Parkinsonism and Related Disorders 65 (2019) 67–72

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Parkinsonian patients do not utilize probabilistic advance information in a grip-lift task

Leif Trampenau[a,*], Johann P. Kuhtz-Buschbeck[b], Thilo van Eimeren[c,d]

[a] Institute for Sexual Medicine and Forensic Psychiatry, Psychiatry, Centre for Integrative Psychiatry (ZIP gGmbH), Niemannsweg 147, D 24105, Kiel, Germany
[b] Institute of Physiology, Kiel University, Hermann-Rodewald-Str. 5, D 24118, Kiel, Germany
[c] Department of Nuclear Medicine, University Hospital Cologne, Germany
[d] Institute of Neuroscience and Medicine (INM-3), Research Center Jülich, Jülich, Germany

ARTICLE INFO

Keywords:
Parkinson's disease
Predictive force scaling
Motor system
Decision-making
Force rate
Probability

ABSTRACT

Introduction: Patients with Parkinson's disease (PD) are known to have decision-making impairments in tasks involving probabilistic information. How PD patients utilize task-relevant probabilistic advance information to plan and initiate common motor tasks like grasping has not yet been studied.
Methods: PD patients (n = 15, OFF medication) and control participants repeatedly grasped and lifted an object, the weight of which could be light, medium, or heavy. Visual cues provided explicit *probabilistic* information about the upcoming weight at the start of each grip-lift trial. This information allows the force of the grasping fingers to be scaled predictively so that it matches the likely weight, with a suitable rate of initial force increase. *Deterministic* cues announced the upcoming weight with certainty in other grip-lift trials. In a weight adjustment experiment, participants associated each probabilistic cue with a specific heaviness.
Results: The weight adjustment experiments showed that the probabilistic cues were understood correctly. However, PD patients utilized the probabilistic information significantly less than controls during the grip-lift task. Specifically, patients did not initiate their grasp more forcefully when probabilistic cues announced a high likelihood (66.7% probability) of a heavy weight, in contrast to controls. Thus, *probabilistic* cues that encouraged a more vigorous action had no effect in PD. Nevertheless, patients and controls scaled their forces appropriately when *deterministic* cues announced the forthcoming weights unambiguously.
Conclusions: PD patients do not invest a high movement effort to initiate a grip-lift unless the necessity of such a vigorous action initiation is decidedly clear.

1. Introduction

Predictions and associated decisions are often based on probabilities rather than on sure information. The choice of appropriate clothes based on weather forecast, the selection of a particular car when purchasing, or a job application: these are all cases in which the outcome is not fully predictable. Even simple motor acts, such as grasping and lifting diverse objects, require prediction of the objects' properties, namely heaviness, grip, and consistency, in order to allow the action to succeed fluently [1]. Unless the items being lifted are familiar, motor planning is based on assuming the most probable properties of the objects [2,3].

Parkinson's disease (PD) is not only associated with motor symptoms, but also interferes with executive functions such as making decisions [4–6]. Several studies have shown impaired decision-making of PD patients in probabilistic tasks [7–10] such as the Weather Prediction Task, where participants need to predict the likely weather outcome ("rain or sun") based on a combination of several probabilistic cues.

The utilization of probabilistic information for motor planning has, to our knowledge, not yet been investigated in PD. We therefore devised a task where participants repeatedly grasped and lifted an object that could have light, medium, or heavy weight, as presaged by visual cues that provided probabilistic information about the upcoming weight just before each trial. A cue could, e.g. indicate that the next weight would be light with a 66.7% probability or medium with a 33.3% probability. Utilization of such probabilistic information allows the force of the grasping fingers to be anticipatorily scaled to match the most likely upcoming weight. The peak rates of the initial force increase are known to reflect such predictive scaling [11]. We compared grip and lift force data of PD patients and healthy control participants.

To demonstrate whether PD patients can use arbitrary cues predicting object weight for motor planning at all [12,13], we included

* Corresponding author.
E-mail address: Leif.Trampenau@uksh.de (L. Trampenau).

https://doi.org/10.1016/j.parkreldis.2019.05.015
Received 14 September 2018; Received in revised form 18 January 2019; Accepted 9 May 2019

further grip-lift trials where deterministic cues announced the upcoming weight with certainty (probability 100%). Finally, to find out how patients and controls interpreted the probabilistic cues, we let them associate each cue with a particular weight by adjusting it gradually until the heaviness matched the participant's expectation. In line with reports of impaired performance in probabilistic decision-making tasks [7–10], we hypothesized that patients with PD might utilize probabilistic information in a grip-lift task less than control persons.

2. Methods

2.1. Participants and paradigm

15 patients with idiopathic PD (6 women; age 59 ± 9 years; UPDRS 41 ± 11; mean ± SD) and 15 healthy controls (6 women; age 59 ± 11 years) gave written informed consent to participate in this study (see supplementary data for details and neuropsychological tests). It had been approved by the local ethics committee (FN 114/12) and was conducted in accordance with the Declaration of Helsinki. PD patients were examined in the OFF state as in related studies [12,14]. Long-acting dopamine agonists were replaced with short-acting formulations 3 days prior to the experiments, and patients were studied after overnight withdrawal from antiparkinsonian medication. All participants were right-handed [15], had normal or corrected-to-normal vision, and did not show symptoms of dementia (supplementary table 1) or psychiatric conditions. They were naïve to the purpose of the study.

The participants sat at a table facing a monitor, their right forearm resting on the desk with a pad supporting the wrist. The grip object was a cuboid block (4 × 4x3 cm) attached to an adjustable lever, and was positioned close to the right thumb and index finger (Fig. 1A). The object's vertical grip surfaces were covered with sandpaper and equipped with force transducers, which measured the grip and load forces of the fingers with a sampling frequency of 50 Hz. The adjustable lever was connected via a non-elastic string to a computer-controlled linear actuator (STA1116, Dunkermotoren, UK), the pull force of which determined the object's weight. Three weights, 300 g (light), 800 g (medium) and 1400 g (heavy), were used. An optical sensor registered object position (see Refs. [16,17] for details).

Four probabilistic visual cues (LM,ML,MH,HM) were shown and explained (Fig. 1B). A blue rectangle could take one of four different positions in a frame. The lowest position (LM cue) indicated that the next object would be light in 66.7% of the trials and medium in 33.3%; the ML cue indicated 66.7% medium/33.3% light; MH indicated 66.7% medium/33.3% heavy; and the topmost position (HM) signified 66.7% heavy/33.3% medium. Hence each probabilistic cue explicitly specified the true probabilities of two possible object weights for the upcoming trial. Moreover, three other deterministic cues (images of bottles filled to distinct levels) were explained, which each indicated the upcoming object weight (light, medium, or heavy) with full prediction (100% certainty). We encouraged the participants to draw on all these cues to prepare their grip-lift actions.

At the onset of each trial, a cue was shown in full size on the monitor for one second (Fig. 1C). It then appeared in smaller (yet well recognizable) size beneath the target zone, indicating that the object should be grasped with a pinch grip between thumb, index and middle finger, and lifted ~3 cm high by a radial adduction of the wrist. Thereby the cue was moved into the target zone. There was no time limit to initiate the grip lift, and after lift-off, the participants had 1.5 s to reach the target zone with their self-selected speed. The small cue remained visible until 1.5 s after lift-off. A release cue then gave the signal to place the object back down and to release it. The next trial followed 3.5 s later. The task was fairly unchallenging with regards to speed and accuracy.

In an initial 10 min practice session, each participant was instructed how to handle the grip object, the cues were explained and all experimental conditions practiced (10 lifts of each weight, followed by 10 lifts with each of the probabilistic cues). In the following grip-lift experiment each participant performed 6 blocks of 25 grip-lift actions, with pauses between blocks. Probabilistic cues announced object

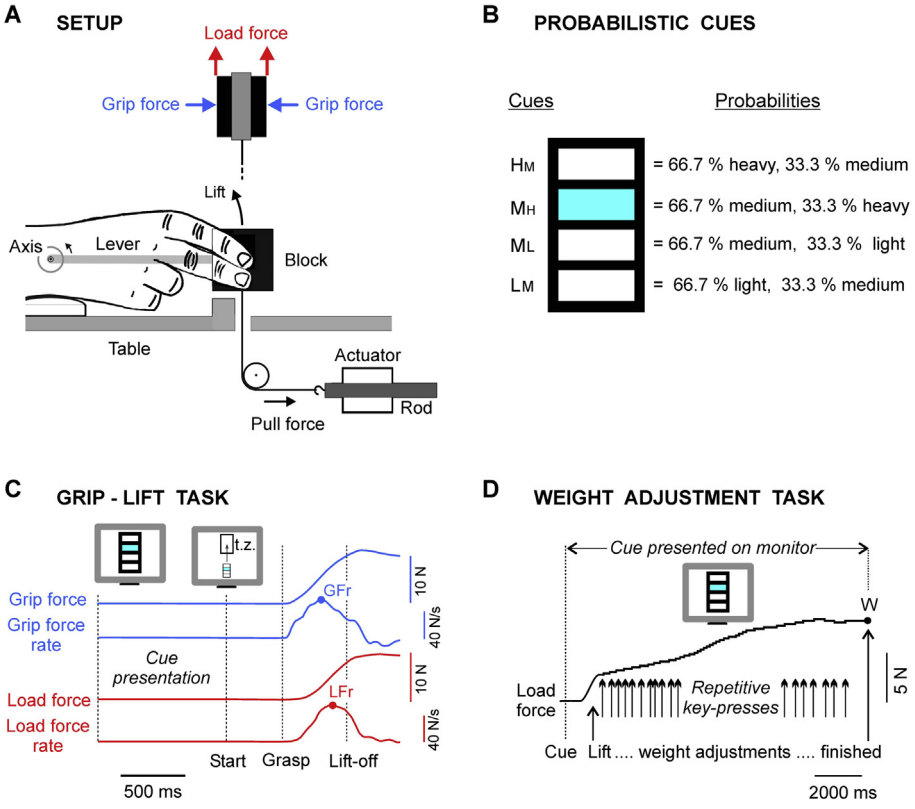

Fig. 1. Methods. **(A)** Setup. The grip object (a block with force transducers) was attached to an adjustable lever and connected via string to a hidden linear actuator, the pull force of which determined the object's weight. Grip force (GF) and load force (LF, vertical lifting force) of the grasping fingers were measured. **(B)** The four probabilistic visual cues (LM, ML, MH, HM). Each position of the blue rectangle in the frame indicated the probabilities of two possible object weights (here cue MH). **(C)** Grip-lift task. A probabilistic cue appeared for one second on the monitor, followed by the cue to start, and the target zone (t.z.). The object was then grasped and lifted. Peak grip force rate (GFr, blue dot) and peak load force rate (LFr, red dot) are typically reached before lift-off. **(D)** Weight adjustment task. A cue was shown and the object was lifted and held. Then its weight was adjusted by repetitive key-presses that changed the pull force of the linear actuator until the perceived weight W matched the probabilistic cue, which remained visible throughout the trial. Note the different time scales in (C) and (D). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

weight in 120 trials, with 60 lifts of the medium weight and 30 lifts each of the light and heavy weights. Deterministic cues (full prediction) announced weight in 30 trials (10 grip-lift trials for each cue/object weight combination). To avoid potential biasing effects of the preceding object weight on motor performance [11–13,18], the trials were performed in a pseudo-randomized order, where lifts of the medium weight announced by the four probabilistic cues were evenly preceded by the three object weights.

From the force curves and their time derivatives (force rate curves, Fig. 1c), six measures were determined: (1) peak grip force GF, (2) peak grip force rate GFr, (3) peak load force LF, (4) peak load force rate LFr, (5) load phase duration (LPD), and (6) time interval between GF onset (= GFr > 5 N/s) and LF onset (= LFr > 5 N/s) at the start of the grip-lift action. LPD lasted from LF onset until the object was lifted from its support (lift-off). No data filtering was performed; analyses were based on subject-wise averages of repeated trials.

In the subsequent weight adjustment experiment (Fig. 1D), participants associated each probabilistic cue with a specific object weight [17]. A cue was shown on the monitor and the object was lifted and held with the right hand; then the participant gradually changed its weight by pressing two keys (↑↓) on a computer keyboard with the left hand, until perceived heaviness matched weight W (unit of measure: gram) that he/she expected according to the probabilistic information. This was confirmed by pressing the space-bar, and the next trial followed. Each key-press changed the pull force of the actuator and thereby the object's weight by ~10 g. The initial (pre-adjustment) weight varied between 250 g and 1550 g. Each probabilistic cue was presented ten times in randomized order, so that 40 wt adjustment trials were performed. In total, the experiments (grip-lift and weight adjustment) lasted about one hour.

2.2. Data analysis

As in previous studies [16,17], we only analyzed trials in which the medium weight was grasped and lifted, yet preceded by the four different probabilistic cues (LM,ML,MH,HM). The peak force rates (GFr, LFr) and the adjusted weights W were plotted against the weights P predicted by the cues (Fig. 2). P was calculated as a weighted combination of the two possible weights, i.e., the P values were 1200 g [(0.67 × 1400 g) + (0.33 × 800 g)] for cue HM, 1000 g for cue MH, 633 g for cue ML, 467 g for cue LM. These values do not represent individual expectations but indicate statistical averages, in line with research that applies statistical decision theory to motor performance [19].

In trials where deterministic cues announced the object weight unambiguously, we tested for weight-dependent changes in the grip-lift variables. Analyses of variance (ANOVA) for repeated measurements with weight as within-subject factor (3 levels) were performed on the subject-wise means. Lifts of the medium weight, preceded by the four different probabilistic cues, were analyzed by testing for cue-dependent changes of the grip-lift variables, using ANOVA for repeated measurements with cue as within-subject factor (4 levels) on the subject-wise means. The same approach tested for cue-dependent changes of W in the weight adjustment experiment. One-tailed paired sample t-tests were calculated to test for cue-dependent increases, with $p < 0.0167$ after Bonferroni correction for multiple comparisons. For each contrast the effect size was calculated as Cohen's $d = (m_1 - m_2)/\sqrt{(s_1^2 + s_2^2)}/2$; [$m_{1,2}$ group means; $s_{1,2}$ standard deviations]. ANOVAs were initially calculated separately for PD patients and controls, followed by post-hoc mixed design within-between ANOVAs that tested for group differences and interactions. Statistical analyses were performed using the R project for statistical computing [20].

3. Results

Deterministic cues. Both controls and parkinsonian patients utilized deterministic cues that announced the upcoming object weight with 100% certainty to initiate their grip-lift actions accordingly. In control persons (Table 1, upper panel), we found significant weight-dependent changes of peak GF (ANOVA $F_{2,14} = 379.64$, $p < 0.001$), peak LF ($F_{2,14} = 15904.2$, $p < 0.001$), peak force rates (GFr: $F_{2,14} = 29.42$, $p < 0.001$; LFr: $F_{2,14} = 106.62$, $p < 0.001$), and of the load phase duration (LPD: $F_{2,14} = 62.20$, $p < 0.001$), which all increased with object weight (light < medium < heavy). Likewise, the patients with PD (Table 1, lower panel) showed significant weight-dependent increases of peak GF ($F_{2,14} = 265.85$, $p < 0.001$), peak LF ($F_{2,14} = 3697.63$, $p < 0.001$), peak GFr ($F_{2,14} = 6.31$, $p < 0.01$), peak LFr ($F_{2,14} = 33.99$, $p < 0.001$), and LPD (ANOVA

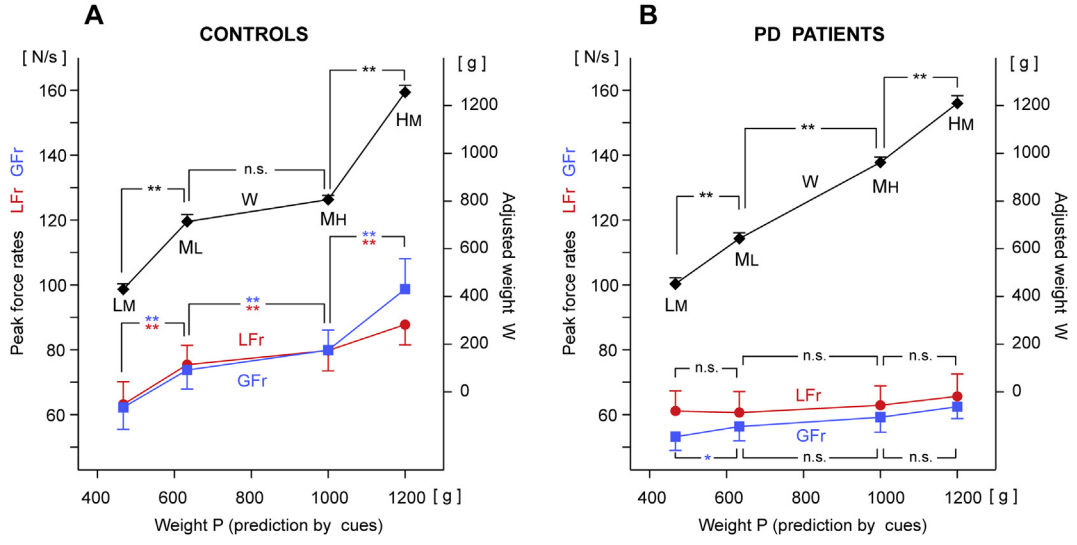

Fig. 2. Results. **(A)** The control participants' peak force rates LFr (red circles) and GFr (blue squares) increased significantly as weight P, predicted by the four probabilistic cues (LM, ML, MH, HM), increased (x-axis). Adjusted weight W (black diamonds), which should match the cues, also increased significantly with P. **(B)** The parkinsonian (PD) patients' grip and load force rates (GFr, LFr) showed little change across cues (only GFr between cues LM and ML [$p < 0.05$], otherwise not significant). Yet adjusted weight W increased significantly ($p < 0.01$) and almost linearly across cues. Actual object weight was always 800 g (medium) for the grip-lift trials shown here. Symbols denote mean values (± SEM). Asterisks indicate significant cue-dependent changes of W, GFr, LFr (paired t-tests, *$p < 0.05$, **$p < 0.01$). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Grip-lift parameters of trials where *deterministic* cues announced object weight unmistakably.

Healthy control participants						
Actual object weight [g]	300 (L)		800 (M)		1400 (H)	
Peak GF [N]	5.60 ± 2.45	d = 2.97 **	10.18 ± 1.72	d = 5.53 **	15.34 ± 1.32	
Peak LF [N]	3.86 ± 0.37	d = 21.87 **	8.60 ± 0.25	d = 28.34 **	14.51 ± 0.35	
Peak GFr [N/s]	56.5 ± 38.5	d = 0.61 **	75.0 ± 26.8	d = 1.35 **	100.2 ± 29.0	
Peak LFr [N/s]	48.3 ± 22.3	d = 1.60 **	74.8 ± 22.7	d = 1.34 **	100.0 ± 24.2	
Load phase duration [ms]	342 ± 127	d = 1.46 **	467 ± 126	d = 1.18 **	606 ± 161	
Interval GF-LF onset [ms]	−28 ± 48		−48 ± 58		−42 ± 49	
Patients with Parkinson's disease (PD)						
Actual object weight [g]	300 (L)		800 (M)		1400 (H)	
Peak GF [N]	7.00 ± 2.48	d = 2.59 **	10.70 ± 1.42	d = 4.89 **	15.16 ± 1.46	
Peak LF [N]	4.00 ± 0.83	d = 9.73 **	8.68 ± 0.48	d = 14.42 **	14.66 ± 0.67	
Peak GFr [N/s]	54.9 ± 22.8	d = 0.29 ns	59.1 ± 18.0	d = 0.64 ns	67.8 ± 20.5	
Peak LFr [N/s]	45.7 ± 19.5	d = 0.97 **	61.4 ± 25.8	d = 0.55 **	71.9 ± 28.2	
Load phase duration [ms]	583 ± 182	d = 1.56 **	776 ± 167	d = 1.93 **	994 ± 151	
Interval GF-LF onset [ms]	−73 ± 132		−44 ± 90		−43 ± 56	

Means ± standard deviations of individual means (n = 15 participants per group; ten trials per object weight per person).
d = effect size (Cohen's d). Asterisks indicate significant differences between values in adjacent columns.
*p < 0.05; **p < 0.01 (t-tests for paired samples; Bonferroni corrected for multiple comparisons). ns, not significant.

$F_{2,14} = 72.15$, $p < 0.001$). Effect sizes were smaller than in controls for the GFr (Table 1, lower panel, Cohen's d). A post-hoc mixed within-between 3 × 2 ANOVA indicated significant interactions between weight and group for GF ($F_{2,56} = 5.021$, $p < 0.01$), GFr ($F_{2,56} = 34.95$, $p < 0.001$), and LFr ($F_{2,56} = 14.4$, $p < 0.001$). The peak force rates were lower in parkinsonian patients than in controls (GFr: $F_{1,28} = 14.68$, $p < 0.001$; LFr: $F_{1,28} = 9.76$, $p < 0.001$), and their load phase lasted longer ($F_{1,28} = 45$, $p < 0.001$). In other words, the patients with PD needed more time than controls to lift the object due to a slower build-up of their forces, but their initial force increase was scaled according to the deterministic cues.

Probabilistic cues. Healthy age-matched volunteers grasped and lifted the same object of medium weight (800 g) in different ways, depending on the probabilistic cue shown at the onset of each trial (Fig. 2A; Table 2, upper panel). ANOVA indicated significant cue-dependent changes of the peak GF ($F_{3,14} = 30.15$, $p < 0.001$), GFr ($F_{3,14} = 26.26$, $p < 0.001$), LFr ($F_{3,14} = 22.57$, $p < 0.001$), and LPD ($F_{3,14} = 12.61$, $p < 0.01$). Peak GF and force rates (GFr, LFr) increased step-wise and significantly ($p < 0.01$) in progression with the predicted weight (LM < ML < MH < HM), while LPD shortened progressively (LM > ML > MH > HM). Thus, initial buildup of the force was enhanced and the 800 g object was lifted earlier by control participants when probabilistic cues predicted higher upcoming weights P. The adjustment task showed significant cue-dependent changes of the adjusted weight W ($F_{3,14} = 189.03$, $p < 0.001$) in controls. This effect was non-linear because cues ML and MH were associated with similar weights (Fig. 2A).

The probabilistic cues had little effect on grip-lift actions of parkinsonian patients. Only two cue-dependent changes of pertinent variables were found (Fig. 2B, lower panel of Table 2). ANOVA showed significant cue-dependent changes of peak GF ($F_{3,14} = 15.16$, $p < 0.001$) and GFr ($F_{3,14} = 7.82$, $p < 0.01$), while the other parameters remained unaltered. Patients lifted the medium weight (800 g) with a slightly reduced grip force rate GFr when it was preceded by probabilistic cue LM, as compared to cue ML (LM < ML). Unlike controls, patients showed no progressive step-wise increases of their force rates when probabilistic cues MH and HM indicated possibly heavier weights (Table 2). In other words, patients did not initiate their grip-lift actions more vigorously when such cues appeared; motor performance was nearly the same for cues ML, MH, and HM (note

Table 2
Grip-lift parameters of trials where *probabilistic* cues predicted the object weight.

Probabilistic cues	LM		ML		MH		HM
Probability ratio	66.7% L/33.3% M		66.7% M/33.3% L		66.7% M/33.3% H		66.7% H/33.3% M
Predicted object weight P [g]	467		633		1000		1200
Actual object weight [g]	800		800		800		800
Healthy control participants							
Peak grip force [N]	9.06 ± 1.41	d = 1.00 **	9.95 ± 1.06	d = 0.76 **	10.57 ± 1.25	d = 1.24 **	12.12 ± 2.14
Peak load force [N]	8.58 ± 0.27	d = 0.04 ns	8.58 ± 0.28	d = 0.12 ns	8.61 ± 0.27	d = 0.06 ns	8.62 ± 0.25
Peak grip force rate [N/s]	62.3 ± 26.1	d = 0.67 *	73.8 ± 22.6	d = 0.37 **	79.9 ± 23.9	d = 0.86 **	98.7 ± 36.4
Peak load force rate [N/s]	63.2 ± 26.7	d = 0.70 **	75.4 ± 23.0	d = 0.26 **	79.8 ± 24.3	d = 0.47 **	87.7 ± 23.9
Load phase duration [ms]	617 ± 174	d = 1.02 **	498 ± 155	d = 0.40 **	456 ± 141	d = 0.40 **	414 ± 152
Interval GF-LF onset [ms]	−20 ± 39		−27 ± 38		−41 ± 47		−45 ± 51
Adjusted weight W [g]	429.6 ± 88.9	d = 3.90 **	713.8 ± 115.5	d = 1.35 ns	805.3 ± 71.6	d = 6.72 **	1255.6 ± 113.3
Patients with Parkinson's disease (PD)							
Peak grip force [N]	9.78 ± 1.08	d = 0.83 **	10.39 ± 1.01	d = 0.50 ns	10.75 ± 1.04	d = 0.37 ns	11.03 ± 1.04
Peak load force [N]	8.52 ± 0.46	d = 0.16 ns	8.57 ± 0.41	d = 0.11 ns	8.54 ± 0.45	d = 0.22 ns	8.60 ± 0.44
Peak grip force rate [N/s]	53.2 ± 16.3	d = 0.27 *	56.4 ± 17.1	d = 0.23 ns	59.2 ± 18.0	d = 0.25 ns	62.5 ± 18.4
Peak load force rate [N/s]	61.1 ± 24.2	d = 0.03 ns	60.7 ± 24.9	d = 0.13 ns	62.9 ± 23.1	d = 0.16 ns	65.8 ± 26.7
Load phase duration [ms]	759 ± 213	d = 0.15 ns	779 ± 154	d = 0.20 ns	757 ± 165	d = 0.10 ns	746 ± 145
Interval GF-LF onset [ms]	−42 ± 94		−38 ± 80		−48 ± 79		−53 ± 58
Adjusted weight W [g]	452.1 ± 97.2	d = 2.81 **	642.2 ± 94.1	d = 4.95 **	961.3 ± 88.0	d = 3.33 **	1209.3 ± 124.3

Each cue specified the probabilities of two out of three possible object weights (L, light; M, medium; H, heavy) for the upcoming trial (see methods). Actual object weight was always 800 g (medium) in the grip-lift trials analyzed here. Means ± standard deviations of the individual means (n = 15 persons per group; with 10–20 trials per cue in each subject). Asterisks indicate significant differences between values in flanking columns; *p < 0.05; **p < 0.01 (t-tests for paired samples; Bonferroni corrected for multiple comparisons). ns, not significant. d, effect size (Cohen's d).

nearly “flat lines” of force rates, Fig. 2B).

Nevertheless, PD patients assigned different weights to the four probabilistic cues in the weight adjustment experiment. ANOVA indicated significant cue-dependent changes of W ($F3,14 = 240.70$, $p < 0.001$), which increased significantly ($p < 0.01$) with the predicted weight (LM < ML < MH < HM) in an almost linear fashion (Fig. 2B). Hence, patients realized the cues' probabilistic predictions, but did not implement this information during the grip-lift actions.

A mixed design 4 × 2 ANOVA indicated significant interactions between probabilistic cue and group for peak GF ($F3,84 = 8.62$, $p < 0.001$), GFr ($F3,84 = 11.96$, $p < 0.001$), LFr ($F3,84 = 10.57$, $p < 0.001$), and for the adjusted weight W ($F3,84 = 9.549$, $p < 0.001$). The group comparison revealed bradykinesia of the patients, with reduced peak force rates, lower peak LF and a prolonged load phase (GFr: $F1,28 = 65.25$, $p < 0.001$; LFr: $F1,28 = 56.28$, $p < 0.001$; peak LF: $F1,28 = 7.04$, $p < 0.01$; LPD: $F1,28 = 265.01$, $p < 0.001$). Higher UPDRS scores were associated with somewhat lower peak LFr and longer LPD during lifts of the medium and heavy object (see supplementary table 2 for correlation coefficients). Typical force and force rate curves are shown as supplementary figures.

4. Discussion

We studied how patients with PD (and healthy volunteers) utilize priori weight information to scale their fingertip forces predictively in a grip-lift task. When object weight was announced unambiguously by *deterministic* cues, patients and controls initiated their actions with rates of force increase that matched the forecast (light, medium, or heavy object). Also an earlier study [12] reported that parkinsonian patients scale the grip force of either hand predictively when arbitrary color cues provide advance information about object weight, an ability that was not influenced by dopaminergic medication. The main new finding of the present study, however, is that PD patients barely utilize explicit *probabilistic advance information* about object weight in grip-lift tasks. In contrast, age-matched control participants exploit such information, as evident from the significant effect had by probabilistic cues on their force rates. Note that the actual weight was always 800 g (medium) in the analyzed trials, so probabilistic advance information changed how the same motor task was executed. This is in congruence with our previous two studies conducted with young volunteers [16,17].

PD patients struggle to process probabilistic information accurately, and therefore struggle with probabilistic decision-making tasks [7–10]. A possible explanation for the present results might thus be that patients misinterpreted the probabilistic cues. However, the weight adjustment experiments contradict this. Here the patients associated the four cues with four markedly different weights (Fig. 2B). Unlike in tasks where participants need to learn about the reliability and validity of probabilistic information predicting an outcome, such as gambling tasks [10], we explained the meaning of the probabilistic cues clearly at the onset of the experiment, and this seemed to have been understood.

So why did PD patients not implement the probabilistic advance information during grip-lift trials? Dissimilar time scales may play a role, since ample time for cognition and continuous proprioceptive and tactile feedback were available for weight adjustments (mean trial duration ~15 s), whereas grip-lifts were initiated within about a second. Interestingly, the patients applied slightly but significantly less grip force (Fig. 2B) when cue LM announced a high likelihood of a light weight, but did not grasp more vigorously when heavier weights were indicated by probabilistic cues MH and HM. Dopamine is known to exert a powerful influence on the vigor, strength and rate of response in a variety of tasks [21]. It is implicated in reward-based learning and accelerates reward-driven choices [22], assigning incentive values to objects or behavioral acts [23]. Rewards can negate the cost of increased effort associated with vigorous movements [24]. We examined PD patients after overnight withdrawal of antiparkinsonian medication. Due to lack of dopamine, they may have had difficulties to invest high movement effort at the moment of grip-lift initiation, when the necessity of such vigorous action was dubious (probabilistic cues); however, they did increase their force rates when this was inevitable, e.g. when a deterministic cue unmistakably announced a heavy weight. There was no extrinsic reward (like monetary gain) for vigorous actions, which may not represent a valuable goal *per se*. In line with this, Mazzoni and colleagues hypothesized that bradykinesia in PD reflects impairments in the link between motivation and the control of movement gain, resulting in a higher sensitivity to movement energy costs [25].

The lower peak force rates and prolonged load phases of patients with PD (compared to controls) indicate bradykinesia, in line with previous grip-lift studies [14,26,27]. Yet we did not find excessive maximum grip forces in those patients who were OFF medication, unlike other reports where GF overshoots possibly occurred as a result of levodopa treatment and/or dyskinesia in PD [28,29]. The grip and load forces were initiated nearly simultaneously and increased largely in parallel in both, PD patients and control participants (see supplementary data).

This study is not without limitations. Due to the rather small number of patients and controls, small (intra-group) effects of the probabilistic cues may have been underestimated, since there is an inverse relationship between variance and sample size. PD patients were exclusively examined OFF medication. Experiments ON medication and correlations with neuropsychological test results (visuomotor processing, decision-making) might be future issues. It could be interesting whether other cues (auditory, tactile) yield similar results. Our paradigm necessitated a rather high total number of 150 grip-lift trials. The sampling rate (50 Hz) of the force transducer, custom-made for fMRI studies that we plan to conduct, was rather low. Still, previous research [16,17] and the original force curves (supplementary material) show that the data are valid for evaluation. The order of the grip-lift and weight adjustment experiments was deliberately fixed, so that the order effect, which we demonstrated earlier [17], remained uniform across participants.

In conclusion, the present study shows for the first time that parkinsonian patients do not exploit relevant probabilistic advance information to plan and initiate a common motor act (grasping and lifting an object). This has implications for physical therapy and rehabilitation of PD patients, where cues guiding movements should be explicit, simple and direct. Examples are the BIG program, adapted from the Lee Silverman Voice Treatment, which aims to increase the amplitude of limb and body movement, and cueing techniques for gait improvement [30].

Acknowledgements

The authors thank the patients and control persons for their participation, and Oliver Granert, Anke Hoff, Kirsten Zeuner, Angelika Troyke, Bettina Möller, Nele Schmidt and Martin Müller for their support with the experiments and the construction of the setup, and Holly McKelvey for diligent proofreading. This study was supported by the Deutsche Forschungsgemeinschaft (DFG) by grant EI 892/3–1 to TvE.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.05.015.

Availability of data

The authors state that other data supporting the findings of this study are available within the supplementary information and in a file that can be downloaded at http://www.physiologie.uni-kiel.de/en/research/sensorimotor-control/research-interests.

Contributions

L.T.: data acquisition, evaluation and interpretation, study design, writing first draft of the manuscript. J.P. K–B: establishing the method, data interpretation, revisions of manuscript, intellectual content. T.v.E.: study concept and design, data interpretation, critical revision of manuscript for intellectual content.

Conflicts of interest

The authors have no conflicts of interest to declare.

Funding

There are no sources of funding to declare.

References

[1] A.M. Gordon, G. Westling, K.J. Cole, R.S. Johansson, Memory representations underlying motor commands used during manipulation of common and novel objects, J. Neurophysiol. 69 (1993) 1789–1796.
[2] G. Buckingham, J.S. Cant, M.A. Goodale, Living in a material world: how visual cues to material properties affect the way that we lift objects and perceive their weight, J. Neurophysiol. 102 (2009) 3111–3118.
[3] L.A. Baugh, M. Kao, R.S. Johansson, J.R. Flanagan, Material evidence: interaction of well-learned priors and sensorimotor memory when lifting objects, J. Neurophysiol. 108 (2012) 1262–1269.
[4] E. Gleichgerrcht, A. Ibáñez, M. Roca, T. Torralva, F. Manes, Decision-making cognition in neurodegenerative diseases, Nat. Rev. Neurol. 6 (2010) 611–623.
[5] D.M. Herz, R. Bogacz, P. Brown, Neuroscience: impaired decision-making in Parkinson's disease, Curr. Biol. 26 (2016) R671–R673 https://doi.org/10.1016/j.cub.2016.05.075.
[6] A. Perugini, J. Ditterich, A.G. Shaikh, B.J. Knowlton, M.A. Basso, Paradoxical decision-making: a framework for understanding cognition in Parkinson's disease, Trends Neurosci. 41 (2018) 512–525.
[7] M. Mimura, R. Oeda, M. Kawamura, Impaired decision-making in Parkinson's disease, Park. Relat. Disord. 12 (2006) 169–175.
[8] A. Ryterska, A.J.L. Harris, A. Ejova, M. Jahanshahi, M. Osman, Investigating decision-making in Parkinson's disease in tasks characterized by probabilistic cue-outcome associations: the role of optimality, Ann. Neurosci. Psychol. 1 (2014) 2–10.
[9] D. Shohamy, C.E. Myers, S. Onlaor, M.A. Gluck, Role of basal ganglia in category learning: how do patients with Parkinson's disease learn? Behav. Neurosci. 118 (2004) 676–686.
[10] T. Gescheidt, K. Czekoova, T. Urbanek, R. Marecek, M. Mikl, R. Kubikova, S. Telecka, H. Andrlova, I. Husarova, M. Bares, Iowa Gambling Task in patients with early-onset Parkinson's disease: strategy analysis, Neurol. Sci. 33 (2012) 1329–1335.
[11] D.A. Nowak, S. Glasauer, J. Hermsdörfer, Force control in object manipulation – a model for the study of sensorimotor control strategies, Neurosci. Biobehav. Rev. 37 (2013) 1578–1586.
[12] D.A. Nowak, M. Ameli, F. Kemper F, A.S. Sarfeld, D. Bensmail, J. Konczak, G.R. Fink, Arbitrary visuomotor mapping during object manipulation in Parkinson's disease, Mov. Disord. 24 (2009) 1925–1933.
[13] M. Ameli, M. Dafotakis, G.R. Fink, D.A. Nowak, Predictive force programming in the grip-lift task: the role of memory links between arbitrary cues and object weight, Neuropsychologia 46 (2008) 2383–2388.
[14] A.M. Gordon, P.E. Ingvarsson, H. Forssberg, Anticipatory control of manipulative forces in Parkinson's disease, Exp. Neurol. 145 (1997) 477–488.
[15] R.C. Oldfield, The assessment and analysis of handedness: the Edinburgh inventory, Neuropsychologia 9 (1971) 97–113.
[16] L. Trampenau, J.P. Kuhtz-Buschbeck, T. van Eimeren, Probabilistic information on object weight shapes force dynamics in a grip-lift task, Exp. Brain Res. 233 (2015) 1711–1720.
[17] L. Trampenau, T. van Eimeren, J.P. Kuhtz-Buschbeck, Processing of probabilistic information in weight perception and motor prediction, Atten. Percept. Psychophys. 79 (2017) 404–414.
[18] K.J. Cole, D.L. Rotella, Old age impairs the use of arbitrary visual cues for predictive control of fingertip forces during grasp, Exp. Brain Res. 143 (2002) 35–41.
[19] D.M. Wolpert, M.S. Landy, Motor control is decision-making, Curr. Opin. Neurobiol. 22 (2012) 996–1003.
[20] R Development Core Team, R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, https://www.r-project.org, (2008).
[21] Y. Niv, N.D. Daw, D. Joel, P. Dayan, Tonic dopamine: opportunity costs and the control of response vigor, Psychopharmacology 191 (2007) 507–520.
[22] P. Smittenaar, H.W. Chase, E. Aarts, B. Nusselein, B.R. Bloem, R. Cools, Decomposing effects of dopaminergic medication in Parkinson's disease on probabilistic action selection – learning or performance? Eur. J. Neurosci. 35 (2012) 1144–1151.
[23] S.M. McClure, N.D. Daw, P.R. Montague, A computational substrate for incentive salience, Trends Neurosci. 26 (2003) 423–428.
[24] E.M. Summerside, R. Shadmehr, A.A. Ahmed, Vigor of reaching movements: reward discounts the cost of effort, J. Neurophysiol. 119 (2018) 2347–2357.
[25] P. Mazzoni, A. Hristova, J.W. Krakauer, Why don't we move faster? Parkinson's disease, movement vigor, and implicit motivation, J. Neurosci. 27 (2007) 7105–7116.
[26] S.J. Fellows, J. Noth, Grip force abnormalities in de novo Parkinson's disease, Mov. Disord. 19 (2004) 560–565.
[27] D. Kandaswamy, M. Muthukumar, M. Alexander, K. Prabhu, M. Gowri, S.B. Krothapalli, Quantitative assessment of hand dysfunction in patients with early Parkinson's disease and focal hand dystonia, J. Mov. Disord. 11 (2018) 35–44.
[28] A.M. Gordon, R. Reilmann, Getting a grasp on research: does treatment taint testing of parkinsonian patients? Brain 122 (1999) 1597–1598.
[29] R. Wenzelburger, B.R. Zhang, M. Poepping, B. Schrader, D. Müller, F. Kopper, U. Fietzek, H.M. Mehdorn, G. Deuschl, P. Krack, Dyskinesias and grip control in Parkinson's disease are normalized by chronic stimulation of the subthalamic nucleus, Ann. Neurol. 52 (2002) 240–243.
[30] S.J. Spaulding, B. Barber, M. Colby, B. Cormack, T. Mick, M.E. Jenkins, Cueing and gait improvement among people with Parkinson's disease: a meta-analysis, Arch. Phys. Med. Rehabil. 94 (2013) 562–570.