The effect of Parkinson’s disease on interference control during action selection

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Abstract

Basal ganglia structures comprise a portion of the neural circuitry that is hypothesized to coordinate the selection and suppression of competing responses. Parkinson’s disease (PD) may produce a dysfunction in these structures that alters this capacity, making it difficult for patients with PD to suppress interference arising from the automatic activation of salient or overlearned responses. Empirical observations thus far have confirmed this assumption in some studies, but not in others, due presumably to considerable inter-individual variability among PD patients. In an attempt to help resolve this controversy, we measured the performance of 50 PD patients and 25 healthy controls on an arrow version of the Eriksen flanker task in which participants were required to select a response based on the direction of a target arrow that was flanked by arrows pointing in the same (congruent) or opposite (incongruent) direction. Consistent with previous findings, reaction time (RT) increased with incongruent flankers compared to congruent or neutral flankers, and this cost of incongruence was greater among PD patients. Two novel findings are reported. First, distributional analyses, guided by dual-process models of conflict effects and the activation–suppression hypothesis, revealed that PD patients are less efficient at suppressing the activation of conflicting responses, even when matched to healthy controls on RT in a neutral condition. Second, this reduced efficiency was apparent in half of the PD patients, whereas the remaining patients were as efficient as healthy controls. These findings suggest that although poor suppression of conflicting responses is an important feature of PD, it is not evident in all medicated patients.

Keywords:
Parkinson’s disease
Basal ganglia
Interference control
Response inhibition
Flanker task
Action selection

Responding optimally in a visual environment often requires attentional navigation of relevant and irrelevant stimuli as well as the capacity to control responses that might be signaled by these stimuli. In some instances, a response to a visual stimulus is overlearned and activation related to this response may be triggered automatically by the presence of the stimulus, even if the stimulus is irrelevant to the task at hand. Depending on the circumstances, this automatic stimulus–response activation can be advantageous or disadvantageous to performance. For instance, when automatic response activation anticipates a preferred course of action, the speed and accuracy of selecting the preferred response is facilitated (Burle, van den Wildenberg, & Ridderinkhof, 2005). In contrast, conflict between an automatically activated response and a preferred response interferes with the speed and accuracy of selecting the preferred response (Botvinick, Braver, Barch, Carter, & Cohen, 2001). In the case of conflict, cognitive control is necessary to suppress the automatic response activation in order to minimize interference with the selection of the preferred action (Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004a; Ridderinkhof, van den Wildenberg, Wijnen, & Burle, 2004b). Anyone who has attempted to type a sentence quickly using a keyboard with an unfamiliar key arrangement can appreciate the amount of cognitive control required to suppress the automatic, overlearned keystrokes (e.g., typing with a Dvorak key arrangement after learning a Qwerty layout).

Frontal–basal ganglia circuits are hypothesized to play an important role in the executive control of action, including the capacity to suppress unwanted response tendencies (Aron & Poldrack, 2006; Aron, Robbins, & Poldrack, 2004; Band & van Boxtel, 1999; Frank, 2005; Mink & Thach, 1993; Mink, 1996; Ridderinkhof, van den Wildenberg, Segalowitz, et al., 2004; van den Wildenberg et al., 2006). Indeed, many influential models of basal ganglia function have proposed that direct, indirect, and, recently, hyperdirect pathways within the basal ganglia architecture implement the selection and suppression of competing response alternatives (Aron & Poldrack, 2006; Chevalier & Deniau, 1990; Groves, 1983;
Hikosaka, 1998; Jackson & Houghton, 1995; Krauthamer, 1979; Krospotov & Etlinger, 1999; Middleton & Strick, 2000a; Middleton & Strick, 2000b; Oberg & Divac, 1979; Redgrave, Prescott, & Gurney, 1999; Robbins & Brown, 1990; Taylor & Saint-Cyr, 1995). This conceptualization implies that the complementary basal ganglia pathways may be uniquely adapted to implement interference control during action selection. That is, when two response alternatives are concurrently competing for the control of action, and the non-preferred response option happens to be the more overlearned or strongly signaled of the two responses, the basal ganglia may play a key role in suppressing this alternative and amplifying the selection of the preferred response (Bogacz, 2007). One test of this idea is to determine if individuals with known basal ganglia dysfunction have greater difficulty resolving response interference and, if so, whether the difficulty arises from stronger activation of competing responses, poorer suppression of competing responses, or some combination of these two processes.

Parkinson’s disease (PD) is a neurodegenerative condition that leads to progressive loss of dopamine-producing neurons in the substantia nigra compacta of the basal ganglia. The substantial dopamine loss due to PD dramatically alters information flow through the basal ganglia, producing well-known changes in motor function (e.g., bradykinesia, tremor, rigidity) as well as various deficits in so-called executive cognitive capacities (Cools, 2006). According to the interference control model of the basal ganglia described above, one possible source of difficulty for PD patients may be related to greater interference during action selection. For instance, PD patients may experience stronger activation of undesired response tendencies that are signaled by external stimuli or have greater difficulty suppressing unwanted response activations (Gaugel, Rieger, & Feghoff, 2004; Praamstra & Plat, 2001; Praamstra, Stegeman, Cools, & Horstink, 1998; Seiss & Praamstra, 2004). In other words, basal ganglia dysfunction produced by PD may create a response selection traffic jam that requires extra time and greater effort to resolve. In the current study, we investigate this possibility by measuring the effects of PD during response selection when an automatically activated response conflicts with a preferred course of action.

1. Interference control and the Eriksen flanker task

A well-established procedure for measuring interference control is the Eriksen flanker task (Eriksen & Eriksen, 1974). In the arrow version of the task, participants are asked to make speeded responses to the direction of a target arrow (e.g., left pointing arrow = left hand button press). Additional arrows, or flankers, are positioned along the horizontal and/or vertical plane that point either in the same or opposite direction as the target, thus signaling a manual response that is congruent or incongruent, respectively, with the response signaled by the target. Reaction time (RT) slows and error rates increase when target and flankers signal incongruent as opposed to congruent responses (i.e., there is a cost of incongruence or interference effect). The presence of incongruent flankers is associated with changes in the properties of the lateralized readiness potential (LRP) derived from the electroencephalogram. The LRP provides an “on line” comparison (i.e., subtraction) of activation recorded from scalp sites over both motor cortices. A shift in the balance of activation in favor of the response signaled by the incongruent flankers occurs prior to the appearance of a shift in LRP activation that favors the motor cortex controlling the response signaled by the target (e.g., Kopp, Rist, & Mattler, 1996; Mattler, 2003; Wascher, Reinhard, Wauchshuhn, & Verleger, 1999; Willemsen, Hoermann, Hohnsbein, & Falkenstein, 2004). This pattern is consistent with the view that the response signaled by the flankers is rapidly and automatically activated before the controlled response to the target is activated and selected. Suppression of the activation induced by incongruent flankers is a time-consuming process that slows overall RT, but ensures selection of the response that is signaled by the target. Based on these dynamics, the flanker interference task provides a powerful context for examining interference control during response selection, and individual differences in interference effects can be used to draw inferences about the efficiency of cognitive control processes engaged to resolve the interference, including the suppression of automatic response activation.

There are now six studies that have investigated the effects of PD on performance in the flanker task. In each study, it was predicted that dysfunction of the basal ganglia would make individuals with PD more vulnerable than healthy matched controls to the interference produced by incongruent flankers. Praamstra et al. (Praamstra et al., 1998; Praamstra, Plat, Meyer, & Horstink, 1999) were the first to demonstrate and replicate the finding that medication-withdrawn PD patients (n = 8, 1998; n = 10, 1999) show larger interference effects than do healthy controls. Using the LRP as an index of differential motor system activation for the competing response hands, they also found that changes in the properties of the LRP supported the conclusion that the enhanced interference effects in PD are driven by a stronger, automatic activation of cortical motor areas that control the conflicting response. A few years later, we (Wylie, Stout, & Bashore, 2005) replicated the behavioral effect reported by Praamstra et al. in a sample of 16 medicated PD patients. In addition, we found that the greater interference induced by incongruent flankers for PD patients could be harnessed to benefit RT if the response activated by the incongruent flankers became the preferred response (i.e., when instructions required a response in the direction opposite to that indicated by the target arrow). In contrast to these studies, greater interference among PD patients was not supported in an early study of 10 medicated PD patients by Lee, Wild, Hollnagel, and Grafman (1999) or in recent studies of 15 medicated PD patients by Falkenstein, Willemsen, Hohnsbein, and Hielscher (2006) and of 20 medicated PD patients by Caggias, Filoteo, Stricker, Rilling, and Friedrich (2007).

Based on these mixed reports, Falkenstein et al. (2006) considered the potential impact of several experimental variables, including clinical characteristics of sampled PD patients and differences in task design and procedures, but no clear and consistent factor could account for the discrepant findings. For example, across all studies, the severity of the disorder in PD patients was mild to moderate as measured by standard clinical rating systems, the Unified Parkinson’s Disease Rating Scale (UPDRS) and the Hoehn and Yahr Scale (1967), and all of the patients studied were free of dementia. Even in studies that found exaggerated interference effects among PD participants, no relationship between disease severity and interference effects was found. Dopaminergic medication status at the time of testing, i.e., during a patient’s normal medication “on” state or in a practically defined “off” state following overnight medication withdrawal, appeared non-contributory as both medicated and medication-withdrawn patients showed larger interference effects in some studies, but normal effects in others.

Here we examine whether individual differences in the efficiency of crucial cognitive processes involved in performing the flanker task (i.e., individual differences in the sensitivity to incongruent response activation and/or in the proficiency of inhibiting this response activation) can account for interference effects in PD. We measured interference effects in a much larger sample of PD patients (n = 50) than has been previously investigated. Based on previous findings from Praamstra et al. and our own work, we predicted that individuals with PD would show larger interference effects compared to healthy controls. Next, we utilized a specific
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