Reilmann is founding director and owner of the George-Huntington-Institute, a private research institute focused on clinical and preclinical research in Huntington's disease, and QuantiMedis, a clinical research organization providing Q-Motor (quantitative motor) services in clinical trials and research. He holds appointments at the Dept. of Radiology of the University of Muenster and at the Department of Neurodegenerative Diseases and Hertie-Institute for Clinical Brain Research, University of Tuebingen. Dr. Reilmann serves as elected member of the Steering Committees of the European Huntington Disease Network (EHDN) and the Huntington Study Group (HSG), co-chair of the Task Force on Huntington's disease and member of the Task Force on Technology of the International Parkinson and Movement Disorder Society (IPMDS). He has provided consulting services, advisory board functions, clinical trial services, quantitative motor analyses, and/or lectures for Actelion Pharmaceuticals, Amarin Neuroscience, AOP Orphan Pharmaceuticals, Cure Huntington Disease Initiative Foundation (CHDI), Desitin, Hoffmann-La Roche, IONIS Pharmaceuticals, Ipsen, Lundbeck, Link Medicine, MEDA Pharma, Medivation, Mitoconix, Neurosearch, Novartis AG, Omeros, Pfizer, Prana Biotechnology, Raptor Pharmaceuticals, Siena Biotech, Temmler Pharma, Teva Pharmaceuticals, uniQure, Vaccinex, Wave Life Sciences, and Wyeth Pharmaceuticals. He has received grant support from the Bundesministerium für Bildung und Forschung (BMBF), the Cure Huntington Disease Initiative Foundation (CHDI), the Deutsche Forschungsgemeinschaft (DFG), the Deutsches Zentrum für Neurodegeneration und Entzündung (DZNE), the European Union 7th Framework Program (EU-FP7), the European Huntington Disease Network (EHDN), the High-Q-Foundation, and the National Science Foundation (NSF). Daniela Berg reports grants from Janssen Pharmaceutica, grants from Michael J. Fox Foundation, grants from Damp foundation, grants from German Parkinson's Disease Association (dPV), grants from BMWi, grants from BMBF, grants from Parkinson

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