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RESEARCH ARTICLE

Leakage of decision uncertainty into movement execution in Parkinson's disease?

Peter Praamstra · Andrea F. Loing · Floris P. de Lange

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Abstract The concept of segregated basal ganglia–cortical loops entails that functional disturbances may result from abnormal processing *within* loops, but also from abnormal communication *between* loops. Cognitive and motor processes subserved by different basal ganglia–frontal loops may interfere with one another as a result of such abnormal communication, leakage, between loops. In Parkinson's disease, movement execution has been found susceptible to decision uncertainty, attributed to this mechanism. Here, we evaluate whether this mechanism of abnormal coupling or leakage extends to perceptual decision-making with trial-by-trial control of decision uncertainty. We examined 10 Parkinson's disease (PD) patients and healthy control subjects in a random-dot motion direction discrimination task with concurrent EEG recording. Random-dot motion was manipulated to make direction discrimination easy or difficult. Reaction times (RT) and movement times (MT) were recorded, and EEG was analysed to extract movement-related potentials. Easy versus difficult direction discrimination produced robust, equally large RT differences in patients and controls (>400 ms), along with a marked difference in error rates, confirming the efficacy of the task. Effects of easy versus difficult discrimination on MT were comparatively small (<50 ms) and did not differ between groups, despite robustly slower MT in patients. Lateralised movement-related EEG potentials reproduced the MT difference between patients and controls. Together, the results do not demonstrate an enhanced effect of decision uncertainty onto movement execution in PD. We surmise that leakage of decision uncertainty into movement execution is probably task-dependent, consistent with the view that the degree to which partial information is allowed to influence the motor system is under strategic control.

Keywords Parkinson's disease · Basal ganglia · Dopamine · Motor cortex · Decision-making

P. Praamstra (✉) · A. F. Loing
Department of Neurology, Radboud University Medical Centre, Radboud University Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands
e-mail: p.praamstra@neuro.umcn.nl

P. Praamstra · F. P. de Lange
Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, The Netherlands

P. Praamstra · A. F. Loing · F. P. de Lange
Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, Nijmegen, The Netherlands

Introduction

The activity of the basal ganglia and cerebral cortex is closely coordinated in the control of behaviour. Basal ganglia–thalamocortical interactions are mediated by a set of parallel circuits connecting different functional regions of the cerebral cortex and the basal ganglia (Alexander et al. 1986; Middleton and Strick 2002; Redgrave et al. 2010). Moreover, a topographical differentiation is maintained throughout the course of these loops from cortex through the basal ganglia and thalamus back to the cortex (for discussion see Bar-Gad and Bergman 2001). This layout of parallel loops provides a powerful concept to explain the great variety of symptoms of basal ganglia disease. However, it is also recognised that the architecture of parallel loops may itself be affected in basal ganglia disease. Thus, it has been proposed that normally independent processes, subserved by different circuits, may interfere with one another as a result of abnormal communication between

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normally segregated loops (Pessiglione et al. 2005). The possibility of such a de-segregation is supported by evidence that the relative independence of these loops is maintained by the dopaminergic innervation of the striatum (Bergman et al. 1998; Filion et al. 1988, 1994). Empirical evidence for interference based on de-segregation was suggested by the observation that movement execution in Parkinson patients is abnormally susceptible to decision uncertainty. Pessiglione et al. (2005) described this susceptibility as abnormal temporal coupling of decision and movement execution processes. Specifically, they observed increased movement times with increased uncertainty in untreated Parkinson patients, reflecting interference between deliberation and execution processes.

To evaluate the range of behavioural manifestations of this pathophysiological mechanism, the present paper examines temporal coupling of decision and movement execution processes in a task very different from the one in which it was originally described. Pessiglione et al. (2005) used a go–nogo task in which participants, by means of trial and error, acquired an implicit learning rule that determined whether a stimulus required a go or a nogo response. Reaction times and movement times during the trial and error learning process were compared with those during successful application of the implicit rule once it was learned. This comparison showed that decision uncertainty slowed reaction times in both control subjects and PD patients. By contrast, movement times were only affected in patients, giving rise to the notion of abnormal temporal coupling of decision and movement execution in PD.

In the present study, we use a well-known perceptual decision task that has been extensively used in investigations into the neural basis of decision-making (Gold and Shadlen 2007; Roitman and Shadlen 2002; Shadlen and Newsome 1996). The perceptual decision concerns the predominant direction of motion in an array of moving dots. The difficulty of this decision can be influenced by varying the amount of dots that move in a coherent fashion in one direction. Decision uncertainty is thus manipulated on a trial-by-trial basis, instead of gradually over the course of multiple trials during the learning of an implicit decision rule, as in Pessiglione et al. (2005). Varying the difficulty of the perceptual discrimination will have an effect on both the decision time (reaction time) and the error rate as indices of decision uncertainty. The subsequent movement expressing the perceptual decision may also be affected by decision uncertainty, with a prolonged movement time when the discrimination is difficult. Any such prolongation should affect PD patients more than controls, if leakage of uncertainty into movement execution in PD generalises to this perceptual task.

Another important feature of this task is that neural indices of motor cortical activity can be exploited to monitor the evolving decision process (Donner et al. 2009; De Lange et al. 2013). Here, we used lateralised movement-related potentials to complement reaction and movement time measures. Beyond timing information, lateralised movement-related potentials, developing during the viewing of the random-dot motion stimuli, might contribute insight into the abnormal coupling of deliberation and movement execution. Specifically, choice-predictive lateralisation of movement-related potentials could differ between patients and control subjects during the build-up of this activity and at the transition between decision-predictive and movement-related activity. At the transition, i.e. at movement onset, one should normally see lateralisation of a fixed amplitude, independent of the reaction time (Gratton et al. 1988). Abnormal termination of the decision phase, with leakage into movement execution, could be manifested in loss of this fixed relationship between movement-related EEG amplitude and movement onset.

Methods

Participants

Ten patients with Parkinson's disease (8 male, 2 female) participated in this study. All but one were right-handed. They all fulfilled established criteria for diagnosis of the disease (Hughes et al. 1992). Demographic details are provided in Table 1. The patients were recruited from the Parkinson Centre in the neurology department of the University Medical Centre Nijmegen. Ten age-matched control subjects (7 male, 3 female; all right-handed) were recruited from a research subject pool of healthy participants.

Table 1 Demographic data of the participating PD patients

Patient no.	M/F	Age	Medication (LED/day, mg)	Time since diagnosis (year)	UPDRS
1	M	65	200	1	29
2	F	54	300	1	18
3	M	56	995	12	55
4	M	60	1,350	11	33
5	M	53	500	2	34
6	M	63	1,325	11	38
7	M	61	525	8	22
8	F	69	1,000	15	37
9	M	59	900	10	19
10	M	71	700	6	33

The UPDRS rating was performed after overnight withdrawal from medication

LED levodopa equivalent dose (Tomlinson et al. 2010), *UPDRS* Unified Parkinson's Disease Rating Scale

The PD patients were selected on the basis of having mild to moderate disease severity and little or no tremor, so as not to induce movement artefacts in EEG recordings. The investigation and Unified Parkinson's Disease Rating Scale (UPDRS) rating were performed after overnight withdrawal from medication (≥10 h after last dosage). The control subjects were free of any history of neurological or psychiatric disease. The study was conducted with the understanding and written consent of all participants and was approved by the regional ethical review board.

Task, apparatus and procedure

The task involved repeated judgements of the motion direction in dynamic random-dot patterns presented on a computer screen. On each trial, a circular array was shown containing dots that moved in random directions and dots that moved to the left or the right. Participants were asked to decide whether motion direction was to the right or to the left and expressed their judgement through a movement of the corresponding hand. The difficulty of the motion direction discrimination was manipulated by varying the percentage of dots that moved coherently to the left or right. Thus, there were low and high coherence conditions for left and right motion directions, yielding four conditions altogether: low coherence right, low coherence left, high coherence right, high coherence left.

The circular array with moving dots consisted of an annulus with outer radius of 9.5 cm and inner radius of 1 cm. At the standard viewing distance of 80 cm, this corresponds to 6.8° and 0.72° of visual angle. Moving white dots (density = 2.2 dots/degree^2; speed = 6°/s) were superimposed on the black annulus, presented on an LCD monitor with refresh rate of 60 Hz. The direction of net motion of the dots was either leftward or rightward. For each frame, a random subset of the dots was chosen to carry the coherent motion. Incoherent dots moved randomly with the same speed as the coherent dots. When dots moved off the annulus, they were replotted at a random location within the annulus. The two levels of motion coherence (low and high) were 15 and 70 %, respectively. These values were based on pilot testing and resulted in a substantial reaction time difference between the conditions. Crucially, the 15 % coherence value in the low coherence condition ensured the direction discrimination to be so difficult that participants felt they were guessing most of the time, while in actual fact they remained above chance performance. The stimuli were presented on a grey background. Stimulus generation and experiment control were realised using the Psychophysics Toolbox (Brainard 1997; Pelli 1997) in MATLAB (MathWorks, Natick, MA, USA), running on a Hewlett-Packard PC with 24-inch monitor.

Moving dot stimuli were displayed until a response was made, to a maximum display time of 3,000 ms. A new trial started with the display of the next moving dot array 2.5 s after the response to the previous stimulus. Subjects were instructed to respond as soon as they perceived the motion direction and to make a choice before the stimulus was extinguished, even if they felt uncertain (forced choice procedure). Responses were made by movement of the left or right hand from a home key to a response key. The keys measured 7 × 7 cm and were mounted virtually level in a response panel. The weight of the resting fingers was sufficient to keep the keys depressed until the subject moved one or the other hand to the response key 20 cm in front of the home key. The home keys for left and right hand were mounted at a distance of 18 cm from one another (centre-to-centre). The distance between the response keys for the left and right hand was 28 cm. Release of the home key and depression of the response key allowed the measurement of reaction time and movement times. Reaction time was defined as the time from the start of the dot pattern until the release of the home key. Movement time was defined as the time between release of the home key and depression of the response key.

The experiment was run in a semi-dark room. Subjects were first familiarised with the task including a brief test to establish whether they were able to perceive motion direction with the coherence values used in the experiment. They were subsequently prepared for EEG recording and then performed one practice block. The experiment itself consisted of 8 blocks of ~5 min duration each. There were a few minutes rest between each block and a 10–15 min break halfway through the experiment. The rest intervals between blocks were also used to encourage participants, who generally tended to get frustrated by the uncertainty engendered by the difficult low coherence condition. Each block consisted of 68 trials, composed of an equal number of trials from each condition and arranged in random order. The number of trials per condition was 136.

EEG recording

EEG was recorded continuously with BioSemi ActiveTwo DC amplifiers from 132 Ag/AgCl scalp electrodes relative to the common mode sense (CMS) and driven right leg (DRL) electrodes, which were placed adjacent to the Cz (vertex) electrode location. Electrodes were placed according to the 10–5 extension of the international 10–20 electrode system (Oostenveld and Praamstra 2001), using a carefully positioned elastic nylon cap. Electrooculography (EOG) electrodes were positioned lateral to the left and right eyes in order to monitor horizontal eye movements. EEG and EOG signals were sampled at 512 Hz (anti-alias filter −3 dB at 102 Hz).

Analysis

The continuous EEG data were re-referenced to an average reference and subsequently subjected to an eye-blink and eye-movement correction based on a source modelling approach (Berg and Scherg 1994) implemented in Brain Electrical Source Analysis 5.1.8 (BESA; MEGIS software GmbH). After eye-blink and eye-movement correction, the continuous data were segmented into epochs from 500 ms before to 2,500 ms after stimulus onset for those trials with a correct behavioural response. The segmented data were checked for artefacts with a semi-automatic procedure and individually adjusted artefact thresholds. Trials with artefacts were rejected. Based on the segmented artefact-free individual trials, averaged data were created for each participant and condition separately. The same procedure was followed to extract averages per subject and condition relative to the response onset (release of the home key) for each trial, and averages relative to response completion (depression of the response key). These latter two response-locked data sets used segments of −3 s before to 2 s after the respective response triggers.

The response-locked averages per subject and condition were used to derive lateralised readiness potentials (LRPs), representing motor cortex activity associated with the preparation and execution of the response. The LRP is computed, for electrodes C3 and C4 overlying the left and right motor cortex, according to the formula $\mathrm{LRP} = ((\mathrm{C3} - \mathrm{C4})_{\text{right hand movement}} + (\mathrm{C4} - \mathrm{C3})_{\text{left hand movement}})/2$. The LRP was computed for each pair of homologous left/right hemiscalp electrodes. Based on inspection of its topography, we pooled the LRP waveforms from electrode pairs C3/C4, C1/C2, FCC3h/FCC4h and CCP3h/CCP4h for further analysis. As the LRP waveforms are computed from signals recorded at homologous electrodes overlying left and right scalp, its topography was evaluated by projecting the LRP over one hemisphere and replicating the waveforms with opposite polarity over the other hemisphere, according to Praamstra et al. (1996).

LRP onset latencies were analysed with a jackknifing procedure, in which every participant's LRP waveform is replaced by a subaverage waveform across the other $n - 1$ participants. The subsample LRP onsets were submitted to a conventional mixed-design ANOVA with between-subject factor Group (PD patients, control subjects) and within-subject factor Difficulty (high coherence, low coherence). To correct for the reduced variance of subsample LRP onset values, F values were adjusted according to Ulrich and Miller (2001). Reaction times and movement times, as well as the coefficient of variation of movement times, were analysed separately with standard ANOVAs for the same design.

Results

Behavioural results

Reaction time

Both PD patients and control subjects were able to do the task and demonstrated near-perfect performance in the high coherence condition and above chance performance in the low coherence condition. The considerable difference in difficulty of motion direction discrimination between high and low coherence conditions produced a desired difference in reaction times, presumably reflecting a difference in decision (un)certainty. Across groups, the reaction time in the high coherence condition was 737 ± 116 ms, against 1,217 ± 222 ms in the low coherence condition, yielding a significant effect of Difficulty [$F(1, 18) = 125.1$, $P < 0.0001$]. While patients were numerically slower than controls in the high coherence condition (776 ± 127 vs. 698 ± 95 ms), the reverse was true in the low coherence condition (1,211 ± 274 vs. 1,224 ± 170 ms). Overall, there was neither a significant Group difference in reaction time ($F < 1$), nor a significant Group by Difficulty interaction [$F(1, 18) = 1.1$, $P = 0.3$].

Movement time

The experiment's critical prediction did not concern reaction time but the question whether differences in reaction time would carry over to differences in movement time, especially in PD patients. Movement time as such was markedly slower in PD patients than in control subjects (547 ± 140 vs. 406 ± 87 ms), yielding a significant effect of Group [$F(1, 18) = 7.4$, $P = 0.014$]. Like the reaction time measure, movement time was sensitive to the difficulty of the direction discrimination, expressed in a significant effect of Difficulty [$F(1, 18) = 8.2$, $P = 0.01$). Critically, however, this effect of Difficulty did not interact with Group [$F(1, 18) = 1.9$, $P = 0.19$], indicating that patients were not more susceptible than control subjects to decision uncertainty influencing the execution of movements. Neither was such an influence evident from the variability of movement times, which we quantified by means of the coefficient of variation (CV), defined as the ratio of the standard deviation to the mean, determined for each participant separately. The CV was significantly different between high and low coherence conditions (effect of Difficulty [$F(1, 18) = 4.9$, $P = 0.04$]. There was, however, no interaction of Difficulty with Group [$F(1, 18) = 2.8$, $P = 0.1$]. The variability did also not differ between Groups [$F(1, 18) < 1$].

It should be noted that while difficulty of motion direction discrimination significantly influenced movement

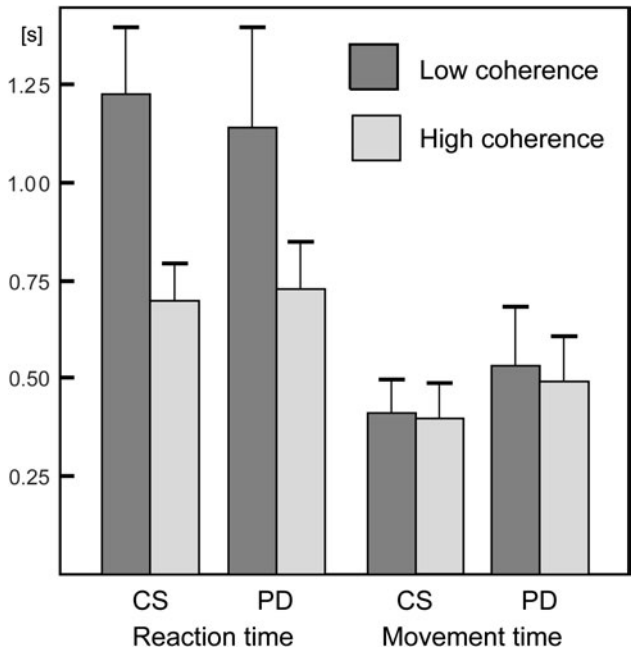

Fig. 1 Reaction and movement times. *Error bar* represents 1 SD

time, the effect was extremely small compared to the very substantial effect it had on reaction times, as illustrated in Fig. 1. Control subjects had movement times of 399 ± 91 and 413 ± 84 ms in the high and low coherence conditions. In patients, these values were 527 ± 123 and 568 ± 161 ms, respectively. The fact that the magnitude of the difference between high and low coherence conditions was numerically larger for patients than for controls (41 vs. 14 ms) raises the possibility that the study was just underpowered. Additional analyses did not support this. Separate analyses of the difference in movement time between high and low coherence conditions showed the difference to be significant in control subjects [$t(9) = 2.8$, $P = 0.022$]. By contrast, the numerically larger difference in patients did not reach significance [$t(9) = 2.2$, $P = 0.055$]. On further exploration of the data, it was found that two patients were responsible for the numerically larger slowing of movement execution in the low coherence condition. Without these two patients, the movement times in the high and low coherence conditions were 505 ± 104 and 522 ± 107 ms, respectively, reducing the difference to 17 ms. The two patients had the highest percentage of correction errors. That is, these patients were more likely to start one response, but then correct with a movement of the other hand. We will return to this observation below and in the discussion.

Errors

Participants found the low coherence condition extremely difficult, which was reflected in the error rates. Errors were frequent in the difficult low coherence condition (32 ± 12 %), but rare in the high coherence condition (4 ± 5 %), yielding a significant main effect of Difficulty [$F(1, 18) = 186.3$, $P < 0.0001$]. Patients made errors more frequently overall (22 ± 6 vs. 14 ± 6 %) [$F(1, 18) = 8.2$, $P = 0.01$], but made also a comparatively higher number of errors in the high coherence condition, yielding a just significant interaction of Group by Difficulty [$F(1, 18) = 4.47$, $P = 0.049$). A subset of errors were trials where the wrong hand moved first, leaving the home key, but the correct hand eventually pressed the response key. Such errors, referred to as corrections, were relatively rare, occurring on 1.4 ± 1.2 % in control subjects, and in 2.8 ± 1.8 % in patients. This difference was significant [$t(18) = 2.86$, $P = 0.019$). The percentage corrections made by the two patients whose movement times suffered most from decision uncertainty (as referred to in the previous paragraph) were 5.6 and 5.1 %, well above the group average. The existence of a relation between the number of corrections and the extra movement time in the low coherence condition was supported by a significant Pearson's correlation coefficient ($r = 0.740$, $P = 0.014$) (see Fig. 2). Hence, correction errors, excluded from the calculation of movement times, signal a tendency to hesitation apparently also manifested in correct trials. Surprisingly, in terms of the UPDRS score, the participants with the most frequent corrections were the most mildly affected patients. That this was not accidental is indicated by a significant negative correlation

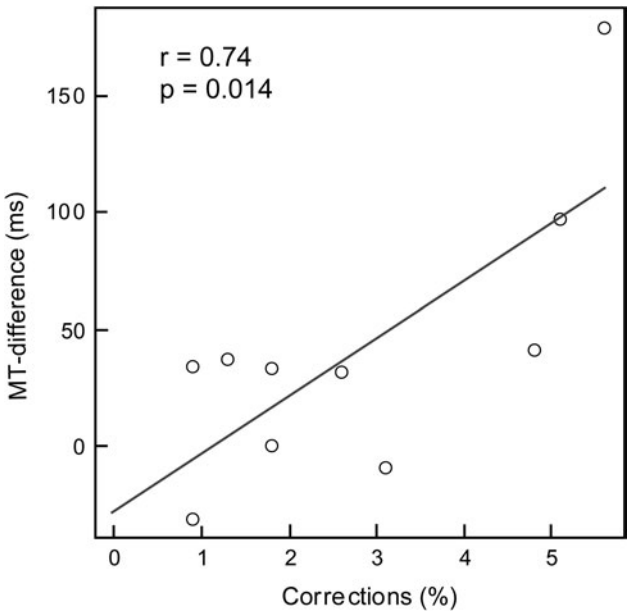

Fig. 2 Correlation of the percentage corrections and the increase in movement time with increasing difficulty of motion direction discrimination. Corrections are defined as trials where the wrong hand releases the home key first, followed by the correct response hand, which then depresses the correct response key

between percentage corrections and UPDRS score (Spearman $r = -0.657$, $p = 0.04$).

EEG results

Reported EEG results are confined to motor cortical EEG activity studied by means of the LRP. The LRP represents lateralised activity preceding and accompanying movements of the contralateral hand. The LRP combines the preparatory activity for the left and right hand and was here derived relative to the release of the home key (reaction time) and relative to the depression of the response key (movement time), designated LRP-RT and LRP-MT, respectively. The LRP was also studied in stimulus-locked fashion relative to the onset of the stimulus. These analyses are not reported, as they provided no additional insight. The response-locked LRPs were compared across groups and conditions in terms of their onset, quantified as the latency at which they reached an amplitude equal to 50 % of the peak amplitude. Note that latencies are measured relative to the response onset or response completion occurring later in time.

The LRP-RT represents covert processes preceding the initiation of the response. In spite of the absence of a group difference in reaction times, the motoric activation leading up to the response could differ in time course. Moreover, the high and low coherence conditions might also differ in time course as a result of the longer decision process in the latter condition. Figure 3 shows the LRPs and suggests that neither was the case. This was borne out by the analyses, revealing mean LRP-RT onsets for control subjects and patients of -295 ± 9 and -307 ± 8 ms, respectively. This small difference was not significant [$F(1, 18) < 1$]. The difference between high and low coherence conditions, across groups, was equally small, with onset values of -294 ± 7 and -309 ± 11 ms, which were not significantly different either [$F(1, 18) = 1.85$, $P = 0.19$). Finally, the Group $\times$ Difficulty interaction was also not significant [$F(1, 18) < 1$], there being no latency difference between high and low coherence conditions in either group.

The LRP-MT represents motor cortical activity preceding the initiation of the response, but also the activity accompanying the transport phase of the hand from release of the home key to depression of the response key. As a

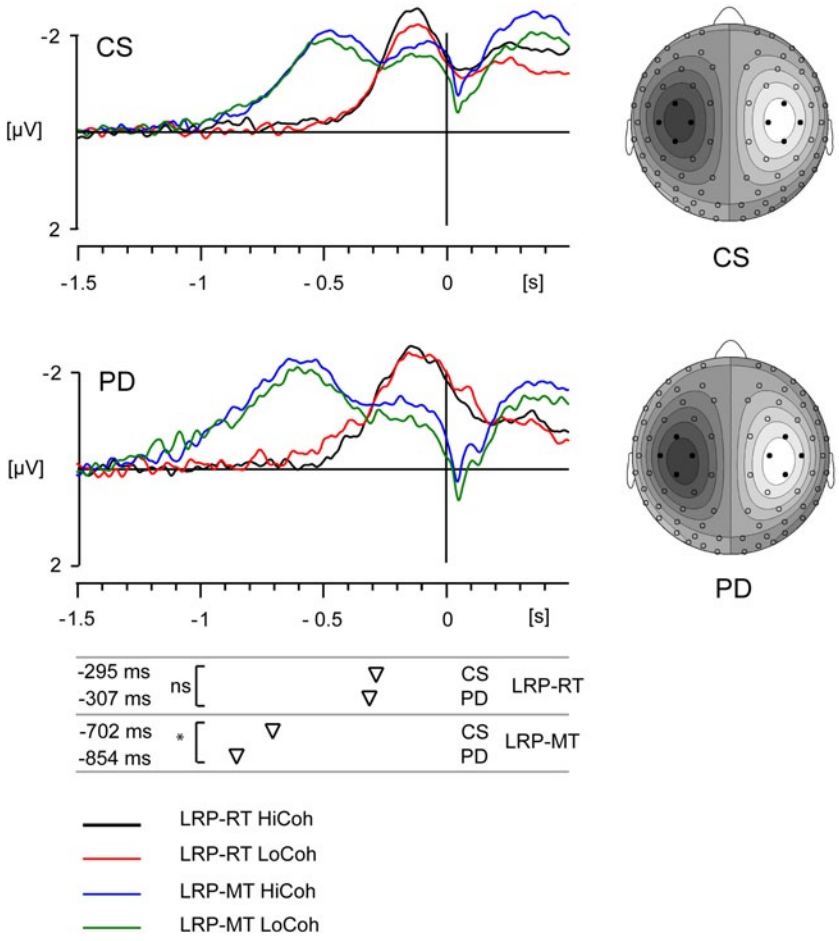

Fig. 3 Lateralised readiness potentials preceding the release of the home key (LRP-RT) and preceding depression of the response key (LRP-MT). Time point 0 is RT (for LRP-RT) and MT (for LRP-MT). The LRP traces are pooled from the marked electrodes closest to the centre of the LRP scalp distribution. Note the absence of a difference in time course between high and low coherence conditions in both groups. The *panel below* the LRP traces gives the mean latencies in numbers and marked with *triangles*. *HiCoh* high coherence condition, *LoCoh* low coherence condition

result, the LRP-MT starts much earlier than the LRP-RT, as is evident in Fig. 3. The figure also shows, more clearly for controls than for patients, separate preparation and movement phases in the LRP-MT. The key result in the LRP-MT analyses is the absence of a difference between high and low coherence conditions. The mean onset latencies for the high and low coherence conditions, across groups, were -786 ± 87 and -770 ± 72 ms, respectively, which was not significant [$F(1, 18) < 1$]. The difference between groups, by contrast, was significant [$F(1, 18) = 5.68$, $P = 0.028$], as is clear from Fig. 3, with values of -854 ± 22 ms for patients and -702 ± 15 ms for controls. This difference, of course, was expected based on the difference in movement time between the groups. The Group by Difficulty interaction was not significant [$F(1, 18) < 1$], as neither group had a latency difference between high and low coherence conditions.

In the Introduction, we discussed the possibility that abnormal coupling of deliberation and movement execution is manifested in a loss of the normally fixed relationship between movement-related EEG amplitude and movement onset. As Fig. 3 shows, the LRP-RT at movement onset was of identical amplitude in low and high coherence conditions, for both groups. No further analyses were therefore performed. Note that Fig. 3 does suggest a group difference in amplitude during the execution of the movement. That is, in patients, the LRP-MT in the interval -400 to 0 ms is ~50 % of the LRP-RT amplitude in this interval. In control subjects, by contrast, there is only a slight reduction in amplitude. Though not further pursued here, this amplitude attenuation of the LRP during movement represents an interesting correlate of the increased movement time in patients.

Discussion

We sought to replicate and extend previous evidence for leakage of decision uncertainty into movement execution processes in Parkinson's disease. The pathophysiological concept of movement being affected by decision uncertainty is based on evidence that the often assumed segregation (but see Haber 2003; Draganski et al. 2008) of basal ganglia–thalamocortical loops is not hard-wired, but modulated by dopamine and compromised in parkinsonian monkeys (Bergman et al. 1998; Filion et al. 1988, 1994). The existing evidence that movement execution is indeed susceptible to decision uncertainty in patients with Parkinson's disease (PD) (Pessiglione et al. 2005) is compelling and of theoretical significance, yet has not received wide attention. Remarkably, the current study indicates that leakage of decision uncertainty into movement execution in PD patients does not generalise to a perceptual discrimination task, in spite of the fact that the decision process in this task is known to be reflected in motor cortical activity. We will first review the task we used, followed by discussion of the results and the implications of the current findings.

Random-dot motion discrimination and decision-making

The random-dot motion direction discrimination task has been widely used in neurophysiological studies of (perceptual) decision-making in monkeys (for review, see Gold and Shadlen 2007). Performance of this task obviously relies on visual processes, especially those subserved by area MT (Shadlen et al. 1996). However, the mapping of perceptual decisions to simple oculomotor or limb motor responses has enabled the study of the dynamics of decision-making, revealed in the time course of neural activity in motor structures. The time course can be conceived in terms of a gradual accumulation of sensory evidence towards a decision bound or threshold (Gold and Shadlen 2007). The accumulation of evidence is visible in gradually increasing activity, measured in terms of increasing neuronal firing rates (Roitman and Shadlen 2002; Shadlen and Newsome 1996). The expression of the deliberative process in motoric activity makes the task eminently suitable to investigate potential pathological leakage of decision uncertainty into movement execution. Another advantage of the random-dot motion direction discrimination task is that it affords manipulation of decision uncertainty on a trial-by-trial basis by varying the percentage of dots moving coherently in one direction.

Previous work in humans has already shown that non-invasive recording of motor cortical activity using magnetoencephalography (MEG) is able to track the decision process in the random-dot motion discrimination task, similar to invasive recordings in monkeys (Donner et al. 2009; de Lange et al. 2013). In this work, the evolving decision process during viewing of the motion stimuli was expressed in a lateralisation of gamma oscillatory power and the power of beta band oscillations over the motor cortex. In the present experiment, we used EEG recording of motor cortical activity with analyses focusing on movement-related potentials.

Leakage of decision uncertainty?

The manipulation of motion coherence in the present investigation produced vastly different reaction times in both controls and patients, in combination with an equally pronounced difference in error rate between high and low coherence conditions (4 vs. 32 %). Together, we take this as evidence that the task achieved its purpose, i.e. to influence the certainty of making a decision. That the difficult low coherence condition also induced a subjective sense of

decision uncertainty was evident to the investigators (see "Methods"), but was not formally evaluated. Decision (un) certainty had only a minor effect (<50 ms) on movement time, compared to the approximately 500 ms effect in Pessiglione et al. (2005). Decision (un)certainty also affected the variability of movement execution. However, the size of these movement execution-related effects did not differ significantly between control subjects and patients. These results contrast with those of Pessiglione and co-workers, who used a go–nogo task in which participants had to discover, by trial and error, an implicit learning rule that determined whether a stimulus required a go or a nogo response. There are several important differences between the tasks that may be relevant to the divergent results and which may, thereby, illuminate the examined pathophysiological concept of information leakage between normally segregated basal ganglia–cortical loops.

One difference concerns the fact that the evidence guiding the decision for a go or nogo response in Pessiglione et al. (2005) accumulates across trials and depends on the recognition of the implicit rule that explains the pattern of feedback (in terms of gain or loss of points). In our task, by contrast, the evidence guiding the decision is in the actually displayed stimulus. This difference in the length of the integration window for evidence accumulation may be relevant. In our task, the movement bringing about the decision terminates the display of a stimulus and the participant's deliberation about that stimulus. Likewise, in the go–nogo task, a go response also terminates the display of a stimulus. At the same time, however, the response expresses a weak and still to be learned stimulus–response relationship, during learning phases of the experiment. In the go–nogo task for stimulus–response learning, the movement carrying out the response may for that reason be more susceptible to decision uncertainty, under conditions of a dysfunctional dopamine system.

One could frame the task difference also in a functional–anatomical perspective and argue that the perceptual decision here exploited depends predominantly on visual area MT, which is not involved in closed feedback loops with the basal ganglia. We do not think this explains why PD patients' movements were no more affected by decision uncertainty than the movements of control subjects. Along with the build-up of choice-predictive visual and motor cortex activity, the random-dot motion direction discrimination task engages a fronto-parietal network of areas, independent of the involved effector (Liu and Pleskac 2011). This supports that not only the motor loop of basal ganglia–cortical circuits but also the cognitive-associative loop contributes to the decision. Hence, leakage between these loops could certainly manifest itself in a perceptual decision task with hands as effectors. In fact, many examples exist of motor behaviour betraying features of perceptual and cognitive decision-making in healthy subjects, exemplifying leakage between cognition and action (Song and Nakayama 2009).

In both tasks, participants made a movement to a target position (touch screen and target key, respectively) and arrival at that position made a displayed stimulus disappear. Behind this resemblance, however, the choice being made in the two tasks (go vs. nogo and left- vs. right-hand response, respectively) was very different. Specifically, while in both cases, the decision was final only once the target was touched, the cost of changing the initial decision was different between the tasks. In the go–nogo choice, a movement towards the touch screen can be abandoned (or initiated/resumed) at any time, there being no difference between a change early and late in the movement (or absence of movement) expressing the choice. In the between-hands choice of our task, by contrast, one could argue that the further advanced the response hand is, the greater the cost of changing one's mind, both in terms of time and energy expenditure (Mazzoni et al. 2007). From a neurophysiological point of view, one might add that top-down and reciprocal interactions between neural structures implementing the response alternatives (Burle et al. 2004; Praamstra and Seiss 2005; Tandonnet et al. 2011), probably contribute to reduce wavering between alternative responses.

Based on these task comparisons, interference between deliberation and movement execution, in PD, is most likely to occur (1) when the task involves a form of stimulus–response learning, and (2) when the task leaves ample room for hesitation. The latter point is reinforced by the observation that in Pessiglione et al. (2005) the increased movement times under decision uncertainty, in PD, are accounted for by hesitations in response execution rather than a reduced peak movement velocity. The fact that, in our study, the patients whose movements were most affected by decision uncertainty were the patients with the highest rate of corrections seems to support this point as well. It has to be acknowledged, on the other hand, that these patients were the least affected in terms of UPDRS score.

Movement-related EEG activity

The timing of lateralised movement-related EEG potentials corroborated the main RT and MT results, but the EEG data did not add further insights. The onset of the LRP-RT preceded the onset of movement by some 300 ms in controls and patients. When time-locked to the depression of the target key instead of the home key, the movement-related potentials, i.e. the LRP-MT, started some 150 ms earlier in patients compared to controls (−854 vs. −702 ms), consistent with and explained by their longer movement times.

In neither group of participants, there were significant differences related to the manipulated decision uncertainty.

The insensitivity of the LRP to differences in the difficulty of motion direction discrimination means that the LRP in the present data only reflects motor cortical activity closely associated with the preparation and execution of the movement, but no choice-predictive activity building up during viewing of the random-dot motion stimuli. If there had been such activity, this would presumably have been manifested in an earlier onset and shallower slope of the LRP-RT in the more difficult low coherence condition, where subjects needed a much longer time to decide. Longer movement times would have shown up in different peak latencies of the LRP-MT in the low and high coherence conditions, as the start and end times of the movements would differ between these conditions.

The absence of choice-predictive lateralisation of the LRP, in the present data, is at variance with previous work reporting such lateralisation in the form of gamma power event-related synchronisation (ERS) and beta power event-related desynchronisation (ERD), during a random-dot motion direction discrimination task (Donner et al. 2009; de Lange et al. 2013). The reason for this discrepancy is not likely the use of MEG instead of EEG in the latter investigations. Nor is there evidence that oscillatory ERS and ERD measures are more sensitive to early choice-predictive lateralisation than movement-related potentials (Cheyne 2013; van Wijk et al. 2009). What may be relevant to these absent predictive effects in the LRP is that during the viewing of the random-dot motion stimuli subjects had to keep the home keys for left and right hand depressed. While the response panel and keys were constructed in such a way that the mere weight of the hands was sufficient to depress the keys, subjects were aware of the keys and may have exerted pressure to make sure they remained depressed until the start of movement. It is conceivable that this may have prevented the development of early choice-predictive lateralisation. Nevertheless, in previous work by one of us (van Wijk et al. 2009), sustained bilateral muscle activity during a delay period did not prevent lateralisation of movement-related potentials and beta ERD, albeit in a movement precuing task with valid directional cues.

Conclusion

The architecture of segregated basal ganglia–thalamocortical loops is central to our understanding of basal ganglia function and dysfunction, notwithstanding debate as to the degree of segregation and the sites of possible information exchange between loops (e.g. Bar-Gad and Bergman 2001; Guthrie et al. 2013). The possibility that some aspects of basal ganglia dysfunction are due to functional de-segregation of these loops is an important pathophysiological concept that may shed light on PD patients' susceptibility to interference. Interference, for instance, of one task by a second task in dual-task paradigms (Caligiuri et al. 1992; Lord et al. 2010; Malapani et al. 1994) or interference in response conflict tasks such as the flanker and stimulus–response compatibility tasks (Praamstra and Plat 2001; van den Wildenberg et al. 2010). An important contribution of the work by Pessiglione et al. (2005) is that it draws attention to the possibility of disruption in the *temporal* organisation of action, caused by de-segregation of basal ganglia–cortical circuits in patients with Parkinson's disease off-medication. The present data, however, collected in a different task, do not replicate the interference of deliberation with movement execution described by Pessiglione and co-workers. We propose that this does not necessarily question the concept of functional de-segregation and the possibility of abnormal temporal coupling of deliberation and movement execution. Rather, the two studies combined suggest that the deficit is strongly task-dependent. Such a task-dependence is, in fact, entailed by the consideration that coupling of deliberation and execution may be strategically modulated (Pessiglione et al. 2005). Empirical evidence to support this is already there, as subjects are able to strategically modulate to what extent perceptual information exerts an early influence over the activation of the motor cortex (Coles et al. 1995).

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