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COGNITIVE NEUROSCIENCE

Effects of stimulus–response compatibility on inhibitory processes in Parkinson's disease

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Abstract

Parkinson's disease (PD) is a neurodegenerative basal ganglia disorder accompanied by deficits in cognitive functions. One important executive function is the inhibition of responses. Due to basal ganglia damage, processes related to the selection of response are also dysfunctional. However, the relevance of deficits in response selection to processes related to response inhibition in PD is not clear. In this study we examined these processes by means of event-related potentials (ERPs) in two Go/Nogo tasks. In one task the stimulus–response mapping was compatible and in the other task it was incompatible with the meaning of the stimuli. The behavioural results show that PD patients were unaffected in the compatible response inhibition task but encountered problems in the incompatible one. In the ERPs the N2, generally reflecting response selection, was delayed for the PD compared to the control group. This suggests that response selection is delayed in PD. Moreover, the N2 was specifically enhanced in Nogo trials. This indicates that premotor inhibition, which is probably reflected by the Nogo-N2, is intensified in PD. The P3 was specifically attenuated and delayed after Nogo stimuli in the incompatible condition for PDs. Assuming that the Nogo-P3 reflects the evaluation of successful motor inhibition, our data show that this process is attenuated and delayed in PD but mainly in the incompatible task. The results suggest that inhibitory deficits in PD are only evident in complex (incompatible) stimulus–response mappings. These effects are probably due to an overstrain of striatal processes.

Introduction

Parkinson's disease (PD) is a neurodegenerative basal-ganglia disorder, accompanied by severe motor symptoms. Besides motor symptoms, PD is characterised by cognitive dysfunctions. These affect memory and executive functions (for review see Caballol *et al.*, 2007). One important executive function is the inhibition of prepared or prepotent responses (Beste *et al.*, 2008). Response inhibition processes can be examined by event-related potentials (ERPs) in Go/Nogo tasks. Here, subjects are asked to respond to one stimulus (Go) and to refrain from responding to the other stimulus (Nogo). Nogo stimuli elicit a frontocentral negative–positive complex (Falkenstein *et al.*, 1999) in the ERP. This has been labelled as Nogo-N2 and Nogo-P3 (Falkenstein *et al.*, 1999; Bokura *et al.*, 2001). These components are considered to be indices of different aspects of inhibition. The Nogo-N2 is assumed to reflect inhibition on a premotor level (e.g. Falkenstein *et al.*, 1999) or response conflict (e.g. Nieuwenhuis *et al.*, 2003). The Nogo-P3 is probably related to motor inhibition (e.g. Bruin *et al.*, 2001; Burle *et al.*, 2004). However, because of its long latency the Nogo-P3 probably does not reflect motor inhibition itself. Rather, it may reflect the evaluation of inhibitory processes (Naito & Matsumura, 1996; Band & van Boxtel, 1999; Bruin *et al.*, 2001; Roche *et al.*, 2005; Beste *et al.*, 2008).

Several findings in the literature suggest that patients with PD may have problems with inhibition. This seems likely as brain regions and systems important for response inhibition processes are dysfunctional in PD (Brooks & Piccini, 2006; Caballol *et al.*, 2007). These brain regions and systems include the anterior cingulate cortex (ACC; Ridderinkhof *et al.*, 2004; Beste *et al.*, 2008), the superior and inferior frontal cortex (Konishi *et al.*, 1998; Beste *et al.*, 2008) and the dopamine system (Fallgatter *et al.*, 1998; Beste *et al.*, 2008). Moreover, and due to the 'antagonist balance model' in PD (for review see Gale *et al.*, 2008) a loss of dopamine in nigrostriatal circuits causes a predominance of inhibitory effects on motor programmes. This may be particularly relevant for the Nogo-N2, supposed to reflect premotor inhibition processes. Dopaminergic decline in nigrostriatal pathways induces striatal dysfunctions, which in turn may affect ACC functions. This may be of particular relevance for processes related to the Nogo-P3 (Fallgatter *et al.*, 2003; Bekker *et al.*, 2005; Beste *et al.*, 2008).

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In particular, Bokura *et al.* (2005) found a reduction and delay of Nogo-N2 and Nogo-P3 in PD patients and hence claimed that patients with PD show impairments in inhibitory functioning. However, Bokura *et al.* (2005) used a task (N-back task) in which subjects had to respond to a stimulus when it was the second after a particular other one. Thus, task complexity differed from a simple stimulus–response (S–R) task. Working memory functions are strongly demanded in this task. As this function is deficient in PD (for review see Caballol *et al.*, 2007) the result found by Bokura *et al.* (2005) may reflect a working memory, rather than an inhibitory, deficit. Falkenstein *et al.* (2006) found that PD patients are less likely to respond to irrelevant stimuli. This suggests an enhancement of inhibitory control in PD. Thus, the evidence for an inhibitory deficit in PD is far from clear.

In the current study we tried to manipulate the degree of difficulty for response selection by imposing different dimensions of S–R compatibility. This was done to extend and link findings on response inhibition processes in PD to response selection processes. This seems reasonable as processes related to response selection are most probably mediated by the basal ganglia medium spiny neurons (Redgrave *et al.*, 1999; Bar-Gad *et al.*, 2003). These neurons are directly affected in PD (Chase & Oh, 2000). Also important for this selection is the dopaminergic modulation of medium spiny neurons via the nigrostriatal system (Gurney *et al.*, 2004), which also shows a decline in PD. As response selection processes are more demanded in incompatible S–R mappings one may expect PD patients to show most pronounced deficits in this condition. Here, longer reaction times (RTs) and/or more false alarm rates are expected in PD patients. Furthermore, the Nogo-N2 and/or the Nogo-P3 should be decreased and/or delayed in the patients compared to the healthy controls. Two tasks were applied to examine these questions. In the one (compatible) task, the stimulus directly signalled the response (Go or Nogo). In the other (incompatible) task the stimulus signalled the opposite of what had to be done.

Materials and methods

Participants

Fifteen non-demented and non-depressive outpatients (seven female, mean age 60 years; eight male, mean age 62 years) with idiopathic Parkinson's disease participated in the study. The patients were on their normal medication, which was L-dopa plus benserazide for most of the patients (n = 10) and dopamine agonists and/or amantadine for the rest. The patients were tested 4 h or later after the last medication intake. They were examined clinically with the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn *et al.* 1987).

To each patient a healthy control subject was matched by age, sex and educational state. All 30 subjects were examined with two standard neuropsychological tests: the modified Wisconsin Card Sorting Test (Nelson, 1975) and the Word Fluency Test (Benton, 1968). The subjects were tested with a battery of binary choice and Go/Nogo tasks which were aimed at inducing conflict and errors. The total administration time was ~80 min. The results of two tasks are reported here. The experiments were undertaken with the understanding and written consent of each subject. The study conforms with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and was approved by the Ethics Committee, Ruhr-University of Bochum.

Task 1

In the first task ('compatible') one out of two words was presented on a PC monitor: 'DRÜCK' (German for press; Go stimulus) and 'STOPP' (German for stop; Nogo stimulus). The stimuli were displayed for 300 ms. The response–stimulus interval was fixed at 1600 ms. Time pressure was administered by asking the subjects to respond within 550 ms. In trials with reaction times exceeding this deadline a feedback stimulus (1000 Hz, 60 dB SPL) was given 1200 ms after the response. This warning stimulus had to be avoided by the subjects. Two blocks of 60 stimuli each were presented in this task. Nogo stimuli and Go stimuli appeared with equal frequency. The subjects had to react with the thumb to the Go stimuli and to refrain from responding to Nogo stimuli.

Task 2

In the second task ('incompatible') the same stimuli were given, but the S–R mapping was reversed, i.e. DRÜCK was the Nogo stimulus and STOPP the Go stimulus. In this task the subjects had to overcome the direct but incorrect giving of a response, which makes inhibition more difficult. The order of the tasks was counterbalanced across subjects.

Data processing and analysis

RTs and error rates (i.e. rate of false alarms) were measured. RTs and error rates were analysed in a repeated-measures ANOVA using the within-subject factor task and the between-subject factor group.

During the tasks the electroencephalogram (EEG) was recorded from 24 electrodes: F3, Fz, F4; F11, F12 (lateral–frontal); FC3, FCz, FC4; C3, C4; P3, Pz, P4; O1, Oz, O2; M1, M2. Cz was used as primary reference. Additionally, eye movements were monitored and recorded by means of two lateral and four vertical electro-oculogram (EOG) electrodes. The sampling rate of all recordings was 500 samples/s. A filter bandwidth 0–80 Hz was applied to the EEG. Electrode impedances were kept < 5 kΩ. EEG was re-referenced off-line to linked mastoids. Artefact rejection procedures were applied twice: automatically with an amplitude threshold of ± 80 μV, and visually by rejecting all trials contaminated by technical artefacts. Horizontal and vertical eye movements preserved in the accepted trials were corrected by means of a linear regression method for EOG correction (Gratton *et al.*, 1983). Subsequent to averaging, N2 and P3 peak amplitudes and latencies in Go and Nogo trials were evaluated. This was done for correct trials only. For statistical analysis peak amplitudes were quantified relative to a baseline 200 ms before stimulus presentation. Amplitudes and latencies of the N2 component were analysed in a repeated-measures ANOVA using the within-subject factors task and Go/Nogo and the between-subjects factor group. For the P3 component another within-subject factor, electrode, was further included in analyses. The Nogo-N2 was defined as the most negative deflection within the range from 150 to 300 ms after stimulus onset. The Nogo-P3 was defined as the most positive peak within a range from 300 to 500 ms after stimulus onset. Amplitudes of the Go-N2 and -P3 were measured at the corresponding time point, where the Nogo component reached its maximum. The components were analysed depending on their distribution in the scalp topography maps. The N2 amplitudes were measured at FCz only, as the maps showed a maximum at this electrode. For the P3, the electrodes Fz, FCz and Pz were analysed, as the distribution of this component spans these electrodes.

Results

Behavioural data

RTs on Go and error rates on Nogo stimuli are reported. For the RTs there were significant main effects of task ($F_{1,27}$ = 15.59, P = 0.001)

and group ($F_{1,27} = 31.29$, $P < 0.001$). RTs were longer in the incompatible (365.7 ± 4.5) than the compatible (348.4 ± 5.0 ms) condition and longer for PD patients (381.3 ± 6.1) than for controls (333.1 ± 5.9 ms). Further, there was a task × group interaction ($F_{1,27} = 6.38$, $P = 0.018$): for the PD group the RTs were markedly delayed for incompatible (395.3 ± 4.3 ms) compared to compatible (367.3 ± 5.2 ms; $F_{1,13} = 19.60$, $P = 0.001$) stimuli. The controls showed virtually no RT difference between conditions (compatible, 330.1 ± 8.4; incompatible, 336.2 ± 7.7 ms; $F_{1,14} = 1.08$, $P = 0.316$). No difference was seen between tasks in the rate of false alarms ($F_{1,27} = 0.79$, $P = 0.382$) or groups ($F_{1,27} = 0.4$, $P = 0.528$). There was also no interaction ($F_{1,27} = 1.29$, $P = 0.265$).

N2

ERPs on Go- and Nogo-Trials are shown in Fig. 1. The Nogo-N2 shows a maximum at Fz.

The repeated-measures ANOVA revealed a main effect of task ($F_{1,27} = 7.03$, $P = 0.013$). The N2 was more negative for the compatible (−0.18 ± 0.76) than for the incompatible (1.23 ± 0.45 mV) task. Moreover, there was a significant main effect of Go/Nogo ($F_{1,27} = 23.74$, $P < 0.001$): the N2 was more negative on Nogo (−0.50 ± 0.53) than on Go (1.55 ± 0.67 mV) trials. The main effect of group was also significant ($F_{1,27} = 6.80$, $P = 0.015$). The N2 was more negative for the PD participants (−0.95 ± 0.79) than for the controls (2.0 ± 0.81 mV). This effect was further modulated by the factor Go/Nogo, as revealed by a Go/Nogo × group interaction ($F_{1,27} = 4.19$, $P = 0.050$). The groups differed significantly on Nogo trials (PD, −2.41 ± 0.7; controls, 1.41 ± 0.7 mV; $F_{1,27} = 13.02$, $P = 0.001$), but hardly on Go trials (PD, 0.5 ± 0.9; controls, 2.6 ± 0.9 mV; $F_{1,27} = 2.43$, $P = 0.130$). In other words, the enhancement of the N2 in Nogo trials was larger in the PD patients than in controls. No other effects reached the level of significance (all $F < 1.10$, $P > 0.300$).

For the latencies there was a significant main effect of task ($F_{1,27} = 11.04$, $P = 0.003$). The N2 latency was prolonged in the incompatible (233.9 ms ± 4.7) than the compatible (222.2 ± 4.6 ms) task. Furthermore, the main effect of Go/Nogo was significant ($F_{1,27} = 10.41$, $P = 0.003$). The N2 latency was prolonged on Nogo-trials (233.8 ± 4.4) compared to Go-trials (220.2 ± 4.9 ms). Finally, the main effect of group was significant ($F_{1,27} = 8.23$, $P = 0.008$). The N2 latency was prolonged in PD patients (239.1 ± 5.8) compared to controls (214.9 ± 6.1 ms). No other effects reached the level of significance (all $F < 1.85$, $P > 0.185$).

P3

As can be seen in the maps for the Nogo condition, the P3 showed considerable activity at Fz, FCz and Pz. Therefore the factor electrode was additionally taken into the repeated-measures ANOVA. Only the main effect of group was significant ($F_{1,27} = 5.26$, $P = 0.030$). Healthy controls showed a larger P3 (12.08 ± 0.5) than the PD patients (9.9 ± 0.6 mV).

Most interesting, the ANOVA revealed an electrode × task × Go/ Nogo × group interaction ($F_{2,54} = 3.98$, $P = 0.025$). Subsequent analyses showed that the task compatibility × Go/Nogo × group interaction was significant for electrode FCz ($F_{1,27} = 13.22$, $P = 0.001$), but not for electrode Pz ($F_{1,27} = 0.77$, $P = 0.388$). For electrode Pz no effect was significant (all $F < 2.5$, $P > 0.125$). For electrode Fz the pattern was similar. Here, no effect was significant (all $F < 1.77$, $P > 0.174$).

Hence only electrode FCz was further analysed and Bonferroni-corrected paired t-tests were used to compare Go and Nogo amplitudes within each group for each task, separately. The results are illustrated in Fig. 2.

PD patients revealed no difference between Go (8.9 ± 1.1) and Nogo (7.60 ± 1.0 mV) amplitudes in the incompatible task ($t_{14} = -1.16$, $P = 0.131$). In contrast, differences were seen in the compatible task (Go, 5.7 ± 0.2; Nogo, 8.76 ± 0.3 mV; $t_{14} = 5.65$, $P < 0.001$). For the control group, differences between the Go and Nogo amplitudes were obtained in both conditions (Go: incompatible, 8.3 ± 1.1; compatible, 10.8 ± 1.0; Nogo: incompatible, 15.1 ± 1.6; compatible 14.8 ± 1.1 mV; incompatible: $t = 4.76$, df = 13, $P < 0.001$; compatible: $t = 3.18$, df = 13, $P < 0.001$).

At electrode FCz a main effect of Go/Nogo was seen ($F_{1,27} = 25.53$, $P < 0.001$). The P3 was larger on Nogo (11.59 ± 0.65) than on Go (8.48 ± 0.55 mV) trials. This effect was further modulated by group as revealed by the Go/Nogo × group interaction ($F_{1,27} = 13.48$, $P = 0.001$). Subsequent univariate ANOVAs revealed that PD patients showed a smaller P3 than controls in the Nogo condition ($F_{1,27} = 26.91$, $P < 0.001$). For the Go condition no group differences were obtained ($F_{1,27} = 1.54$, $P = 0.225$). In summary, the frontocentral P3 enhancement in Nogo trials was smaller in the patients than in the controls, particularly for the incompatible task.

For the latencies the repeated-measures ANOVA revealed a significant main effect of Go/Nogo ($F_{1,27} = 33.17$, $P < 0.001$). P3 latencies were longer for the Nogo (408.2 ± 5.1) than for the Go (381.3 ± 6.0 ms) trials. This effect was further modulated by the factor task (Go/Nogo × task interaction, ($F_{1,27} = 7.61$, $P = 0.010$). Subsequent analyses showed that the difference in latencies between Go and Nogo trials was larger for the incompatible (33.1 ± 3.4) than for the compatible (19.3 ± 3.5 ms; $F_{1,27} = 5.55$, $P = 0.020$) task.

The factor group further modulated the Go/Nogo effect, as indicated by the Go/Nogo × task compatibility × group interaction ($F_{1,27} = 11.23$, $P = 0.005$). Subsequently, Bonferroni-corrected paired t-tests were used to compare Go and Nogo latencies within each group for each task, separately. For the control group differences were obtained between Go and Nogo trials in both tasks (compatible: Go, 371.0 ± 9.5; Nogo 395.9 ± 9.7 ms; $t_{13} = 2.88$, $P = 0.008$; incompatible: Go, 380.1 ± 8.8; Nogo 398.8 ± 6.5 ms; $t_{13} = 2.67$, $P = 0.013$). For PD patients a similar effect was seen (incompatible: Go, 383.1 ± 6.2; Nogo, 427.4 ± 5.0 ms; $t_{13} = 6.33$, $P < 0.001$; compatible: Go, 389.9 ± 10.5; Nogo, 408.7 ± 9.3 ms; $t_{14} = 2.99$, $P = 0.006$).

While latency differences between Go and Nogo trials showed no group differences for the compatible task (PD, 19.2 ± 7.3; controls, 24.9 ± 7.2 ms; $F_{1,27} = 0.10$, $P = 0.733$), differences were obtained for the incompatible task (PD, 44.3 ± 6.4; controls, 20.2 ± 6.8 ms; $F_{1,27} = 7.99$, $P = 0.010$). All other main or interaction effects were not significant (all $F < 1.10$, $P > 0.300$). In summary, the P3 latency difference between Go and Nogo trials was small for healthy controls and for PD patients in the compatible task. In contrast, there was a delay in PD patients in the incompatible task.

Discussion

In this study we examined processes related to response inhibition in PD in two Go/Nogo tasks by means of ERPs. These tasks differed in compatibility of S–R mappings. RTs were longer in PD patients than in controls. Similarly, they were also longer in the incompatible than the compatible task. These effects were caused by the PD group. The error rates did not differ between groups. However, as the PD group

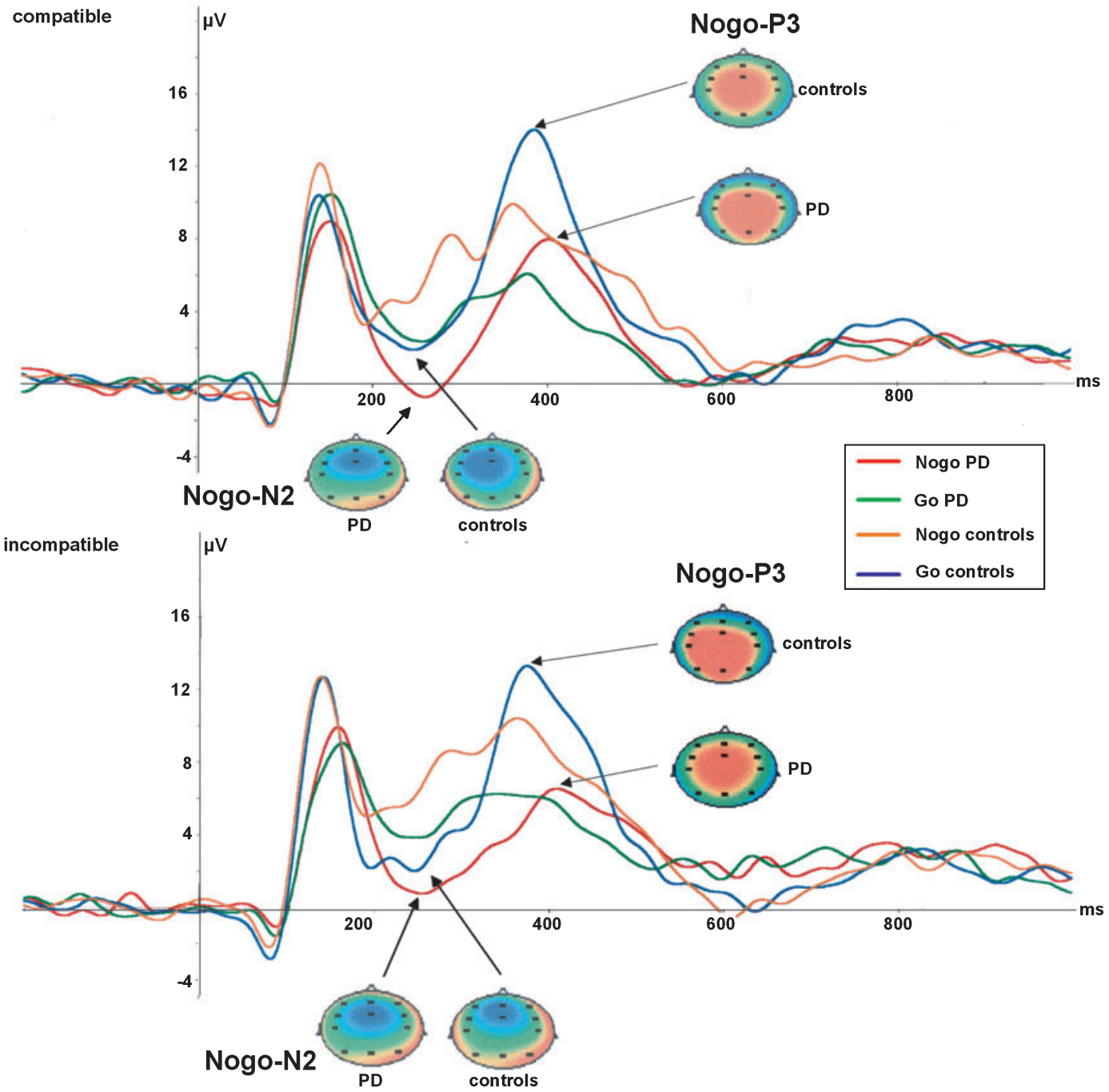

FIG. 1. (Top) Time course of ERP components in the compatible task. (Bottom) Time-course of ERP components in the incompatible task. Time point 0 denotes the point of Go or Nogo stimulus presentation. For both conditions topographical maps are given, separated for the Nogo-N2 and Nogo-P3, for each group.

spent more time on a response they reduced the risk of false alarms, i.e. they made more deliberate decisions when to respond and when to refrain from responding. This led to similar error rates, but at the expense of the RTs. Hence a behavioural deficit in the PD patients is due not to their accuracy but rather to their speed of responding. As deficits in PD patients were only evident in the incompatible task, it cannot be ruled out that slower RTs mask an inhibitory deficit. However, there is no definite evidence for this. As the order of the tasks was counterbalanced across subjects, the effects obtained are not due to possible decreases in effort and arousal.

N2

Effects of the task were seen in amplitudes and latencies. The N2 was reduced and delayed in the incompatible task. Task effects were not specific for the Nogo trials. This suggests that the N2 contains a general component which is common to Go and Nogo trials and which is delayed in the incompatible task. This component, which may be evident in both trial types, can hardly reflect conflict monitoring by the ACC (Nieuwenhuis *et al.*, 2003) because conflict should be virtually absent in Go trials. We assume that this common component reflects response selection, as claimed recently by Gajewski *et al.* (2008).

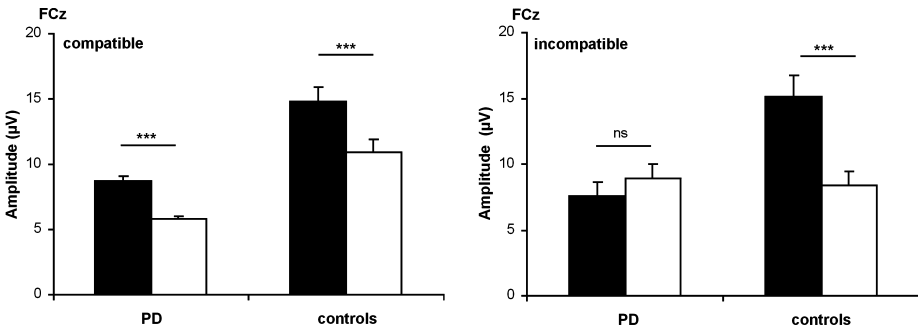

FIG. 2. Amplitudes of the Go-P3 (white bars) and Nogo-P3 (black bars), separated for the compatible and incompatible condition for the PD and control groups. The mean and SEM at electrode FCz is given. ***$P < 0.001$.

However, several authors have tested the inhibition vs. conflict interpretation of the N2. Falkenstein *et al.* (1999) showed larger and earlier N2s in subjects who committed fewer false alarms. Kopp *et al.* (1996) showed the N2 to be dependent on response priming. Both groups interpreted their results as evidence that the N2 reflects the inhibition of an inappropriate response tendency. Also, the N2 has been reported to be smaller in children with ADHD, who are supposed to suffer from an inhibitory deficit (Pliszka *et al.*, 2000; Overtoom *et al.*, 2002). In contrast, several other groups found evidence against the inhibition hypothesis. Nieuwenhuis *et al.* (2003), who varied the frequency of Nogo vs. Go trials, also found an N2 with a frontocentral maximum in rare Go trials. Similarly, Donkers & van Boxtel (2004) also showed a N2 in trials in which subjects had to press with maximum force rather that inhibiting a response. While these data are at odds with the idea that the N2 reflects response inhibition at the motor level, they are still in line with the assumption of 'premotor inhibition', i.e. a revision of a motor programme. However, this result is in contrast with those of Bokura *et al.* (2005), who found a smaller Nogo-N2 in patients with PD than in controls. The reason for this difference may be the tasks applied. Bokura *et al.* (2005) used a task sharing many features of a working memory task (i.e. 2-back task; Gevins & Cutillo, 1993). Such tasks involve several cognitive subprocesses, i.e. updating, matching and shifting (Chen *et al.*, 2008). As these functions have been shown to be dysfunctional in PD (Gilbert *et al.*, 2005; Caballol *et al.*, 2007; Williams-Gray *et al.*, 2008), it may be speculated that dysfunctions in these processes overlap with processes reflected by the Nogo-N2, hence leading to a reduced N2 in this task.

Nogo-P3

Regarding the P3 amplitude, the results show that the difference between the Go and Nogo amplitude is modulated by group and task compatibility. The frontocentral P3 enhancement in Nogo vs. Go trials (i.e. the Nogo-P3) was smaller in the patients than in the controls. This effect was most pronounced in the incompatible task, in which the delay was also largest. Assuming that the Nogo-P3 reflects the evaluation of successful motor inhibition (e.g. Burle *et al.*, 2004), our data show that these processes are attenuated and delayed in PD, but mainly in the incompatible task. This pattern observed in the Nogo-P3 latency strongly resembles the results for the reaction times in Go trials. Hence, the impairment observed in incompatible S–R mappings does also seem to be a general one. The RTs show an impairment in the Go trials while the ERPs unveil a similar impairment in Nogo trials. Altogether, both response activation and response inhibition appear to be delayed in PD for incompatible S–R relations. This may suggest that response selection processes as a whole are impaired, which fits the pathophysiology in PD (see below, Possible neuronal mechanisms). These impaired response selection processes may entail dysfunctions in response inhibition processes, i.e., the evaluation of a successful inhibition. The results cannot be due to effects of decreases in effort or arousal changes throughout the session because the order of the tasks within the session was counterbalanced across subjects.

Possible neuronal mechanisms

Processes reflected by the Nogo-N2 may relate to premotor inhibition (Falkenstein *et al.*, 1999), i.e. the inhibition of a motor programme. An enhanced N2 in the patients reflecting an increased inhibition of a motor programme would be in line with the 'antagonist balance' model of PD (for review see Gale *et al.*, 2008). This model assumes that a loss of dopamine (DA) affects the direct and the indirect pathway in the basal ganglia. A loss of DA causes the direct pathway (normally facilitating movements) to become less active and the indirect pathway (normally suppressing movements) to become more active. Thus, the overall inhibitory effect of the indirect pathway predominates (Gale *et al.*, 2008), leading to an increased inhibition of motor programmes.

Processes reflected by the (Nogo)-P3 have been shown to be mediated via prefrontal networks, including the ACC (Fallgatter *et al.*, 2003; Bekker *et al.*, 2005; Beste *et al.*, 2008). The ACC and the basal ganglia are both affected in PD (Brooks & Piccini, 2006). Due to damage of the substantia nigra and subsequent dysfunction of nigrostriatal pathways, striatal structures themselves become dysfunctional in PD. This in turn probably affects striatal–cingulate interactions. However, dysfunctions in response evaluation became apparent only when incompatible S–R mappings were required. These encompass higher demands on action (response) selection arising due to incompatible S–R mappings. Here, the basal ganglia (Bar-Gad *et al.*, 2003), and especially GABAergic interactions between medium spiny neurons, are of importance (Bar-Gad *et al.*, 2003; Plenz, 2003). These neurons are also directly affected in PD (Chase & Oh, 2000) and are modulated by dopaminergic fibres from the midbrain (Fisone *et al.*, 2007), the locus of primary dysfunction in PD.

The results suggest that disease-related damage to neuronal systems mediating the evaluation of response inhibition only get critical in PD when demands on the basal ganglia–prefrontal interactions are increased. For simple (i.e. compatible) responses, processing capacities seem to be sufficient. When the task requires additional resources of frontostriatal circuits (i.e. incompatible response selection), performance declines. This decline is probably due to an overstrain of processing resources at a frontostriatal level, which have been reported in other basal ganglia disorder studies dealing with tasks of increasing psychomotor demands (e.g. Beste *et al.*, 2007). Based on all these, it may be hypothesised that the primary deficit in PD is due to problems in response selection that entail dysfunctions in response inhibition processes.

Summary and conclusion

The current study reveals that a neurophysiological indicator of premotor inhibition (Nogo-N2) is generally enhanced in PD compared to healthy controls. In contrast, the evaluation of response inhibition (Nogo-P3) is attenuated and delayed in patients with PD compared with healthy controls but only for incompatible S–R relations. These effects are probably due to an overstrain of striatal response selection processes. The results extend findings on problems of PD patients with incompatible S–R mappings to inhibition-related processes.

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Abbreviations

ACC, anterior cingulate cortex; ERP, event-related potential; PD, Parkinson's disease; RT, reaction time; S–R, stimulus–response; UPDRS, Unified Parkinson's Disease Rating Scale.

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