

Backward inhibition in Parkinson's disease

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Received 16 May 2005; received in revised form 4 October 2005; accepted 3 November 2005

Available online 12 December 2005

Abstract

Parkinson's disease has been associated with executive dysfunction, especially task-switching deficits. One factor contributing to task-switching costs is backward inhibition, as measured by less efficient performance when switching back to a task from which one has recently switched away. This alternating-switch cost is considered to be due to persisting inhibition of elements of the previous task set after a switch. In this study, patients with mild to moderate Parkinson's disease and controls performed three tasks (A–C) in an intermixed fashion. Patients with mild to moderate Parkinson's disease and controls showed equivalent response times. However, the patients made significantly more errors during an alternating switch (i.e., ABA) than did control participants. In contrast, there was no group difference in accuracy in the comparable condition of two consecutive switches between different tasks (i.e., CBA). In addition, accuracy for the two groups was similar for trials in which the task was repeated. These data suggest that Parkinson's disease is associated with either increased backward inhibition, or a reduced ability to overcome this inhibition when reactivating a recently abandoned task set.

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Keywords: Parkinson's disease; Task switching; Executive function; Backward inhibition; Alternating-switch costs; Basal ganglia

Parkinson's disease (PD) has been associated with executive dysfunction and task-switching deficits in particular (Brown & Marsden, 1988; Cools, Barker, Sahakian, & Robbins, 2003; DuBois, Boller, Pillon, & Agid, 1991; Gauntlett-Gilbert, Roberts, & Brown, 1999; Woodward, Bub, & Hunter, 2002). Patients with PD appear to show switching impairments primarily in the presence of "crosstalk" trials (that is, with stimuli that evoke both the irrelevant task as well as the target task). This finding (Cools, Barker, Sahakian, & Robbins, 2001; Hayes et al., 1998) suggests that PD patients have a deficit in selecting against distracting information, which has been interpreted as a problem with maintaining a relevant task set in working memory due to impaired attentional processes (Bowen, Kamieny, Burns, & Yahr, 1975; Brown & Marsden, 1988; Flowers & Robertson, 1985; Pollux, 2004).

Because of deficits in maintaining task set, patients with PD may compensate by increasing inhibition of competing task sets. In neurologically intact subjects, switching from one task to another involves inhibiting some aspects of the previous task

set (Mayr & Keele, 2000). This backward inhibition (BI) is revealed as poorer performance when the participant must switch back to this task set. BI is thus measured as the cost associated with an alternating switch. If participants are performing three tasks (A–C) in an intermixed fashion, alternating-switch costs are measured as an increase in response time, or a decrease in accuracy, for the third trial in the alternating sequence ABA compared to the third trial in a non-alternating sequence (CBA). This cost presumably reflects persisting inhibition that makes task A harder to re-activate in the first case.

BI has been interpreted as a mechanism for preventing perseveration by aiding in the disengagement from task sets that are no longer wanted. By this view, BI may be an automatic process that is applied to facilitate switching between tasks. If patients with PD exhibit abnormal alternating-switch costs, it may reflect abnormal BI in this group, which could contribute to task-switching deficits. Exaggerated BI in patients with PD would result in greater costs for intermixed trials as compared to blocked trials because of difficulty in reactivating previously inhibited task sets. On the other hand, decreased BI could contribute to task-switching deficits by hindering the disengagement of the previous task set. In either case, altered BI would contribute to task-switching problems in PD.

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Studies of alternating-switch costs have recently focused on identifying what aspects of the task are inhibited when switching away from it. Initial experiments (Mayr & Keele, 2000) suggested that backward inhibition is applied to high-level, abstract task sets, rather than to specific stimuli or responses. In subsequent work, Schuch and Koch (2003) proposed that BI may be applied to response-related components of the task set, in particular, the set of stimulus–response mappings that are required for a particular task. According to this interpretation, BI is applied to the outgoing set of response rules (e.g., “if the object is red, press right” and “if the object is blue, press left”), in order that the rule set for the incoming task may be loaded in. If BI is applied at the level of response rules, abnormal BI may contribute to the sensitivity to response competition during task switching in patients with PD (Ravizza & Ciranni, 2002).

The automatic nature of the application of BI suggests that the striatum, and the basal ganglia in general, may be involved in this process. Thus, for example, Mink (1996) proposed that in executing a well-learned (habitual) movement, the basal ganglia might select in favor of the posture needed for a given movement, and against all competing postures that would prevent the movement. Similarly, Redgrave, Prescott, and Gurney (1999) suggested that the basal ganglia operate as a selection device to resolve competition for cognitive resources. By these views, BI could play a role in this selection process. Taken together, the existing literature suggests that cortico-striatal loops are involved in inhibiting response sets during switching, while additional prefrontal regions are engaged in reactivating inhibited task sets. In patients with PD, exaggerated alternating-switch costs could result from increased striatally mediated inhibition due to overactivity in the indirect loop (Jellinger, 2002). However, it is also possible that PD is associated with decreased BI, if cortico-striatal dysfunction results in decreased inhibition of competing task sets.

Another possibility is that BI is normal in PD, but patients will exhibit greater alternating-switch costs due to difficulties in reactivating inhibited task sets. By this view, patients with PD may have difficulty in overcoming BI due to impairments in directing attention to the new task set. Thus, patients with PD may have particular difficulty with alternating-switch trials because they have a disproportionate difficulty in marshalling the resources needed to reactivate a recently inhibited task set. This possibility is consistent with the idea that deficits in shifting attention to the new task set underlie switching deficits in PD (Brown & Marsden, 1988; Woodward et al., 2002).

In the present study, we propose to examine switch costs and alternating-switch costs in patients with PD to explore the role of BI in task-switching performance in this group. We will also

examine the relationship between performance on standardized measures of frontal lobe function and alternating-switch costs in patients and control subjects. If individuals with poorer frontal function exhibit alternating-switch cost abnormalities, it may be that BI is related to executive dysfunction. On the other hand, a divergence in performance would suggest that regions other than the prefrontal cortex contribute to BI.

1. Methods

1.1. Participants

Twenty-one patients with mild or mild/moderate PD participated in the study. The patients were recruited from the UCLA Movement Disorders Clinic and were paid US\$ 10 per hour for their participation. The severity of PD was assessed using the *Hoehn and Yahr scale* (1967), with the scores of the patients ranging from 1 to 3 (mean = 2.0) when optimally medicated. The mean time since diagnosis was 5.8 (S.D. 3.5) years. Exclusion criteria included evidence for significant depression as measured by a score of >20 on the Beck Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), or the presence of dementia as measured by a score of <25 on the Mini-Mental Status Exam (Folstein, Folstein, & McHugh, 1975). Patients were also excluded if they had neurological or serious medical conditions other than PD.

All patients were being treated with medications affecting the dopamine system. Each of the patients was receiving dopamine precursor treatment and/or a dopamine agonist. Seven of the patients were being treated with additional medications that inhibit the breakdown of dopamine. Four of the patients were also receiving amantadine, a drug with mixed effects including increased dopamine release. All testing occurred when the patient was optimally medicated.

A group of 25 healthy volunteers served as control subjects. These participants were recruited through an advertisement in a community newspaper and were paid US\$ 10 per hour for their participation. This group was matched to the patient group in terms of mean age and educational attainment. Exclusion criteria included the presence of a neurological or serious medical condition, a score of >20 on the Beck Depression Inventory (Beck et al., 1961), or a score of <25 on the Mini-Mental Status Exam (Folstein et al., 1975). Demographic information for the two groups is shown in Tables 1a and 1b.

1.2. Materials

1.2.1. Task-switching test

The task-switching test was similar to that used by Arbutnott and Frank (2001). Three different two-choice classification tasks were used: a letter classification (upper- or lower-case), a digit classification (even or odd) and a symbol classification task (curved or straight). Stimuli were presented on a G3 Macintosh computer screen using Superlab software. On each trial the relevant task was shown at the top of the screen, and three characters arranged vertically below it. The three characters consisted of one letter (**d**, **h**, **t**, and **G**, **M**, **R**), one digit (**2**, **4**, **6** and **3**, **5**, **7**), and one symbol (⌘ § † and ✱ ✚ ✛). The characters were presented in pseudo-random position (within the vertical arrangement), subject to the constraint that each type of character (digit, letter, symbol) fell equally often in each position, both when it was the target character for the trial, and when it was a distractor.

Trials were arranged in sets of five, each adhering to the pattern: “AABCB”. Thus, for the three tasks—letter (L), digit (D), and symbol (S), there were six possible arrangements for a quintuplet: DDLSL, DDSLS, LLDSL, LLSDS,

Table 1a
Participant demographics

	N	Age	Gender	Education	MMSE	BDI
Controls	25	68.8 (9.6)	13 M, 12 F	16.5 (2.6)	29.0 (1.2)	5.0 (5.2)
PD	21	66.9 (8.2)	13 M, 7 F	16.9 (2.3)	28.8 (1.4)	7.8 (3.8)

Note: The table shows mean values (and standard deviations) for the patient and control groups.

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