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The Effect of Parkinson's Disease on the Dynamics of On-line and Proactive Cognitive Control during Action Selection

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Abstract

■ Processing irrelevant visual information sometimes activates incorrect response impulses. The engagement of cognitive control mechanisms to suppress these impulses and make proactive adjustments to reduce the future impact of incorrect impulses may rely on the integrity of frontal–basal ganglia circuitry. Using a Simon task, we investigated the effects of basal ganglia dysfunction produced by Parkinson's disease (PD) on both on-line (within-trial) and proactive (between-trial) control efforts to reduce interference produced by the activation of an incorrect response. As a novel feature, we applied distributional analyses, guided by the activation–suppression model, to differentiate the strength of incorrect response activation and the proficiency of suppression engaged to counter this activation. For situations requiring on-line control, PD (n = 52) and healthy control (n = 30) groups showed similar mean interference effects (i.e., Simon effects) on reaction time (RT) and accuracy. Distributional analyses showed that although the strength of incorrect response impulses was similar between the groups PD patients were less proficient at suppressing these impulses. Both groups demonstrated equivalent and effective proactive control of response interference on mean RT and accuracy rates. However, PD patients were less effective at reducing the strength of incorrect response activation proactively. Among PD patients, motor symptom severity was associated with difficulties in on-line, but not in proactive, control of response impulses. These results suggest that basal ganglia dysfunction produced by PD has selective effects on cognitive control mechanisms engaged to resolve response conflict, with primary deficits in the on-line suppression of incorrect responses occurring in the context of a relatively spared ability to adjust control proactively to minimize future conflict. ■

INTRODUCTION

Inhibition of stimulus-driven response impulses is an essential aspect of human cognitive control. In some instances, these impulses are beneficial to the speed and accuracy of the emitted responses. In other instances, activation of an unwanted response may interfere with selection of a desired response or lead to a response error. In the case of incorrect response activation, theories of cognitive control propose mechanisms to suppress this activation ("on-line control") and subsequently adjust control mechanisms to better adapt to future response conflict ("proactive control"). Here, we focus on the effects of Parkinson's disease (PD) on on-line and proactive control efforts to overcome conflicting response impulses so as to ensure correct selection of a goal-directed response.

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Simon Task: Measuring On-line and Proactive Control of Response Interference

The elicitation and suppression of conflicting response tendencies have been studied using response interference tasks, which induce conflict between a response impulse that is driven automatically by an irrelevant feature of a stimulus display and a response that is selected deliberately by the processing of relevant stimulus features. The Simon task, used in the present investigation, produces one of the most sensitive measures of response interference (Simon, 1969; cf., Lu & Proctor, 1995; Simon, 1990). In this task, interference arises from automatic processing of the spatial location of an imperative stimulus within the sensory field that, even though task irrelevant, triggers a response impulse that influences reaction time (RT) and accuracy. For example, subjects might be instructed to make a speeded left- or right-hand response on the basis of the color of a stimulus that is presented either to the left or right of visual fixation. Although the spatial location of the colored circle is irrelevant to successful performance on the task, faster RTs and higher accuracy rates occur when the circle is presented in the hemifield

that corresponds to the response side signaled by the color of the circle. Conversely, RT slows and accuracy rates decrease when the response signaled by the color of the circle does not correspond (i.e., is noncorresponding) to the spatial location of the circle (e.g., a colored circle calling for a left-hand response presented in the right hemifield). The detrimental influence on performance of noncorresponding trials relative to the facilitative influence on corresponding trials is called the *Simon effect*.

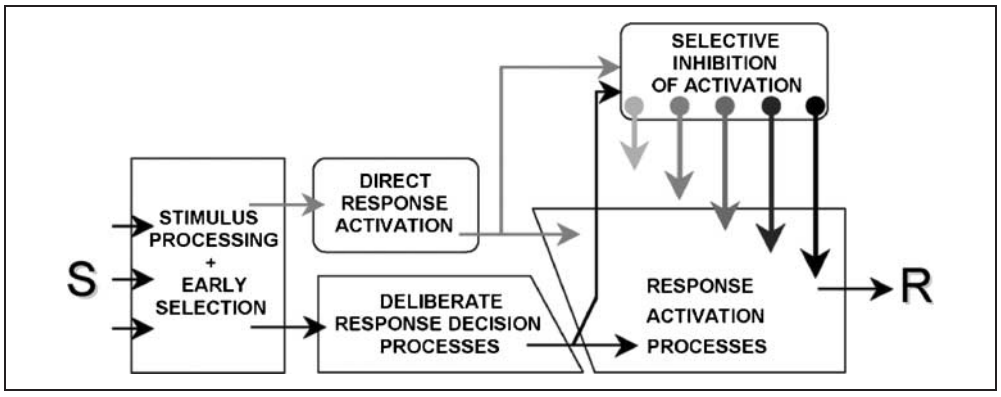
Simon effects are typically explained on the basis of dual-route processing models (Ridderinkhof, 2002a; Eimer, Hommel, & Prinz, 1995; de Jong, Liang, & Lauber, 1994; Kornblum, Hasbroucq, & Osman, 1990). These models posit that the spatial location, or irrelevant dimension, of the stimulus automatically and rapidly activates the corresponding response via a direct processing route, whereas the relevant stimulus feature engages a deliberate processing route that utilizes a slower controlled processing mechanism to translate the relevant stimulus feature into a correct response according to task instructions (see Figure 1). On corresponding trials, the direct route and the deliberate processing route converge on activation of the same response and, in so doing, facilitate both RT and accuracy. In contrast, on noncorresponding trials, the response activated by the automatic processing of the circle's spatial location and the response selected by the deliberate processing of the circle's color conflict, thereby slowing RT and increasing error rates. It is theorized that the size of the Simon effect reflects the extra demands and time required to suppress the interference caused by the incorrect response activation produced in noncorresponding trials that are absent in corresponding trials due to the facilitation from direct route processing (Ridderinkhof, 2002a) (Figure 1). Thus, individual and group differences in the magnitude of the Simon effect are used to infer the proficiency of suppression, as an act of cognitive control, with larger effects associated with less efficient resolution of response interference.

An interesting feature of Simon and related interference effects is that the magnitude of the effect is typically reduced following trials with response conflict (i.e., noncorresponding trials) compared to trials without such conflict (i.e., corresponding trials) as well as following trials in which an error was made compared to trials in which the correct response was issued. These findings have motivated the hypothesis that interference control mechanisms can be adjusted proactively between trials (Ridderinkhof, 2002b; Botvinick, Braver, Barch, Carter, & Cohen, 2001; Gratton, Coles, & Donchin, 1992). Some have argued that control processes are slackened following trials without conflict, but tightened for trials that follow conflict or response errors (cf., Egner, 2007). Although the specific mechanisms of between-trial adjustments are debated, variability in the amount of adjustment to the interference effect can be used to study the proficiency of proactive cognitive control. Thus, the Simon task provides measures of both on-line (i.e., the within-trial Simon effect) and proactive control (i.e., the between-trial conflict or error adaptation effects) of response interference.

PD and the Control of Response Interference

The basal ganglia, via elaborate connections with prefrontal and motor areas of frontal cortex, are hypothesized to contribute to the neural mechanisms involved in the focused selection and inhibition of action (Aron, 2007; Redgrave, Prescott, & Gurney, 1999; Hikosaka, 1998; Mink, 1996; Mink & Thach, 1993; Robbins & Brown, 1990; Alexander, DeLong, & Strick, 1986). Essential to this idea is the demonstration that, at rest, GABAergic output neurons of the basal ganglia maintain tonic inhibitory control over thalamo-cortical motor pathways (cf., Grillner, Hellgren, Menard, Saitoh, & Wikstrom, 2005; Alexander & Crutcher, 1990). To release motor pathways from inhibition, the output structures of the basal ganglia that correspond to a particular movement ensemble must be selectively inhibited by upstream basal ganglia projections (Kropotov & Etlinger, 1999). In particular, the direct pathway of the basal ganglia, which comprises monosynaptic inhibitory (i.e., GABAergic) projections from basal ganglia input structures (e.g., neostriatum) to basal ganglia output nuclei

Figure 1. Dual-route model.



(e.g., globus pallidus interna, substantia nigra reticulata), provides inhibitory control over the output structures and has been argued to convey a *go* signal that facilitates the release (i.e., the selection) of motor commands from inhibition (Frank, 2005). A complementary indirect pathway of the basal ganglia, which comprises a series of projections from input structures through various intermediate basal ganglia nuclei (e.g., globus pallidus externa, subthalamic nucleus), exerts an opposite effect by exciting basal ganglia output structures, thereby increasing inhibition over thalamo-cortical motor pathways. Thus, the basal ganglia can facilitate and suppress response commands that are competing for access to the motor system (cf., Mink, 1996). The basal ganglia are strongly influenced by inputs from prefrontal cortex, which may provide a top–down control signal for guiding the resolution of response competition that amplifies one response command and suppresses competing commands according to task goals (Miller & Cohen, 2001). Moreover, the activity of a series of hyperdirect pathways involving direct projections from prefrontal cortex to the subthalamic nucleus of the basal ganglia, which is a key structure along the indirect pathway that provides excitatory glutamatergic input to the basal ganglia output structures, has been linked to experimental situations that induce a need to suppress unwanted action commands quickly or urgently (Forstmann, Jahfari, et al., 2008; Forstmann, van den Wildenberg, & Ridderinkhof, 2008; Aron, Behrens, Smith, Frank, & Poldrack, 2007; Aron & Poldrack, 2006; Nambu, Tokuno, & Takada, 2002; Casey et al., 2000).

Naturally, this model of basal ganglia function fueled the hypothesis that basal ganglia dysfunction, such as occurs in PD, affects the proficiency of resolving response conflict (Praamstra, Stegeman, Cools, & Horstink, 1998). More specifically, it has been hypothesized that the ability to suppress conflicting responses might be especially vulnerable due to the basal ganglia dysfunction caused by PD, which in turn should lead to exacerbated interference effects (Wylie, Stout, & Bashore, 2005; Praamstra et al., 1998). This prediction has been supported in several studies of PD using the flanker task (Eriksen & Eriksen, 1974), which induces response conflict between an incorrect response signaled by irrelevant distractors in the visual field and a response signaled by an imperative stimulus (cf., Wylie et al., 2009). Support for this idea from investigations of the Simon effect in PD has been mixed so far, with some studies reporting larger Simon effects on RT and accuracy rates among PD compared to healthy control (HC) subjects and other studies reporting equivalent effects (Schmiedt-Fehr, Schwendemann, Herrmann, & Basar-Eroglu, 2007; Fielding, Georgio-Karistianis, Bradshaw, Millist, & White, 2005; Praamstra & Plat, 2001; Cope, Georgiou, Bradshaw, Iansek, & Phillips, 1996). Two of these studies also investigated between-trial adjustments made following trials associated with conflict (i.e., noncorresponding trials; Fielding et al., 2005; Praamstra & Plat, 2001). Both studies reported that PD patients showed less reduction of the Simon effect following trials that induced response conflict, suggesting that proactive control was less effective in PD patients than in HCs.

The Current Investigation

Although there has not been unanimity in the results of previous research, this work does suggest that PD patients may have difficulty with both on-line and proactive control of response interference. To examine this possibility in more depth, we used a novel approach that emerges from the activation–suppression model of Ridderinkhof (2002a). This approach enhances the precision with which group differences in the strength of automatic response activation, what we refer to as *response capture*, can be distinguished from differences in the subsequent engagement of on-line control to suppress this activation. The activation–suppression model refines dual-route models of interference effects by incorporating specific hypotheses about the temporal dynamics of top–down suppression of automatic response capture. To do so, it employs distributional analyses of interference effects to expose the dynamics of interference control that are masked by measures of mean interference effects such as those typically reported in the literature. Specifically, it postulates the existence of both an early automatic response capture and a later controlled top–down response suppression mechanism. Differences in the strength of automatic response capture are thought to be revealed by the pattern of relations between errors and RT. Stronger initial response capture is presumed to lead to an increase in fast errors as less time is available for the buildup of suppression to counter this incorrect activation (Kornblum et al., 1990). Thus, plotting accuracy rates as a function of RT (i.e., *conditional accuracy function*) provides a means for studying group differences in the strength of automatic response capture, with stronger capture associated with a higher frequency of fast errors. In contrast to the rapid engagement of the response capture mechanism, top–down suppression takes time to buildup and, therefore, is most evident as response speeds slow. For instance, the faster one responds, the less likely it is that suppression will have accrued to a level that is sufficient to counteract response capture. Rather, slower responses are more likely to benefit from the buildup of suppression to resolve interference. Thus, plotting the Simon effect as a function of response speed (i.e., *a delta plot*) should reveal a pattern of increasing interference across faster RTs, but a reduction of interference toward the slow end of the RT distribution as the suppression mechanism becomes more fully engaged. Several studies have now confirmed this pattern in the Simon and related interference tasks in young adults (Wiegand & Wascher, 2007; Burle, van den Wildenberg, & Ridderinkhof, 2005; Ridderinkhof, van den Wildenberg, Wijnen, & Burle, 2004; Burle, Possamaï, Vidal, Bonnet, & Hasbroucq, 2002; Ridderinkhof, 2002b; Stuermer, Leuthold, Soetens, Schröter, & Sommer, 2002; de Jong et al., 1994).

Moreover, the magnitude of the reduction in the interference effect at the slowest segment of the RT distribution has been shown to be sensitive to the degree to which response inhibition is engaged (Wijnen & Ridderinkhof, 2007; Burle et al., 2002), to distinguish individuals and groups with predicted deficiencies in inhibitory control (Wylie et al., 2009; Wylie, Ridderinkhof, Eckerle, & Manning, 2007; Bub, Masson, & Lalonde, 2006; Ridderinkhof, Scheres, Oosterlaan, & Sergeant, 2005), and to be associated with the activity of prefrontal areas empirically linked to inhibitory action control (Davelaar, 2008; Forstmann, Jahfari, et al., 2008; Forstmann, van den Wildenberg, et al., 2008).

Working within the conceptual framework of the activation–suppression model, we investigated how PD affects the strength of response capture and the proficiency of suppression in the context of both on-line (within-trial) and proactive (between-trial) control of response interference. Compared to previous studies, we used a significantly larger sample of PD patients ($n = 52$), which increased the power of effects and permitted the examination of the association between clinical features of PD and Simon effects. We predicted that group differences would emerge when the underlying dynamics of the processing were exposed by distributional analyses. Our main prediction regarding on-line control was that PD patients would show stronger incorrect response capture and be less proficient in reduction of interference. This prediction was based, in part, on our previous work showing these effects among PD patients relative to HCs on a flanker task (Wylie et al., 2009) and, in part, on past findings that have demonstrated a larger Simon effect among PD patients. The demonstration of stronger response capture and poorer response suppression in the Simon task among PD patients would further strengthen and extend the notion that deficits in interference control during action selection are a fundamental, situation-independent feature of PD.

With respect to proactive control of interference, we based our predictions on previous findings that PD patients are less effective at adjusting to conflict between trials. Compared to HCs, we predicted that PD patients would show less dramatic reduction of mean Simon effects following conflict trials. However, in the current study, the activation–suppression model guided our expectations about the effects of proactive control on the strength of initial response capture and the proficiency of suppression following a conflict situation. For HCs, we predicted that proactive control would lead to fewer fast errors, suggesting that this type of control involves a reduction in the strength of initial response capture caused by automatic processing. In fact, this pattern has been demonstrated in a recent study of healthy young adults (Stins, Polderman, Boomsma, & de Geus, 2007). We also investigated whether proactive control by HCs would influence the proficiency of the suppression process, revealed by a reduced interference effect on trials following noncorresponding trials than on trials following corresponding trials. Based on these expected patterns, we examined the extent to which poor proactive control among PD patients involved less effective reduction in the strength of initial response capture and/or interference suppression. We also reasoned that if PD patients experience a fundamental reduction in the ability to adjust cognitive control proactively, they would also show poorer proactive control after making a response error compared to HCs. Thus, we expected that the Simon effect would be diminished to a lesser degree among PD patients than HCs after a response error was committed.

METHODS

Participants

Fifty-two individuals diagnosed with PD and 30 HCs similar in age, education, and sex ratio (ps $> .10$) participated in this study. Table 1 shows group demographics. The groups did not differ ($p > .10$) on a measure of global mental status (Mini-Mental Status Exam [MMSE]; Folstein, Folstein, & McHugh, 1975). Participants with PD were recruited from the Movement Disorders Clinic at the University of Virginia and diagnosed with idiopathic PD by a neurologist specializing in movement disorders. They voluntarily completed the study on the same day or within a few weeks of their regularly scheduled Movement Disorders Clinic visit. Patients completing study participation on the same day as their clinic visit were screened for adverse clinical events (e.g., fatigue, stress, concerns about poor symptom control) that might have affected their task performance. All PD patients were rated Stage III or less using the Hoehn and Yahr (1967) scale, with an average rating of 2.1. Just 6 of the 52 patients rated a Stage III. Thus, all patients were considered to have a mild to early moderate disease presentation. Fifty-one of the 52 PD patients were taking medications to improve dopaminergic function and were tested during the optimal "on" state of their medication cycle. All of these patients showed a positive medication response, evidenced by a reduction of clinical symptoms. Of the 51 patients taking medications, 45 were taking levodopa, and 20 of these patients were concurrently taking a dopamine agonist. Of the six patients not taking levodopa, five were taking a dopamine

Table 1. Demographic Data for PD and HC Groups

	HC	*PD*
Sample size	30	52
Age (years)	63.3 (7.9)	65.9 (8.2)
Education (years)	15.9 (3.6)	15.9 (2.6)
Sex (M:F)	19:11	33:19
MMSE (raw score)	29.4 (0.9)	28.7 (1.4)
Years since PD onset	–	7.7 (4.6)
Hoehn & Yahr rating	–	2.1 (0.5)

Standard deviation shown in parentheses.

agonist only and one was taking anticholinergic medication only (i.e., amantadine). Fifteen patients were also taking antidepressant medication at the time of testing, but all reported stable mood functioning and denied significant levels of depression.

Healthy controls were occasionally family members of PD patients or recruited from the local community via advertisement. Exclusion criteria for all participants included the following: history of other neurological condition; untreated or unstable mood disorder; history of bipolar affective disorder, schizophrenia, or other psychiatric condition known to compromise executive cognition; untreated or unstable medical condition known to interfere with cognition (e.g., diabetes, pulmonary disease). All participants had corrected-to-normal vision. All participants provided informed consent prior to participating in the study, which was fully compliant with standards of ethical conduct in human research as regulated by the University of Virginia human investigation committee.

Task and Procedures

Control of the Simon task was accomplished using an IBM-compatible computer. Participants were seated comfortably about 1 meter from a 17-in. computer monitor on which the experimental stimuli were presented. Stimuli consisted of a small square fixation point and blue- or green-colored circles against a white background. Responses to the imperative stimuli, the colored circles, were registered via right- and left-thumb button presses using handheld grips. Each trial began with the presentation of a fixation point shown in the center of the computer screen. After a variable duration ranging from 1750 to 2250 msec, a blue or green circle appeared 0.6 cm (0.34° visual angle) to the left or to the right of the fixation point and remained on the screen until the participant either made a response or 1500 msec elapsed. The circle diameter was 2.1 cm (visual angle = 1.20°). Participants were instructed to make a button press with the right or left thumb based on a predetermined mapping between circle color and response side (e.g., green circle, right-thumb press; blue circle, left-thumb press). The mappings between circle color and response side were counterbalanced across participants. After a response, the circle disappeared and the next trial began. The fixation point remained on the screen at all times.

Two trial types were defined by the correspondence between the spatial location of the circle and the response signaled by its color. For *corresponding* trials, the side of fixation on which the circle appeared matched the side of the response signaled by the color of the stimulus (e.g., a green circle calling for a right-hand response appeared on the right side of fixation). For *noncorresponding* trials, the circle appeared on the side of fixation opposite the side of the response signaled by the circle's color (e.g., a green circle calling for a right-hand response appeared on the left side of fixation). Trials were also partitioned on the basis of the preceding trial type or *trial sequence*. Trial sequence was mixed randomly within a block of trials, with the constraint that roughly equal numbers of trials were preceded by corresponding or noncorresponding trials.

To learn the color–response mapping, participants first completed a block of 100 practice trials in which the circle appeared in the same center location as the fixation point. Next, a block of 60 practice trials was completed in which circles were displaced to the right or left of fixation as described above. Five blocks of 60 experimental trials were then performed. Within each block of trials, corresponding and noncorresponding trial types were presented randomly, but equiprobably. Participants completed 150 corresponding and 150 noncorresponding trials.

Statistical Techniques

Extreme RT values, either excessively fast or slow, were removed from the analysis using a conservative trim procedure (RT values > 3 standard deviations above or below the mean) to indicate suspected outliers and after visual inspection of each trial within an experimental cell to verify each value as a clear outlier (see also Wylie et al., 2009). This procedure resulted in the elimination of less than 0.2% of trials per subject. Anticipatory responses faster than 100 msec were also eliminated from analyses, accounting for less than 0.0005% of trials per subject. RT and square-rooted accuracy data were submitted to separate overall mean analyses (repeated measures ANOVA) to determine group differences in average Simon effect. The experimental factors in this analysis were correspondence (corresponding, noncorresponding) and group (PD, HC). For the analysis of postconflict effects, a third factor, trial sequence (preceding trial corresponding [PTC], preceding trial noncorresponding [PTN]) was added to the ANOVA. For the analysis of post-error effects, a third factor, accuracy sequence (preceding trial accurate [PTacc], preceding trial error [PTerr]) was added to the ANOVA.

As a measure of the strength of response capture, the proportion of fast errors was revealed by conditional accuracy functions (CAFs), which plot Vincentized accuracy rates as a function of the entire RT distribution. For each level of correspondence, RTs were rank-ordered and partitioned into seven segments (septiles; Segments 1–7).[1] Accuracy rates were then calculated for each segment, thus generating seven accuracy values each for corresponding and noncorresponding trials. These accuracy rates were then plotted against the average RT for each bin. The strength of response capture was analyzed by focusing on a group comparison of accuracy rates for the fastest RT segment of the CAFs across levels of correspondence. The proficiency of suppression was studied using delta plots, which plot the Simon effect (i.e., mean RT for the noncorresponding condition minus mean RT for the corresponding condition) as a function of RT. Delta plots were also constructed by Vincentization procedures

that involved rank-ordering RTs for each level of correspondence, partitioning these values into seven segments, and calculating the mean RTs for each level of correspondence in each segment. Next, a Simon effect was computed for each segment. The resulting seven Simon effect values were plotted as a function of the average RT for each bin. The slopes between the Simon effect values (i.e., *delta values*) were computed. The slope of the slowest RT segment connecting the two slowest RT bins was the primary dependent measure and has been linked to the proficiency of inhibitory control (Ridderinkhof, 2002a).

RESULTS

The results are organized as follows. First, we present the analyses of group effects on on-line control processes, including mean effects and distributional effects. Second, the results of the analyses of group effects on proactive control processes that are engaged after experiencing response conflict are described. Next, group effects on proactive control processes that are engaged after committing a response error are presented. Finally, associations between clinical features of PD and measures of on-line and proactive control are described.[2]

Influence of PD on the Dynamics of "On-line" Control

Mean RT and Accuracy Effects

The overall mean RTs and accuracy rates of PD patients and HCs are depicted in Figure 2A. PD patients were 36 msec slower to react than HC subjects, but equally as accurate [Group: RT, $F(1, 80) = 4.36$, $p = .04$; accuracy, $F(1, 80) = 0.86$, $p = .36$]. In addition, as illustrated in Figure 2B, variations in the correspondence of the stimulus location with the side of the response produced parallel effects on the mean RTs and accuracy rates of both groups. RTs were slower and accuracy rates were lower for noncorresponding than for corresponding trials (i.e., the Simon effect) [correspondence: RT, $F(1, 80) = 180.79$, $p < .001$; accuracy, $F(1, 80) = 31.58$, $p < .001$], and the cost of noncorrespondence on both measures, shown in Figure 2C, did not differ between the two groups [Group × Correspondence: RT, $F(1, 80) = 0.11$, $p = .75$; accuracy, $F(1, 80) = 2.07$, $p = .16$]. Indeed, the magnitude of the Simon effect was nearly identical in the two groups for RT (PD = 37 msec; HC = 35 msec) and very similar for accuracy (PD = 4.3%; HC = 2.5%).

Group Effects on Response Capture

The CAFs shown in Figure 3A reveal that most of the errors on the Simon task were fast errors made on noncorresponding trials. Slow responses on noncorresponding trials, as well as both fast and slow responses on corresponding trials, were associated with near-perfect accuracy. Moreover, PD patients and HCs showed similar patterns of fast errors. To verify these visual impressions, we restricted our analysis to the accuracy rate from the first bin of corresponding and noncorresponding trials to isolate these patterns of fast errors. A repeated measures ANOVA, with *correspondence* (Corresponding, Noncorresponding) as a within-subject factor and *group* (PD, HC) as a between-subjects factor revealed that more fast errors occurred on noncorresponding than on corresponding trials [correspondence, $F(1, 80) = 61.53$, $p < .001$]. The groups did not differ in the percentage of fast errors [PD = 87.6%; HC = 88.3%; group, $F(1, 70) = 0.05$, $p = .83$] and the Group × Correspondence interaction was not significant (all $p > .10$). According to the activation–suppression and dual-route models, PD patients and HCs experienced

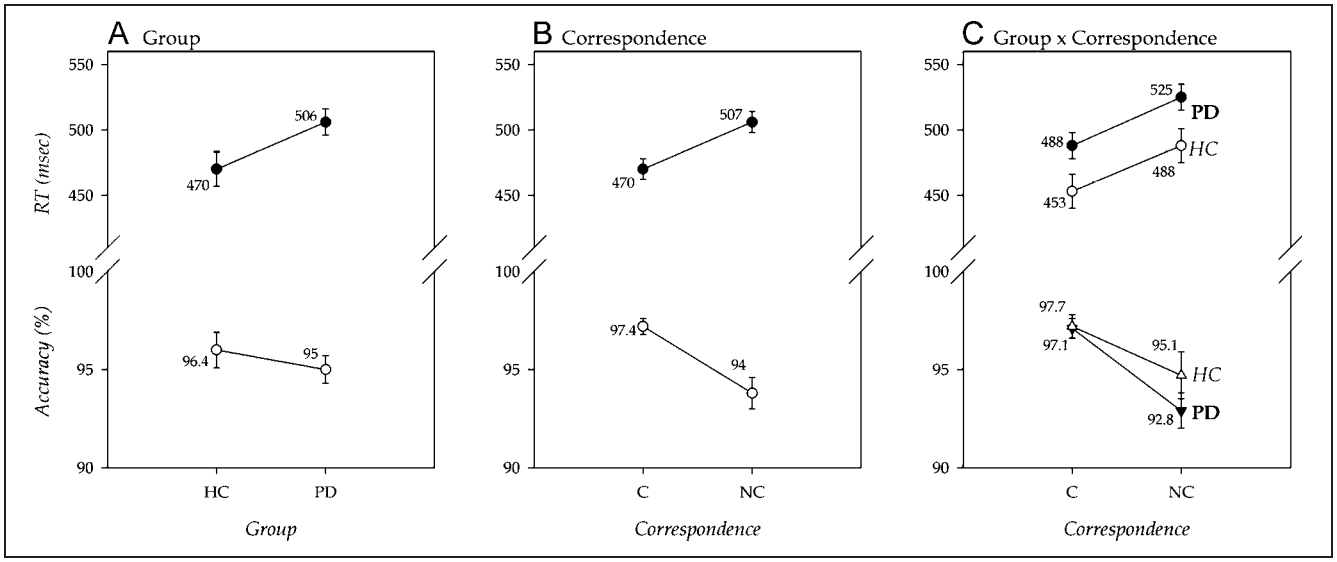


Figure 2. Mean RTs and accuracy rates (% correct) as a function of (A) group (PD, HC), (B) Simon correspondence (corresponding [C], noncorresponding [NC]), and (C) the interaction between group and Simon correspondence. Error bars reflect standard error of the means.

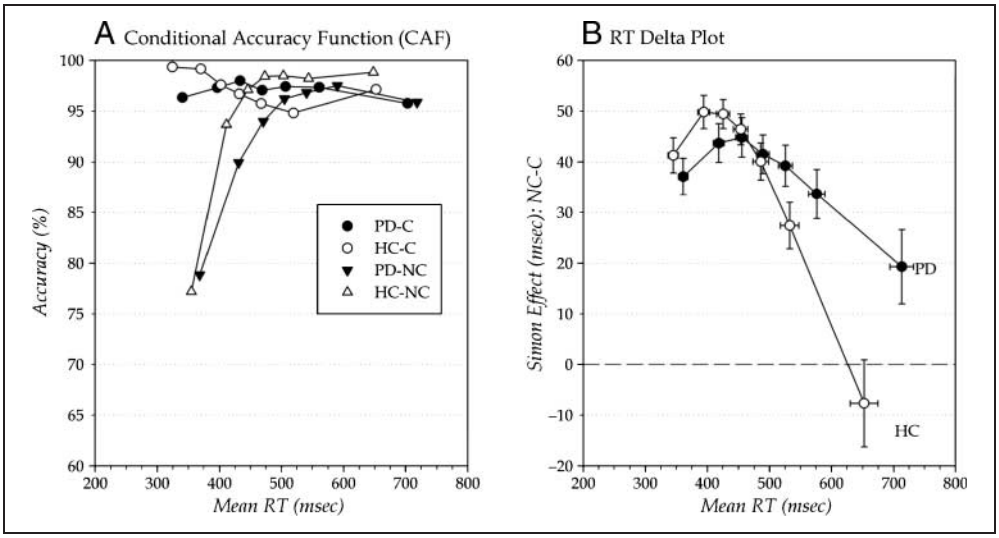


Figure 3. (A) Conditional accuracy functions for corresponding [C] and noncorresponding [NC] trial types in individuals with PD and HCs. For both groups, errors are associated with the fastest RTs on NC trials, but the pattern of error rates does not differ between groups. (B) RT delta plots for PD and HC groups. Group delta slopes diverge at the slow end of the distribution, suggesting less efficient suppression of incorrect response activation among PD patients.

similar levels of initial response capture from the automatic processing of conflicting spatial information.

Group Effects on Selective Suppression

The delta plots for the PD and HC groups shown in Figure 3B clearly illustrate the absence of uniformity in the Simon effect across the RT distribution. As predicted by the activation–suppression model, the hypothesized buildup of inhibitory control results in a decline of the Simon effect for the slowest RTs. In fact, the Simon effect actually reverses among HCs for the slowest RT segment. The slope connecting the final two segments of the delta plot is tied empirically to the effectiveness of inhibitory control, and it is more steeply negative-going among HCs than among PD patients. This visual impression was verified by a planned contrast that revealed that the slope of the final segment of the delta plot was more negative-going among HCs ($m = -0.29$) than among PD patients ($m = -0.10$) [$F(1, 80) = 9.39$, $p = .001$, one-tailed test].[3] This difference in slope, according to the activation–suppression model, suggests that PD patients were less effective at resolving response interference by suppressing incorrect response tendencies than were HCs.

Influence of PD on the Dynamics of "Proactive" Control

Mean RT and Accuracy Effects

In order to evaluate conflict adaptation effects, we added a third experimental factor to the analysis, *trial sequence*, that consisted of two levels; trials preceded either by corresponding (PTC) or by noncorresponding (PTN) trials. Thus, the design included two within-subjects factors, correspondence (corresponding, noncorresponding) and trial sequence (PTC, PTN), and one between-subjects factor, group (PD, HC). Our discussion centers on the presence of sequential effects on RT and accuracy because, as expected, the effects of variations in group and correspondence replicated the results of the initial analyses. Mean RTs were slower and accuracy rates were higher, as shown in Figure 4A, for trials that followed noncorresponding as opposed to corresponding trials [trial sequence: RT, $F(1, 80) = 15.88$, $p < .01$; accuracy, $F(1, 80) = 11.21$, $p = .001$]. However, this effect varied for both RT and accuracy with the correspondence effects of the current trial [Correspondence × Trial sequence: RT, $F(1, 80) = 214.72$, $p < .001$; accuracy, $F(1, 80) = 86.64$, $p < .001$]. The sources of the interaction are clear for both measures, as can be seen in Figure 4B. Specifically, planned comparisons revealed that a large Simon effect was observed on both RT and accuracy for the subset of trials that were preceded by corresponding trials [RT, $F(1, 81) = 435.01$, $p < .001$; accuracy, $F(1, 81) = 77.90$, $p < .001$], whereas the effect vanished for the subset of trials that were preceded by noncorresponding trials [RT, $F(1, 81) = 0.01$, $p = .92$; accuracy, $F(1, 81) = 0.001$, $p = .98$].

We see, then, that when faced with conflict on an immediately preceding trial, participants were able to adapt to this conflict and minimize it when it occurred on the subsequent trial. Of particular importance are our observations that the effects of variations in trial sequence did not differ between the two groups and this pattern was not altered by the correspondence of the stimulus and response mapping for either RT or accuracy [Group × Trial sequence: RT, $F(1, 80) = 2.65$, $p = .11$; accuracy, $F(1, 80) = 0.10$, $p = .75$; Group × Trial sequence × Correspondence: RT, $F(1, 80) = 0.21$, $p = .65$; accuracy, $F(1, 70) = 0.09$, $p = .77$]. The stability of this pattern of effects is depicted in Figure 4C and D. In Figure 4C we show the effect of variations in correspondence between the two groups on a given trial when the preceding trial was corresponding, and in Figure 4D we illustrate this effect when the preceding trial was noncorresponding. These patterns indicate

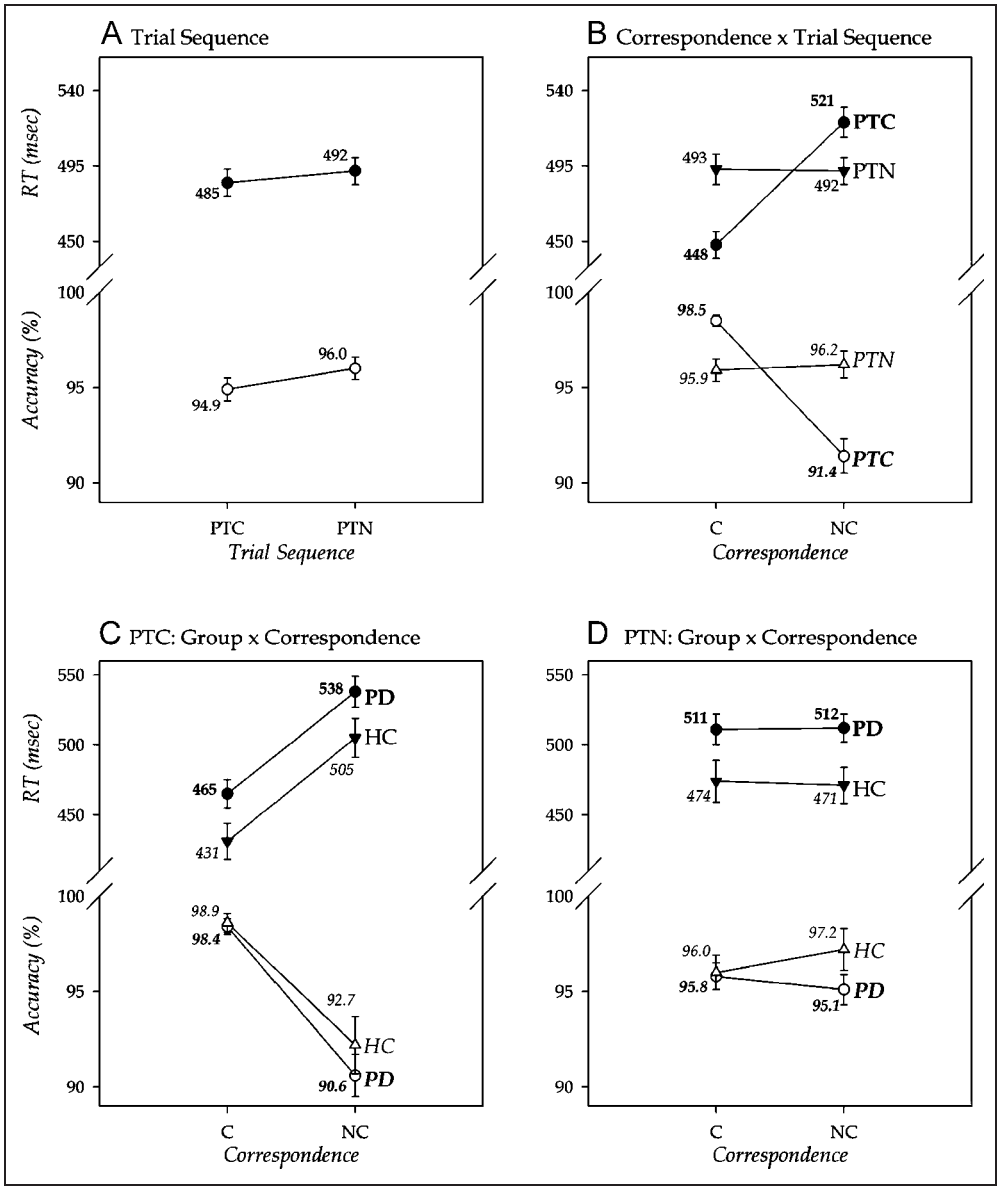


Figure 4. Mean RTs and accuracy rates (% correct) based on (A) trial sequence (preceding trial corresponding [PTC], preceding trial noncorresponding [PTN]), (B) the interaction between trial sequence and Simon correspondence (corresponding [C], noncorresponding [NC]), (C) the interaction between group and Simon correspondence for trials preceded by corresponding trials (PTC), and (D) the interaction between group and Simon correspondence for trials preceded by noncorresponding trials (PTN). Error bars reflect standard error of the means.

that PD patients were similar to HCs in their ability to adapt proactively to conflict between trials.

The Effect of Proactive Control on Response Capture

Figure 5 depicts the group CAFs separately for trials preceded by corresponding (Figure 5A) and by noncorresponding (Figure 5B) trials. Most striking from these graphs is what appears to be a clear increase in incorrect response capture (i.e., fast errors) when noncorresponding trials were preceded by corresponding as opposed to noncorresponding trials. This pattern accords with the view that following noncorresponding trials a conflict adaptation process is engaged that reduces the impact of incorrect response capture on the subsequent trial. To support these visual impressions, we analyzed the pattern of fast errors (i.e., accuracy rates for the fastest RT bin) as a function of correspondence (corresponding, noncorresponding), trial sequence (PTC, PTN), and group (HC, PD).

Fast errors were more prevalent for noncorresponding than for corresponding trials [correspondence, $F(1, 80) = 54.46$, $p < .001$] and for trials preceded by corresponding as opposed to noncorresponding trials [trial sequence, $F(1, 80) = 40.60$, $p < .001$]. The increase in fast errors for noncorresponding trials compared to corresponding trials depended on the preceding trial type [Correspondence × Trial sequence, $F(1, 80) = 70.03$, $p < .001$]. Specifically, the susceptibility to fast errors was diminished for trials that followed noncorresponding trials compared to those that followed corresponding trials [$F(1, 81) = 67.83$, $p < .001$]. This suggests that after facing and resolving the conflict induced by a noncorresponding trial, participants proactively activated control processes to minimize automatic response capture on the next trial.

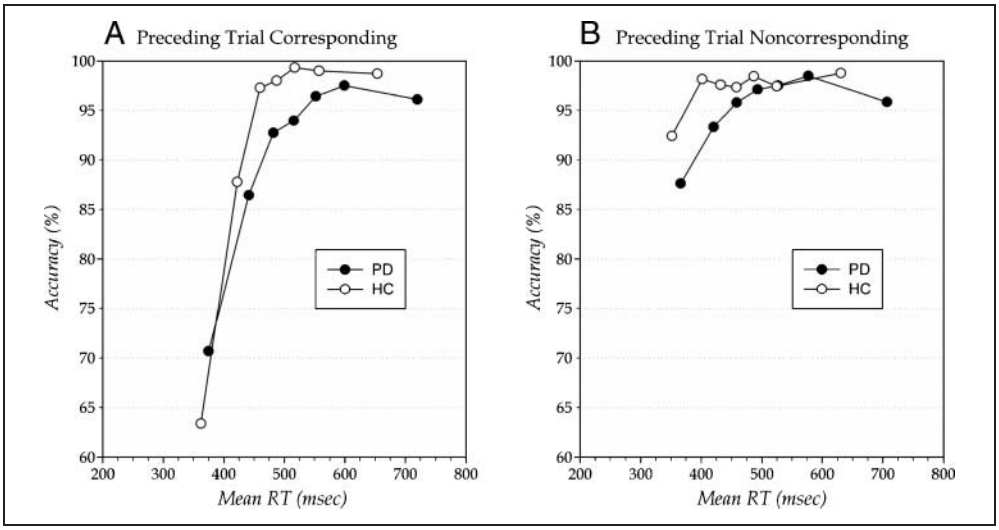


Figure 5. Conditional accuracy functions in individuals with PD and HCs for noncorresponding (i.e., conflict) trials preceded by (A) corresponding trials and (B) noncorresponding trials.

The groups did not differ in their overall pattern of fast errors [Group, $F(1, 80) = 0.03$, $p = .87$]. However, the two groups were found to differ in their production of fast errors on trials following noncorresponding trials [Group × Trial sequence, $F(1, 80) = 7.40$, $p < .01$]. Planned comparisons indicated that HC participants made fewer fast errors than did PD patients following noncorresponding trials [$F(1, 80) = 4.15$, $p < .05$], suggesting they achieved better control over initial response capture following conflict. However, the percentage of fast errors following corresponding trials did not differ between the two groups [$F(1, 80) = 1.12$, $p = .29$].

The Effect of Proactive Control on Selective Suppression

Figure 6 shows the RT delta plots as a function of trial sequence. As previously determined in the mean RT analysis, Simon effects are clearly sensitive to sequential effects; they are much larger for trials preceded by corresponding than by noncorresponding trials. Guided by the activation–suppression model, we isolated the final slope of the delta plot to determine differences in inhibitory control that might be sensitive to sequential effects. The analysis showed no effect of trial sequence on the final delta slope [$F(1, 80) = 0.78$, $p = .38$]. However, the magnitude of the final delta slope was more negative-going among HCs than among PD patients [group, $F(1, 80) = 6.07$, $p < .01$], but this difference was not influenced by the trial sequence [Group × Trial sequence, $F(1, 80) = 0.03$, $p = .86$]. Thus, PD patients showed less efficient inhibition (i.e., less of a negative-going delta slope) than did HCs, but this difference was independent of the sequencing of corresponding and noncorresponding trials.

Influence of PD on Post-error "Proactive" Control

Mean RT Effects

To evaluate post-error proactive control, we added a third experimental factor to the main analysis, accuracy sequence, which consisted of two levels; trials preceded either by an accurate (preceding trial accurate, PTacc) or by an error (preceding trial error, PTerr) response. Thus, the design included two within-subjects factors, correspondence (corresponding, noncorresponding) and accuracy sequence (PTacc, PTerr), and one between-subjects factor, group (PD, HC). Our discussion centers on the presence of post-error sequential effects on RT because, as expected, the effects of variations in group and correspondence replicated the results of the initial analyses and because post-error proactive control effects primarily influence the speed of responding on a subsequent trial. Because errors occur less frequently than accurate responses, fewer trials

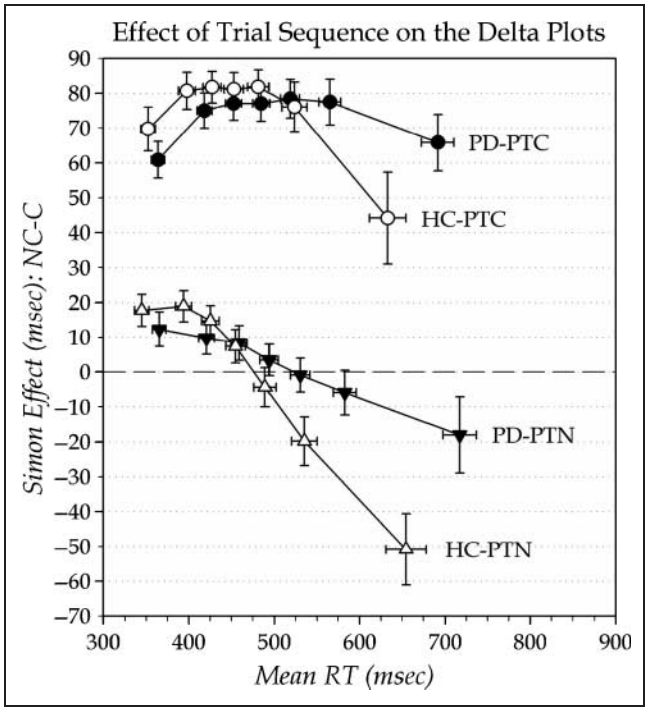


Figure 6. RT delta plots for PD and HC groups for trials preceded by corresponding trials (PTC) and by noncorresponding trials (PTN).

fall into the subset of trials that are preceded by an error (i.e., PTerr) than fall into the subset of trials preceded by an accurate response (PTacc). Furthermore, a small percentage of participants did not make enough errors to permit a comparison of corresponding and noncorresponding trial types on the subsequent trial. Thus, the sample sizes included in the following analysis were reduced slightly for PD (n = 43) and HC (n = 27) groups.

Mean RTs were slower for trials that followed an error as opposed to an accurate trial [accuracy sequence: RT, $F(1, 68) = 114.33, p < .001$] in both groups [Group × Accuracy sequence: RT, $F(1, 68) = 0.64, p = .43$]. However, the sequence effect varied as a function of the spatial correspondence in the current trial [Correspondence × Trial sequence: RT, $F(1, 68) = 26.42, p < .001$]. The source of this interaction is clear, as can be seen in Figure 7. Planned comparisons revealed a large Simon effect on RT (32 msec) for the subset of trials that was preceded by an accurate response trial [$F(1, 69) = 149.32, p < .001$], but a numerically reversed effect (−20 msec) for the subset of trials that was preceded by a trial in which the participant responded incorrectly [$F(1, 69) = 5.08, p < .05$]. Thus, after making an error, participants not only slowed their RTs on a subsequent trial, but engaged control processes between trials to reduce the interfering effects of conflict on the subsequent trial. Of particular importance is our observation that this interaction did not vary by group [Group × Accuracy sequence × Correspondence: $F(1, 68) = 1.06, p = .31$], which is clearly depicted in Figure 7 by parallel effects among both groups. These patterns indicate that PD patients were similar to HCs in their ability to adapt proactively after making a response error.

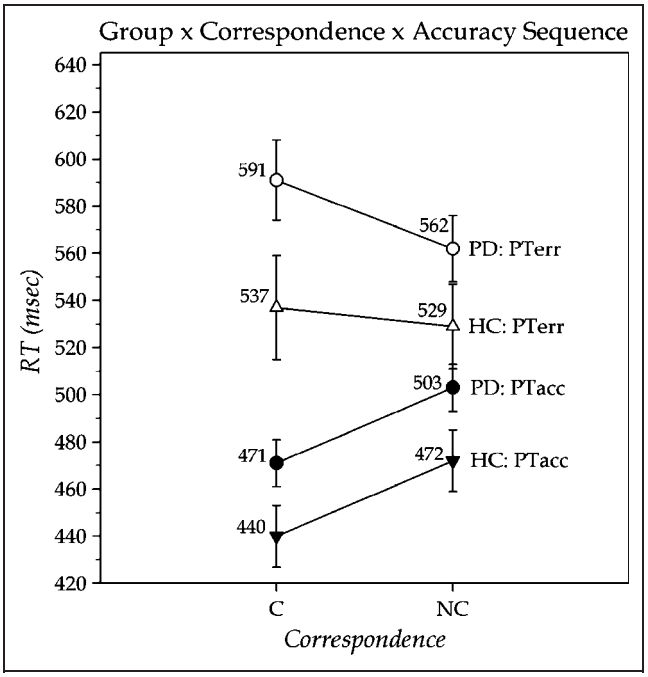


Figure 7. Correspondence effects on mean RT for trials preceded by accurate (PTacc) and error (PTerr) responses. Error bars reflect standard error of the means. C = corresponding; NC = noncorresponding.

Association of Performance Variables to Clinical Features of PD and Subgroup Analysis

On-line Control

The severity of motor symptoms associated with PD was assessed using the motor subscale of the Unified Parkinson's Disease Rating Scale (UPDRS) in 46 of the 52 PD patients. Although motor symptom severity did not correlate with overall RT ($r = .14, p = .36$), more severe symptoms were associated with larger Simon effects on both RT ($r = .42, p < .01$) and accuracy ($r = -.46, p < .01$); a higher proportion of fast errors on noncorresponding ($r = -.37, p = .01$) but not on corresponding ($r = .03, p = .85$) trials; and a reduction in the negative-going slope of the delta plot between the slowest segments of the RT distribution ($r = .31, p < .05$). The latter two results suggest, respectively, an increase in response capture and less proficient suppression of the incorrect response with increases in motor symptom severity.

Proactive Control

Motor symptom severity was unrelated to measures of proactive control following correct or incorrect trials. There was no relationship between increases in motor symptom severity and reductions in the Simon effect for either RT ($r = .01, p = .96$) or accuracy ($r = .06, p = .69$) on trials that were preceded by correct responses on noncorresponding trials. Similarly, motor symptom severity was unrelated to a reduction in the Simon effect ($r = -.16, p = .34$) on trials following an error or to a slowing in RT on corresponding ($r = .04, p = .81$) and noncorresponding ($r = -.14, p = .40$) trials that were preceded by an error.

PD Subgroup Analysis

Motor symptom severity of PD was related to within-trial on-line control of response interference. To study this interesting finding further, we rank-ordered the motor UPDRS scores for 45 PD patients and divided them into three equal-sized subgroups (one patient's UPDRS score was eliminated randomly to create groups of equivalent size). Bearing in mind that all patients were of mild to moderate disease severity, the three subgroups reflected patients within the sample who showed less severe, moderately severe, and most severe motor symptoms. Notably, the three subgroups did not differ in age or age at disease onset (ps > .10), but did differ in disease duration ($p = .03$), with the difference reflecting a longer disease duration for patients with the most severe compared to those with the least severe motor symptoms ($p = .03$). Next, we analyzed subgroup differences in the strength of response capture on noncorresponding trials and the proficiency of

inhibitory control (i.e., the slowest delta slope). Figure 8A and B shows the CAF and delta plots for subgroups of patients with the least severe, moderately severe, and most severe motor symptoms. As depicted in Figure 8A, the strength of response capture (i.e., proportion of fast errors) varied by subgroup [$F(2, 42) = 5.53, p = .007$]. Pairwise comparisons (Bonferroni-adjusted) showed that the PD patients with the most severe motor symptoms made significantly more fast errors than patients with the least severe ($p = .003$) and patients with moderately severe ($p = .04$) symptoms. Figure 8B also shows that the last delta slope between the slowest RT segments varied by motor symptom severity [$F(2, 42) = 4.14, p < .05$]. Pairwise comparisons (Bonferroni-corrected) confirmed slope differences between the least severe and most severe subgroups ($p < .01$), with the moderately severe group falling intermediate to these two subgroups, but not differing statistically from either group ($p > .10$).

DISCUSSION

Conflict tasks provide the opportunity to study the strength of stimulus-driven activation of a conflicting response and the effectiveness of top–down control to suppress this activation and then make proactive changes in control to reduce future conflict. It was our aim to determine whether PD differentially affects these dynamic control processes in the setting of a Simon interference task.

On-line Control of Response Interference

Simon interference effects were produced successfully, as reflected in both mean RT and accuracy rates, but the magnitude of these mean effects did not differ between PD patients and HCs. Based on conventional interpretations, these data suggest that PD patients did not experience enhanced conflict or show impairments in their proficiency at resolving response conflict induced by automatic processing of irrelevant spatial information. Indeed, both groups showed conflict effects that prolonged mean RT by about 37 msec and increased mean error rates by about 3% to 4%.

An important limitation of using mean interference effects is that the underlying processing dynamics that give rise to the interference and its resolution cannot be easily distinguished. That is, mean interference effects cannot determine whether groups differ in terms of the strength of incorrect response capture induced by automatic processing or in terms of the proficiency of suppression engaged to reduce the interference from incorrect response capture. Stronger incorrect response capture or inefficient suppression could separately or collectively contribute to an increase in Simon interference effects. We used the activation–suppression model to study these processing dynamics more directly. The strength of initial response capture was inferred on the basis of the proportion of fast errors. In fact, both PD patients and HCs showed a clear pattern whereby errors in the noncorresponding condition were primarily confined to the fastest RTs. In contrast, slower RTs in the noncorresponding condition were associated with near-perfect accuracy, as were RTs across the entire distribution of corresponding trials. Importantly, the pattern of fast errors on noncorresponding trials did not differ between groups, supporting the inference that the strength of initial response capture was equivalent for the two groups.

Next, we considered the effects of PD on the proficiency of response suppression by determining how much the Simon effect on RT was reduced at the slowest segment of the RT distribution. The slope of the segment connecting the slowest RT bins of the delta plot can be used as a measure of the efficiency of inhibitory control, with more

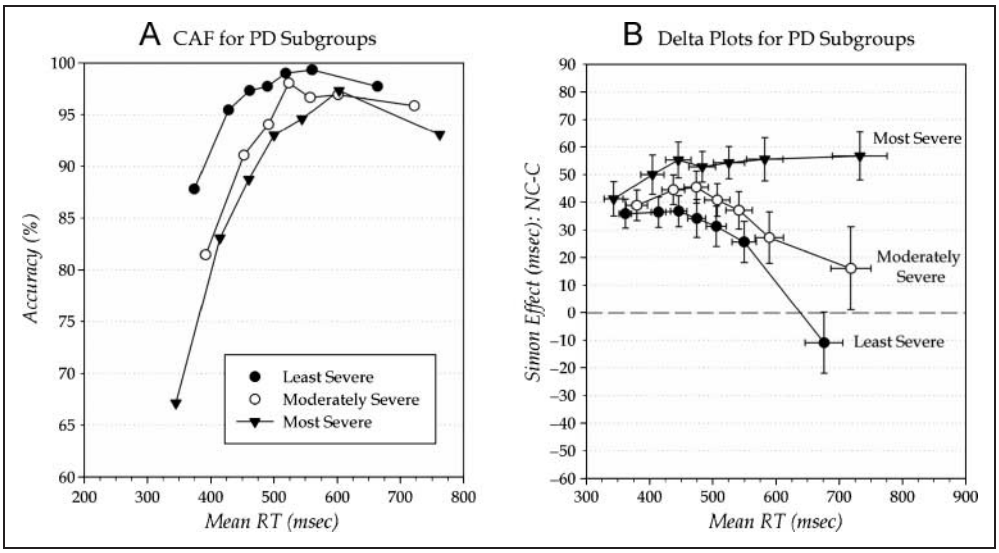


Figure 8. (A) Conditional accuracy functions for noncorresponding [NC] trial types for subgroups of PD patients based on the severity of their motor symptoms. The PD subgroup with the most severe symptoms shows a higher proportion of fast errors than the moderately and least severe subgroups. (B) RT delta plots for PD subgroups. The PD subgroup with the most severe symptoms shows a significantly reduced negative-going delta slope compared to the subgroup with the least severe symptoms, suggesting less proficient suppression of incorrect response activation with more severe disease presentations.

efficient inhibition associated with a steeper, negative-going delta slope (Ridderinkhof, van den Wildenberg, Wijnen, et al., 2004). Consistent with this prediction, the Simon effect declined sharply for the slowest responses. Moreover, the reduction of interference was significantly greater among HCs compared to PD patients, even reversing at the slowest RT segments, suggesting that PD patients were less proficient at suppressing the interference arising from incorrect response capture.

The interpretation that PD patients are less efficient at suppressing response interference is consistent with other studies that have found poor interference control among PD patients on flanker tasks, which measure interference from distractors in the visual field rather than the spatial location of the imperative stimulus (Wylie et al., 2005, 2009; Praamstra, Plat, Meyer, & Horstink, 1999; Praamstra et al., 1998; although see Falkenstein, Willemssen, Hohnsbein, & Hielscher, 2006). The ability to suppress initiated, but yet to be executed, responses as measured by the stop-signal task is also disrupted by PD and influenced by its treatment (van den Wildenberg et al., 2006; Gauggel, Rieger, & Feghoff, 2004). Taken together, these results continue to strengthen the hypothesis that one important feature of PD is a dysfunction in inhibitory control processes that operate during action selection, especially in situations where there is response conflict.

A novel extension of this work is the finding that measures of on-line interference and control, including the magnitude of Simon interference, the strength of automatic response capture, and the reduced proficiency in suppressing response impulses, varied with the severity of PD motor symptoms. Importantly, motor symptom severity did not correlate with overall RT. Partitioning PD patients on the basis of motor symptom severity clearly showed, however, a pattern of stronger response capture and less proficient suppression of response impulses with increasing motor severity. The relationship between Simon interference effects and motor symptom severity was somewhat surprising given the absence of a relationship between motor symptoms and flanker interference effects that we reported previously (Wylie et al., 2009). Although a different sample, the ages and clinical features of the patients in the current study were similar to those described in the latter study. Thus, the activation and suppression of response impulses, as measured by the Simon task, appear more sensitive to the progression of PD symptoms than do the effects induced by flanker interference.

Proactive Control of Response Interference

After experiencing response conflict, healthy adults are able to adjust cognitive control proactively to minimize the interfering effects of conflict that might occur on a subsequent trial. In the Simon task, this is evidenced by a reduction of the Simon effect on RT and accuracy rates for the subset of trials that follows conflict (i.e., noncorresponding) trials compared to the subset of trials that follows corresponding trials. Past investigations using the Simon task have suggested that individuals with PD are less effective at adapting to response conflict (Fielding et al., 2005; Praamstra & Plat, 2001). Contrary to these findings, the current group of 52 PD patients showed clear proactive control of response interference as revealed in mean RT and accuracy rates that were similar in magnitude to HCs. PD patients and HCs alike produced fewer errors and eliminated the Simon effect on RT on trials that were preceded by conflict, and both groups slowed their RT and eliminated the Simon effect on RT on trials that were preceded by a response error. In the distributional analysis of sequence effects based on whether the preceding trial was corresponding or noncorresponding, only one group difference emerged. Whereas both groups showed a pattern of reduced response capture (i.e., fewer fast errors revealed in the CAF) on trials that were preceded by conflict, the magnitude of the reduction was smaller in PD patients than in HCs. Thus, among PD patients, proactive control was less effective at reducing the strength of response capture by the direct route.

Turning to the impact of proactive control on response suppression, several important observations can be made from the delta plots in Figure 6 and related analyses. First, proactive control involved a global depression of the interference effect that was evident even at the fastest RTs. Second, regardless of preceding trial type, the delta slopes toward the slow end of the distribution revealed a sharp reduction of interference which, according to the activation–suppression model, is consistent with the engagement of selective suppression for both trial types. Importantly, and consistent with the main analysis, selective suppression was less efficient among PD patients for both preceding trial types. Third, the sharp reduction of the Simon effect is so dramatic for trials preceded by conflict trials that the interference effect reverses (i.e., becomes negative) for both groups. Thus, after facing conflict, proactive control of initial response capture allows one to respond more quickly to noncorrespondence than to correspondence on a large percentage of trials. PD patients also show this negative interference effect, but it is reduced in magnitude among them, consistent with their reduced proficiency in selective suppression following all trial types.

Overall, the current analysis paints a slightly different picture of proactive control abilities among PD patients than has been reported previously. The analyses of mean effects suggested that PD patients were just as effective as HCs at adjusting control proactively after they had faced response conflict or had committed a response error. Group differences in sequential effects only emerged in the CAFs, which showed that PD patients reduced, although less effectively than HCs, the strength of incorrect response capture after they had faced and resolved a conflict situation. PD patients continued to show less effective suppression of this incorrect response activation, but this deficit did not vary with the correspondence of the preceding trial. Moreover, whereas the severity of PD motor symptoms was significantly related to the efficiency of on-line

control of response interference, no associations between motor severity and any of the measures of proactive, between-trial control were significant.

Alternative Theoretical Considerations and Study Limitations

The activation–suppression model provided a powerful framework within which to interpret the present results in that the distributional analyses conformed accurately to the model's predictions and the results pointed to the hypothesized reduction of inhibitory control among PD patients. However, we recognize that alternative accounts of Simon interference and conflict adaptation effects may be offered in explanation of the current findings. For example, the leveling off of the Simon effect toward the slow end of the RT distribution may also involve a process of passive decay of the initial response activation by the direct route (Hommel, 1994). However, passive decay is unlikely to account for the dramatic reversal of the Simon effect. The negative Simon effect is evident in the delta plot of the overall Simon effect for the HC group and for both groups when plotting the Simon delta values for trials that are preceded by noncorresponding trials. A negative interference effect would seem to require an active process of suppression of the incorrect response activation during noncorresponding trials that leads to faster response selection for these trials. Notably, the Simon effect reverses only for trials preceded by conflict (i.e., noncorresponding) trials. For Simon interference effects calculated on trials that were preceded by corresponding trials, a reduction in the effect is observed at the slow end of the RT distribution, but neither group shows a reversal of the effect. The reversal of the Simon effect following conflict trials cannot be fully explained by suppression of direct route processing because complete blocking of the direct route after noncorresponding trials should result in a zero Simon effect (cf., Stuermer et al., 2002). After facing conflict, suppression may be engaged in a proactive manner to prevent response activation arising from the direct route. It follows that this proactive suppression would be beneficial to response selection when the next trial is noncorresponding and contains conflicting information, but detrimental to response selection on subsequent trials containing corresponding configurations and the direct route conveys correct information. In the latter situation, response time would be slowed by the additional time needed to overcome the proactive suppression of the correct response activated along the direct route. The direct activation followed by suppression and subsequent re-engagement of corresponding responses might explain the proactive pattern of negative Simon effects.

A hotly debated issue concerns the extent to which sequential effects reflect an adaptive, top–down act of cognitive control or reflect the between-trial carryover effects of episodic memory processes. The latter account is described by the feature integration model (Hommel, Proctor, & Vu, 2004), which contends that features of a stimulus and the response to it for each trial are coded into a memory event that can be activated by overlapping features in the subsequent trial. For example, if, on the next trial, one or more features are present, the entire memory event is activated, which produces facilitation effects in the case of feature and response replications or interfering effects when features and/or responses mismatch. Based on this reasoning, some studies using conflict tasks have demonstrated that sequential effects disappear when trial repetitions, overlaps, and alternations are taken into account (Nieuwenhuis et al., 2006; Mayr, Awh, & Laurey, 2003). The literature remains unclear for the Simon task, however, as several studies have demonstrated the persistence of sequential effects after taking these trial sequences into account (Wuhr, 2005; Stuermer et al., 2002). Two excellent reviews of these findings propose that both processes (and potentially others, see Egner, 2007, for a description of the expectancy priming account) are likely to contribute to sequence effects (Akcay & Hazeltine, 2007; Egner, 2007). Unfortunately, we did not design our task to balance trial sequence repetitions, alternations, and feature overlaps. Although our results conform well to the predictions of the activation–suppression model, it will be necessary to consider these opposing views of sequential effects in future studies of PD. This is particularly important as previous investigations have demonstrated that PD can alter aspects of stimulus- and response-related priming and repetition effects (Cagigas, Filoteo, Stricker, Rilling, & Friedrich, 2007; Troche, Trenkwalder, Morelli-Canelo, Gibbons, & Rammsayer, 2006; Shook, Franz, Higginson, Wheelock, & Sigvardt, 2005; Filoteo, Rilling, & Strayer, 2002).

A limitation in the current study is that the effects of dopamine-altering medication cannot be determined as all but one of the PD patients in the study were tested while taking their dopaminergic medications. Thus, it remains unclear how dopamine-altering medications affect the underlying processing dynamics involved in the Simon effect. This could be addressed using a within-subject "on" versus "off" dopamine medication design or in a study of drug-naïve patients before and after starting dopamine medication.

Potential Neural Mechanisms

We have hypothesized that one effect of PD is a disruption to interference control mechanisms operating during action selection (Wylie et al., 2005). Basal ganglia structures are hypothesized to play an important role in the focused selection and inhibition of responses, providing a potential neural circuitry for implementing interference control (Aron & Poldrack, 2006; Band & van Boxtel, 1999; Hikosaka, 1998; Mink, 1996). As a result, a particular problem arising from PD is a reduction in the capacity to suppress automatic capture by conflicting responses, which in turn increases interference during response selection.

One mechanism by which the pathology of PD may disrupt inhibitory control is through altered subthalamic nucleus (STN) activity (Blandini, Nappi, Tassorelli, & Martignoni, 2000). The STN is a portion of the neural circuitry that has been tied to inhibitory control in several recent studies by virtue of its direct connections with regions of prefrontal cortex (e.g., ventrolateral prefrontal cortex) empirically linked to inhibition (Aron, 2007; Aron & Poldrack, 2006; Frank, 2006; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004; Nambu et al., 2002). A recent study has shown that the improvement in clinical motor symptoms in PD patients following STN deep brain stimulation is accompanied by improvements in the ability to suppress unwanted action (van den Wildenberg et al., 2006). This result provides further support for a potential role of altered STN activity in accounting for inhibitory control deficits in PD, although more work is clearly needed to strengthen this hypothesis. That the current deficits in on-line inhibitory control of response interference may be mediated by abnormal basal ganglia activity induced by dopamine depletions is also supported by the systematic association we found between motor symptom severity and reductions in the efficiency of selective response suppression.

Conclusion

The basal ganglia are hypothesized to play an important role during action selection, including the suppression of unwanted or unintended actions that might interfere with the selection of a desired action. Here we add to an emerging literature demonstrating that PD, which alters normal basal ganglia function due to dopamine depletions, leads to reduced efficiency in the ability to suppress incorrect response impulses. We have contributed further to this literature by demonstrating that the vulnerability of PD patients to capture by an incorrect response impulse and their ability to suppress this capture vary with motor symptom severity. We have also found that the ability of PD patients to adjust cognitive control so as to reduce interference from future response conflict is generally intact and that the proficiency of these proactive adjustments is unrelated to motor symptom severity. These findings offer a dramatic example of how distributional analyses can isolate processes involved in the cognitive control of interference effects with greater precision than can mean measures.

Acknowledgments

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Notes

1. Seven RT segments were selected because (1) this number provides a reasonably detailed temporal window on the RT distribution, allowing for the computation of six slope values, and (2) yields mean delta and RT values of about 20 corresponding RTs and 20 noncorresponding RTs per segment, which is reasonable in terms of obtaining sufficient observations. To verify that our results do not depend on the number of segments, we followed a reviewer's suggestion to sample bins of various sizes around the 7-bin solution. Thus, we calculated a group difference in the final slope using fewer bins with more trials per bin (e.g., 5 and 6 bins) and more bins with fewer trials per bin (8 and 9 bins). Using any of these bin sizes produced equivalent results as the 7-bin solution, with PD patients showing a significantly reduced negative-going final delta slope compared to the HC group. These analyses show the robustness of the group effects.
2. As requested by one reviewer, the analyses were recomputed on a subset of 30 PD patients matched on an individual basis to the 30 HC participants according to age, sex, and education. The patterns of results were identical to those reported here using the larger group of PD patients with the exception that the selectively matched groups did not differ in overall RT. These results are not reported due to space limitations.
3. Based on previous studies and theoretical notions derived from the activation–suppression model, we zoomed in on the final delta slope to study the proficiency of inhibitory control. As requested by one reviewer, we computed a Group × Slope interaction that included all slopes from the delta plot function. This analysis confirmed a significant Group × Slope interaction with planned comparisons adjusted for multiple comparisons, showing that only the slope between the slowest RT bins differed significantly between the PD and HC groups, a finding that is consistent with the theoretical model and further justifies the focused analysis on the final slope.

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