

# Impaired inhibitory oculomotor control in patients with Parkinson's disease

Prakash Joti · Shrikanth Kulashékhar ·  
Madhuri Behari · Aditya Murthy

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**Abstract** A hallmark of voluntary control is the capacity to inhibit or change partially prepared responses, an ability thought to be compromised in patients with Parkinson's disease (PD). To test this hypothesis in relation to oculomotor control, PD patients and age-matched controls performed a redirect task in which they were instructed to cancel a partially prepared saccade on some random fraction of trials. Using a race model framework, the time it takes to cancel a saccade, the target switch reaction time (TSRT), was estimated for PD and control subjects. While saccadic reaction times of control and PD subjects were similar, the average TSRT in PD subjects was 139 ms, and was significantly greater than the TSRT in controls, which was 113 ms. These results support the hypothesis that poor voluntary control exhibited by PD patients in a variety of complex behaviors may be caused by impaired inhibitory control as a result of basal ganglia dysfunction.

**Keywords** Countermanding · Double-step · Saccades · Reaction-time

## Introduction

Numerous studies have suggested that Parkinson's disease (PD) patients exhibit poor voluntary control in a variety of tasks that might be caused by an underlying deficit in inhibitory control. Consistent with this hypothesis studies have shown that PD patients are poor at suppressing prepotent behaviors across a variety of tasks (Henik et al. 1993; Praamstra et al. 1998, 1999; Cools et al. 2001; Filoteo et al. 2002; Poliakoff et al. 2003; Mari-Beffa et al. 2005; Wylie et al. 2005). More explicit evidence of impaired inhibition in PD derives from the go-nogo task in which subjects are instructed to respond to one type of stimulus and withhold their response to another. Using the go-nogo task, individuals with PD have been reported to exhibit an inability to suppress manual responses (Cooper et al. 1994; Bokura et al. 2005). While the aforementioned studies do suggest a role for basal ganglia in inhibitory control, it is likely that these tasks are more sensitive to automatic inhibition in situations where conflicting responses tend to be activated simultaneously. Less is known about the nature of deficits in PD in tasks that require inhibition of a planned or ongoing motor response in a voluntary fashion (Angel et al. 1970; Desmurget et al. 2004).

A behavioral paradigm that has been designed to isolate online inhibitory processes is the stop/switch-signal task (Vince 1948; Lappin and Eriksen 1966; Logan and Cowan 1984; DeJong et al. 1995). Here, in most trials subjects are presented with a GO signal to which they must respond to immediately. On infrequent random trials subjects are presented with an imperative STOP/SWITCH signal to which subjects must respond to by inhibiting or changing the planned

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P. Joti · S. Kulashékhar · A. Murthy (✉)  
National Brain Research Centre, Nainwal More,  
Manesar, Haryana 122 050, India  
e-mail: aditya@nbc.ac.in

M. Behari  
Department of Neurology, C.N. Centre,  
All India Institute of Medical Sciences,  
Ansari Nagar, New Delhi 110029, India

movement, respectively. A subject's ability to control voluntarily the production of movement is probed by varying the delay between the presentation of the GO signal and the onset of the STOP/SWITCH signal. Performance in the stop/switch signal task is probabilistic and has been successfully modeled as a race between two opposing processes: a GO process that leads to the production of a movement, and a STOP process (initiated by the STOP/SWITCH signal) that attempts to cancel the planned movement. On a given trial if the reaction time of the GO process is slow enough to be canceled by the STOP process then the outcome of the race will result in successful inhibition of the planned response. Therefore, by measuring the probability of successfully responding to the STOP/SWITCH signal and the reaction times only when the GO process was instantiated, a race model can be used to predict the time it takes to respond to the STOP signal to inhibit a response, called the stop signal reaction time (SSRT). The SSRT represents the mean latency of the STOP process and is an index of one's ability to inhibit a planned response. As in the go-nogo task PD patients are reported to have longer manual SSRTs, implicating the basal ganglia in inhibitory control (Rieger et al. 2003; Gauggel et al. 2004; Bokura et al. 2005).

The view that basal ganglia is involved in behaviors such as response inhibition, that are typically associated with frontal lobe function, is consistent with numerous anatomical investigations showing that different parts of the basal ganglia and frontal cortex are reciprocally connected to each other via basal ganglia-thalamocortical circuits (Strick and Schell 1984; Ilinsky et al. 1985). These circuits are thought to implement a number of functionally distinct loops involving different modalities in which information from somatomotor, oculomotor, cognitive and limbic systems are processed in parallel (Parent and Hazrati 1993; Strick et al. 1995). However, in this context it remains unknown whether the deficits in inhibitory control shown by PD individuals measured in the go-nogo task and the stop signal task are restricted to the somatomotor loop (manual responses), or whether it reflects a more general deficit of online inhibitory control involving other functional domains as well.

To test whether online inhibitory control in the oculomotor loop in PD is also impaired we used an oculomotor version of the stop signal paradigm previously used to investigate mechanisms underlying gaze control (Hanes and Schall 1995; Hanes et al. 1998; Hanes and Carpenter 1999; Cabel et al. 2000). In this task, called the redirect task (Murthy et al. 2000; Ray et al. 2004), which is a modified version of the classic

double-step task (Westheimer 1954; Wheelless et al. 1966; Komoda et al. 1973; Lisberger et al. 1975; Becker and Jürgens 1979; Aslin and Shea 1987), the appearance of the second peripheral target on infrequent random trials served as a "redirect" signal instructing subjects to cancel a planned saccade and direct gaze to the location of the newly specified target. In this paper we use the redirect task to measure the time needed to cancel a planned saccadic eye movement and specifically test whether PD patients' online ability to inhibit planned saccadic eye movements is compromised.

## Methods

Eleven Parkinson's patients and 13 age-matched control subjects with normal or corrected vision performed a visually guided saccade task while their eye movements were recorded with their heads stabilized by means of a chin rest. Patients were from the All India Institute of Medical Sciences (AIIMS), New Delhi, diagnosed as having idiopathic PD in the absence of dementia by a consultant neurologist, their motor disabilities being responsive to anti-Parkinsonian medications. For all subjects (except MN and PT) tests were conducted at least 4 h after their last medication, by which time all patients began exhibiting Parkinsonian symptoms. Two patients MN and PT were tested in the morning 12 h after they took their last medication and were considered in the so-called OFF state. Disease severity varied between Hoehn-Yahr stages 1 and 3 (Hoehn and Yahr 1967). All subjects gave their informed consent in accordance with the institutional human ethics committee of National Brain Research Centre and the Declaration of Helsinki. Table 1 describes the main characteristics of the 10 PD patients and 11 age-matched control subjects whose data formed the basis of this study.

Experiments were under computer control using TEMPO/VIDEOSYNC software (Reflective Computing, St. Louis, USA) that displayed visual stimuli and sampled and stored eye position and other behavioral parameters. Eye position was sampled at 200 Hz with an infrared pupil tracker (ISCAN, Boston, USA) that interfaced with the TEMPO software in real time.

The task shown in Fig. 1a combines a standard saccadic reaction time task to single targets with a modified version of the double-step task (Wheelless et al. 1966; Lisberger et al. 1975; Becker and Jürgens 1979; Hou and Fender 1979; Aslin and Shea 1987; Murthy et al. 2000). On the majority of trials (60%), referred to as no-switch trials, following fixation for a random duration that ranged from 300 to 800 ms, a

**Table 1** Background data for Parkinson's patients and age-matched control subjects

Patient	Age	Gender	H & Y	Duration (years)	Trials
BS	37	Male	2.5	7	428
DN	65	Male	3	21	242
KB	55	Male	1	2.5	401
MK	56	Male	2	5	507
MN	57	Male	1	9	590
PT	67	Male	1	3	437
RB	57	Male	2.5	4	349
RG	65	Male	1	4	260
SB	54	Male	2.5	13	266
SI	63	Male	2	13	425
Mean	58				
Controls					
BK	59	Male			477
BS	62	Male			443
HG	67	Male			412
IR	56	Female			469
JC	52	Male			430
KS	62	Male			420
NJ	51	Female			452
NK	55	Female			429
NP	61	Female			454
RS	57	Male			310
WM	56	Male			466
Mean	58				

single red target ( $1^\circ$  by  $1^\circ$ ) appeared on the screen. The location of targets was randomized such that they appeared in one of eight evenly spaced locations centered on an imaginary circle with a radius typically of  $10^\circ$ . For these trials subjects were also encouraged to respond quickly by imposing a 300–400 ms deadline to make the saccade.

On the remaining trials (40%), called switch trials, following presentation of the first red target, a second green target ( $1^\circ$  by  $1^\circ$ ) appeared unpredictably at another location on the screen. Subjects were instructed to make saccades to the initial red target in case of no-switch trials and gaze directly to the later appearing green target in case of switch trials. Therefore unlike traditional double-step trials in which a single target unexpectedly jumped to a new location (often called a pulse-step), the initial target remained visible to subjects but was rendered inappropriate by the appearance of the second target, which served as a redirect (or switch) signal to subjects. To distinguish this from the original double-step task we have called this task a REDIRECT task (Ray et al. 2004). Successful performance in switch trials required subjects to cancel the programmed saccade to the initial target and instead generate a saccade directly to the newly specified target.

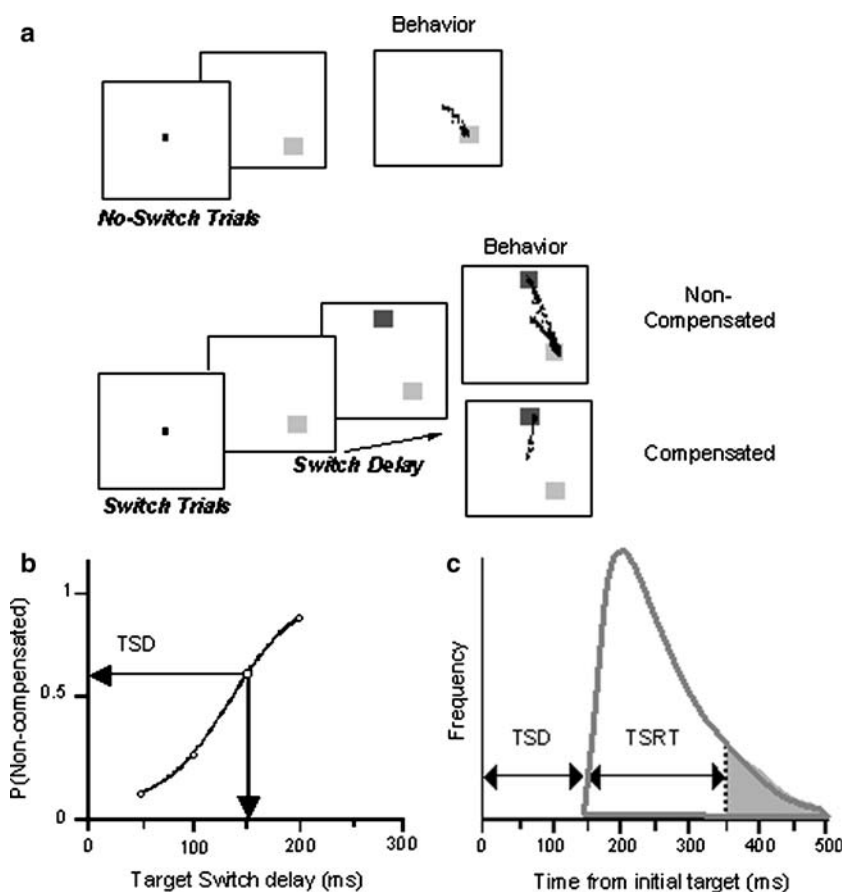
The target switch delay (TSD), which is the time of appearance of the second target relative to the first

target, was varied randomly in steps of 50 ms. A TTL pulse synchronized on the video frames in which the stimuli were displayed captured the actual time of occurrence of the target switch and was stored in the TEMPO computer along with other behavioral data. Since the display monitor and PC running VIDEO-SYNC software, that displayed stimuli, was independent of the PC running the TEMPO software, where the target switch delays were specified, we observed an additional 14.3 ms jitter due to the refresh rate of the monitor (70 Hz). As a result, offline analyses revealed that target switch delays, relative to the beginning of the vertical retrace, occurred at 43 and 57 ms; 100 ms; 143 and 157 ms; and 200 ms. Since target switch delays were randomized across positions a maximum jitter of  $\pm 14.3$  ms was also introduced by pooling the various combinations of target switches and normalizing for the appearance of targets relative to their appearance on the screen. To limit the variability of target switch delays to a minimum, while maximizing the number of target switch trials we could use for the analyses, we grouped the target switch delays into bins, centered at 50, 100, 150, 200 ms, with each bin width being 32 ms wide. Target switch delays not falling into any of the specified bins were not considered in the analyses.

Subjects were given written and verbal instructions with practice trials. Subjects were expected to participate in ~500 trials. The recording sessions were accompanied with breaks as and when indicated by the subjects (usually every 100 trials). Subjects were given initial practice sessions till they were comfortable with the task. The number of trials that each subject performed is shown in Table 1. Trials were scored as successful if subjects fixated the target within  $\pm 2.5^\circ$ . This was determined online by means of an electronic window centered on the target. Successful trials were accompanied by a sound that provided auditory feedback.

#### Calculation of target switch reaction time

The reaction times of no-switch trials together with the compensation function, which describes the probability of non-compensated saccades as a function of target switch delay, provide the necessary data to estimate the time it takes to cancel the partially prepared non-compensated saccade (see Fig. 1b, c). This duration, referred to as the target switch reaction time (TSRT), is analogous to the SSRT in stop signal tasks. It is important to note that the TSRT or SSRT is a measure that is not directly available in the behavioral data. However, the application of a race model (Logan and



**Fig. 1** **a** Illustration of the temporal sequence of the stimuli and behavior in the redirect task. Subjects are instructed to cancel the planned eye movement to the initial target and direct gaze to the newly specified target. Switch trials are interleaved randomly with no-switch trials where a second target did not appear. **b**, **c** Method for calculating the target switch reaction time (TSRT) based on the race model. **b** The compensation function plots the proportion of target switch trials in which a saccade was generated to the initial target as a function of target switch delay. **c** Illustration of the predictions of the race model.

Comparison of the plots in **b** and **c** indicates how the probability of making the non-compensated saccades can be used to measure target switch reaction time (TSRT) at a given target switch delay (TSD). The vertical dotted line indicates the finish time of the STOP process, which is equal to the TSD plus the TSRT. The fraction of the distribution signified by the shaded area corresponds to the proportion of compensated responses in which saccades were successfully redirected at the TSD. The fraction of the distribution signified by the open area corresponds to the proportion of non-compensated saccades at the TSD.

Cowan 1984), which has been successfully adapted to study the control of saccades (Hanes and Schall 1995; Hanes et al. 1998), provides a means of estimating the duration of this covert process. According to the race model, saccade production is the outcome of a race between two stochastic processes: a  $GO_1$  process, initiated following presentation of the initial target; and a STOP process, initiated following presentation of the new target. Instances in which the  $GO_1$  process finishes prior to the STOP process leads to a non-compensated saccade to the old target. If the STOP process finishes prior to the  $GO_1$  process, preparation of the non-compensated saccade is aborted. This allows a second  $GO_2$  process to proceed to completion resulting in a compensated response to the newly specified target location.

The race model can be used to estimate the TSRT. The basis of this calculation derives from the statistics of the distributions of relative finish times of the  $GO_1$  process and the STOP process, which are assumed to be independent and stochastically distributed. The earlier the finish times of the  $GO_1$  process occur relative to the finish times of the STOP process, the greater are the chances of making an erroneous saccade to the initial target. Therefore the probability of making an error is influenced by three factors: the finish times of the  $GO_1$  process; the duration of the STOP process; and the target switch delay. Since the probability of error is measured from the compensation function; the finish times of the  $GO_1$  process is measured from the reaction times of the no-switch reaction times; and the TSD is determined by the investigator, the duration

of the STOP process or TSRT can be estimated. Stated more formally, to calculate the TSRT at a particular TSD the probability of making a non-compensated response is determined from the compensation function. The time at which this probability equals the proportion of saccades made in the no-switch distribution subtracted from the TSD gives the TSRT at that target switch delay. In other words, the no-switch latency value giving that proportion represents the finish time of the compensation process, i.e., the minimum latency of no-switch saccades that would have been reprogrammed had a target switch occurred. To derive a single measure that reflects a subject's ability to inhibit an eye movement the TSRTs estimated for each TSD were averaged.

In addition to TSRT another measure of potential pathological significance is the variability of the inhibitory process. Since the slope of the compensation function results from the variability of the two independent processes in the race model, the STOP and GO processes, it follows that by normalizing for the no-switch reaction time variability, an estimate of the variability of the STOP process can be made. Variability in TSRT from the slope of the normalized compensation function was estimated from the standardized relative finishing time (ZRFT), analogous to the procedure described by Logan and his colleagues (Logan and Cowan 1984; Osman et al. 1986; Schachar and Logan 1990). The ZRFT was determined for each participant across each TSD to compare the performances of PD patients relative to controls. The normalization was done using Logan and Cowan's (1984) formula:

$$\text{ZRFT} = \frac{\text{Mean of NSRT} - \text{TSD} - \text{TSRT}}{\text{Standard Deviation of NSRT}}$$

where NSRT is the reaction time corresponding to the no-switch trials; TSD is the target switch delay; and TSRT is the target switch reaction time.

Since the ZRFT takes into account the variability of the no-switch reaction time, the slope of the value of the best-fit linear regression through the ZRFT function is related to the variability of the STOP process.

All offline analysis was performed using Matlab (Mathworks, USA). The analogue eye position data were smoothed from which blinks were removed. A velocity threshold of 30°/s was used to demarcate the beginning of saccades. The saccade detection algorithm was subsequently verified manually for every saccade. All blink-perturbed saccades were eliminated from analysis. All statistical tests were done using SigmaStat or Matlab.

## Results

The temporal sequence of events in the redirect task and the resulting behavior is shown in Fig. 1a. In switch trials subjects exhibited two types of responses: a compensated saccade to the new target location; and a non-compensated saccade to the old target location. Compensated saccades occur when subjects are able to successfully cancel the partially prepared saccade to the original target location, while non-compensated saccades occur when subjects fail to cancel the partially prepared saccade.

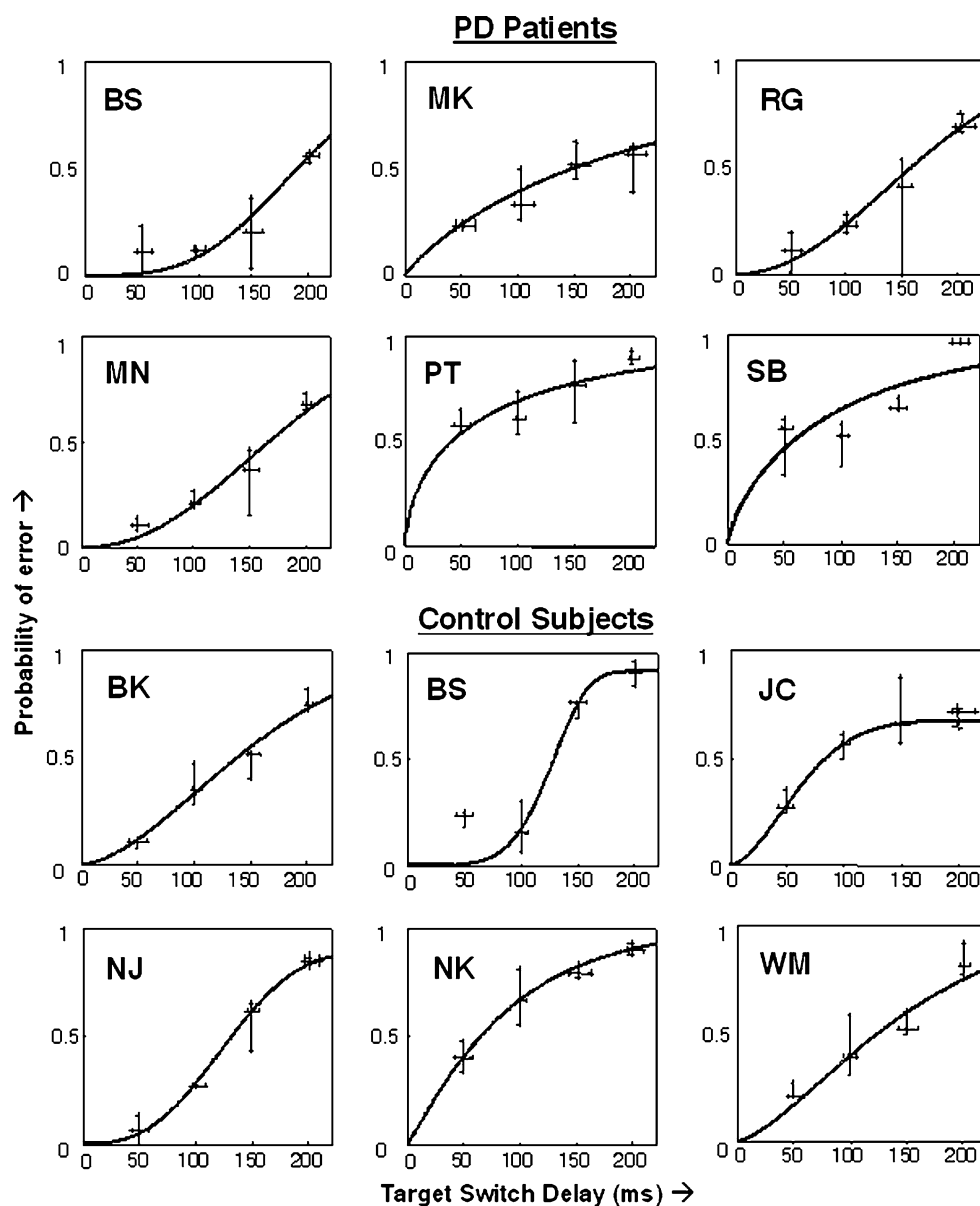
The performance of subjects was assessed by means of a compensation function, which describes the probability of making a non-compensated saccade as a function of TSD (Fig. 2). To compute the range of error associated with each data point we measured the means associated with each of the two bins (of bin-width 16 ms) comprising each target switch delay. As shown in Fig. 3 the probability of making erroneous non-compensated saccades increases with target switch delay. The increasing compensation function arises because at increasing target switch delays the onset of the STOP process, increasing the probability that the GO<sub>1</sub> process will finish before the STOP process.

Subjects' performances were quantified by fitting the best-fit cumulative Weibull function weighted by the inverse of the error associated with each data point.

$$W(t) = \gamma - (\gamma - d) \exp\left(-\left(\frac{t}{\alpha}\right)^\beta\right)$$

where  $t$  is the target switch delay,  $\alpha$  is the time at which the function reaches 64% of its full growth;  $\beta$  is the slope;  $\gamma$  is the maximum value of the function and  $\delta$  is the minimum value of the function. We used the cumulative Weibull function to estimate the degree of monotonic progression of the data across the four target switch delays in order to assess subjects' performance. Since the term  $(\gamma - \delta)$  describes the increase in the probability of making a saccade directed at the first target, we used it as a cancel index to describe the monotonic dependence of the data as a function of TSD and to quantify the degree of cancellation. Of the 11 PD patients and 13 age-matched controls, 1 PD patient and 2 age-matched controls showed cancel indices less than 0.2. On the basis of the logic of the countermanding and redirect paradigms, we assume that saccades to the first target were never programmed and hence were never covertly canceled (Ray et al. 2004). Rather these subjects simply delayed saccade preparation to achieve their goals. Their data was therefore not analyzed further.

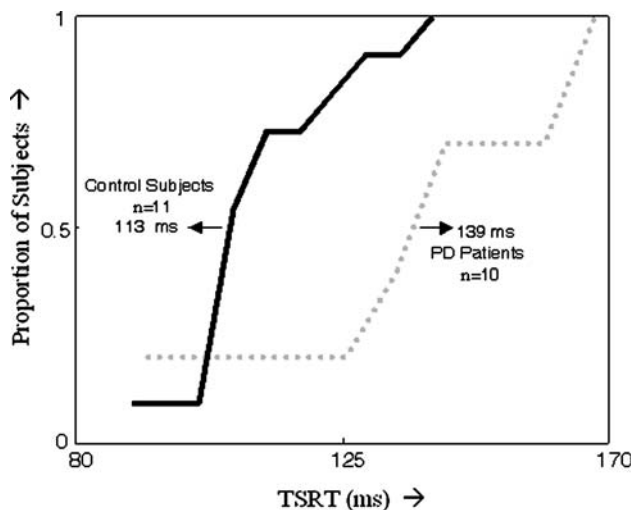
**Fig. 2** Performance of Parkinsonian and age-matched control subjects in the redirect task. The compensation function plots the probability of making a saccade directed at the initial target location which increases with the target switch delay. At comparative target switch delays PD subjects show a propensity to elicit a higher fraction of non-compensated responses. The curve through the data points are the best fit cumulative Weibull functions constrained to pass through the origin



For subjects whose compensation function was consistent with the redirect behavior, compensated saccades were made with the shortest latencies (control mean =  $202.3 \pm 5.9$  ms; PD mean =  $236.9 \pm 15.4$  ms); non-compensated saccades latencies were slightly longer (control mean =  $226.6 \pm 7.7$  ms; PD mean =  $263.5 \pm 15.6$  ms), while the latencies of no-switch saccades were the longest (control mean =  $273.6 \pm 12.8$  ms; PD mean =  $285.9 \pm 15.9$  ms). Comparisons between PD patients and control subjects for no-switch saccades yielded no significant difference ( $P = 0.5$ ;  $t = 0.6$ ;  $df = 19$ ), while non-compensated and compensated saccades were significantly different ( $P = 0.04$ ;  $t = 2.2$ ;  $df = 19$  and  $P = 0.04$ ;  $t = 2.2$ ;  $df = 19$ , respectively) and larger for PD patients than controls.

The reaction times of no-switch saccades together with the compensation function provide the necessary data to estimate the time it takes to cancel the partially prepared saccade to the initial target or the TSRT by the method of integration outlined graphically in Fig. 1b, c.

The TSRT of PD patients and controls calculated for each TSD were found to be significantly greater for PD patients (two way ANOVA;  $P = 0.002$ ). TSRT for each TSD was calculated and averaged to give an average TSRT for each subject. Figure 3 summarizes the data obtained from PD patients and age-matched controls. While the mean TSRT for the control group was  $113 \pm 4.5$ , it was  $139 \pm 9.4$  for PD patients and was significantly longer ( $P = 0.03$ ;  $df = 19$ ). This analysis



**Fig. 3** Cumulative distributions of TSRTs of Parkinsonian and age-matched control subjects estimated from the compensation function. Significantly longer TSRTs in Parkinson's patients relative to age-matched controls suggests impaired inhibitory control

indicates that PD patients had an impaired capacity to inhibit planned eye movements.

We also estimated whether PD patients were more variable in their ability to stop ongoing responses by normalizing their compensation functions based on the method of Logan and co-workers (see [Methods](#)). Figure 4 illustrates the normalized compensation functions or standardized relative finishing time (ZRFT) functions for the PD group and controls. Since the standardized relative finishing time takes into account the no-switch reaction time ( $GO_1$ ) and its variability, as well as the TSRT (STOP), it follows from the logic of the race model that at a ZRFT value of 0, which corresponds to the instance when the GO process and the STOP process are equally likely to finish the race (i.e. numerator of ZRFT = 0), should correspond ideally to a probability of subjects making an error of 0.5. Since at longer ZRFTs, the finish times of the STOP occur progressively before the GO process, the probability of making an error decreases with increasing ZRFT. These basic trends are observed across PD and control subjects as illustrated in Fig. 4.

Further, since the variability in the no-switch reaction times is accounted for in the calculation of the normalized compensation function, the slope of the best-fit regression line is an estimate of the variability of the TSRT. To determine whether PD patients exhibit a greater variability in their ability to inhibit planned saccades, we estimated the mean slope of the best-fit regression line for PD subjects as well as controls. While the mean slope was  $-0.41 \pm 0.03$  for

controls, it was  $-0.51 \pm 0.04$  for PD patients, and was not significantly different ( $P = 0.06$ ).

## Discussion

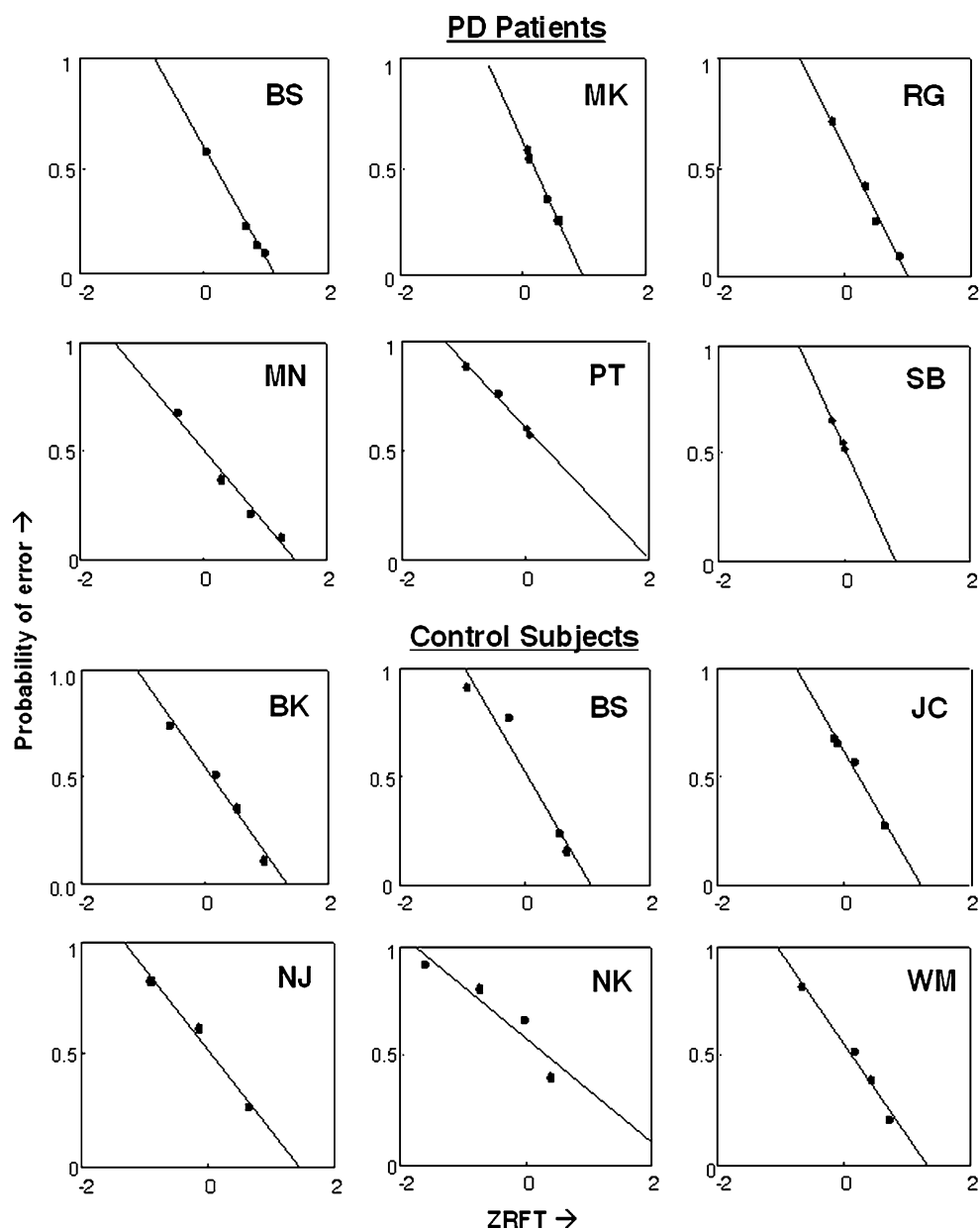
The purpose of this study was to test the hypothesis that PD patients have impaired inhibitory oculomotor control. Using the target switch reaction time or TSRT as an index of inhibitory control we show that PD patients are significantly slower to inhibit partially prepared eye movements. The slower inhibitory responses were not reflective of a general slowing of reaction times since no-switch saccadic reaction times of PD patients were not significantly different from those of age-matched controls.

## Relation to previous studies

The general consensus after numerous studies accessing saccadic performance in PD patients is that while they have difficulty in making voluntary saccades requiring suppression of pre-potent responses, (Corin et al. 1972; Shibasaki et al. 1979; Teravainen and Calne 1980; Carl and Wurtz 1985; Ilinsky et al. 1985; Kitagawa et al. 1994; Crevits and De Ridder 1997; Hikosaka 1997; Briand et al. 1999; Crevits et al. 2004; Chan et al. 2005) reaction times of reflexive saccades are unaffected (Carl and Wurtz 1985; Crawford et al. 1989a, b; Lueck et al. 1990; Ventre et al. 1992; Fukushima et al. 1994; Kitagawa et al. 1994; Vidailhet et al. 1994; Shaunak et al. 1999) or even facilitated (Kingstone et al. 2002; Roll et al. 1996; Briand et al. 1999; Chan et al. 2005). Consistent with these findings we observed no significant deficits in saccadic reaction times of PD patients with respect to visually guided saccades in no-switch trials. However, a significant slowing of compensated and non-compensated saccadic reaction times as well as TSRT was observed, indicating compromised voluntary control. Such differential sensitivity to voluntary versus reflexive saccades parallels converging evidence suggesting that these types of saccades are controlled by different neural systems with the basal ganglia/ frontal cortex being important for voluntary control.

Typically, successful performance in tasks requiring voluntary control is inhibition of a prepotent behavioral response. For example, performance in the anti-saccade task not only entails making a voluntary saccade to the location opposite to the stimulus (a non-standard stimulus response mapping), but also involves inhibiting the prepotent prosaccade prepared to the

**Fig. 4** Normalized compensation functions or standardized relative finishing time (ZRFT) functions as a function of target switch delay for PD patients and controls subjects shown in Fig. 3



location of the stimulus (Chan et al. 2005). As a result it is difficult to interpret deficits in performance to exclusively one or the other process, both of which require some aspect of voluntary control. The redirect task overcomes this difficulty by attempting to directly isolate and measure the inhibitory process using the framework of the race model. Together with previous studies (Cooper et al. 1994; Rieger et al. 2003; Gauggel et al. 2004; Bokura et al. 2005; Chan et al. 2005) these results suggest that poor voluntary control exhibited by PD patients in a variety of complex behaviors could well be a manifestation of an underlying impaired inhibitory control mechanism as a result of basal ganglia dysfunction.

#### TSRT as an index of inhibitory control

Inhibitory control has been previously measured using the stop signal paradigm (Vince 1948; Lappin and Eriksen 1966; Logan and Cowan 1984; Osman et al. 1986, 1990; DeJong et al. 1995) and has been adapted to probe the control of saccadic eye movements (Hanes and Schall 1995; Hanes and Carpenter 1999; Cabel et al. 2000; Logan and Irwin 2000; Asrress and Carpenter 2001; Kornlyo et al. 2003). Here subjects' ability to withhold a partially prepared saccade is probed by presentation of an imperative STOP signal on some random fraction of trials during a reaction time task. Because the correct behavior is to cancel a saccade that

is being prepared, it is necessary to hypothesize that some mechanism serves as an explicit STOP process. Behavioral results from the stop signal task have been successfully modeled by assuming a race with two independent processes: a STOP process that cancels movements, and a GO process that prepares movements. However, within the context of the redirect task, where subjects change the upcoming movement instead of simply stopping it, performance can be modeled as a race between two GO processes with an intervening STOP process. Alternatively, behavior in the redirect task can also be modeled as a race between two GO processes that program mutually exclusive movements, namely, the compensated and non-compensated response (i.e.,  $GO_2$  reaching threshold effectively cancels  $GO_1$  and thereby generates a compensated saccade) without the explicit necessity for a STOP process. However, a simple analysis of the reaction times of the compensated and non-compensated saccades suggest that in order to simulate the observed compensation functions (Fig. 2) the distribution of compensated saccade latencies produced need to be significantly faster than the observed behavioral data. Since compensated saccades are generally observed to be approximately 25 ms faster than non-compensated saccades, this implies that at target switch delays of 25 ms the finish times of compensated and non-compensated saccades should be the same, producing compensated and non-compensated saccades with the same probability ( $P\{\text{error}\} = P\{\text{cancel}\} = 0.5$ ). However, compensation functions from controls reveal that at such target switch delays the probability of cancelation was much greater than 0.5, or conversely the probability of error was much less than 0.5 (Fig. 2). This discrepancy makes it unlikely that a direct race between compensated and non-compensated saccades can account for the observed data. Instead we suggest that a race between the GO process leading to the non-compensated saccade and an intervening STOP process leading to cancelation of the partially prepared response can explain the observed performance curves.

For our purpose, the most critical feature of the proposed race model is the ability to estimate the TSRT or the time it takes to cancel a partially prepared movement, and modify behavior as suddenly demanded by the target switch. In this respect TSRT is formally equivalent to stop signal reaction time, and our estimate of 113 ms closely matches the SSRT values estimated from the studies of (Hanes and Carpenter 1999; SSRT = 125–145 ms; Cabel et al. 2000; SSRT = 113 ms; Asrress and Carpenter 2001; SSRT = 128 ms) using versions of the oculomotor visual countermanding paradigms.

## Basal ganglia and inhibitory control

While changes in brain organization as a result of PD may preclude a straightforward interpretation of relating deficits in inhibitory control to normal basal ganglia function, an anatomically and physiologically well characterized GABA mediated inhibitory input from the substantia nigra pars reticulata to the superior colliculus, a critical node in the generation of saccadic eye movements (Hikosaka and Wurtz 1989), could instantiate the process leading to the stopping of partially planned eye movements. Alternately the mapping of inhibitory control on basal ganglia circuitry may be more complex. One such possibility, which is motivated on the grounds of anatomical and functional connections that has been described in the literature, assumes that the basal ganglia is functionally organized along two main pathways that are mutually antagonistic: an excitatory pathway from the subthalamic nucleus (STN) to the internal segment of the globus pallidus (GPi), the main output nucleus of the basal ganglia; and an inhibitory pathway from the striatum to the GPi. Mutual interactions between these pathways may provide a basis to prevent potentially conflicting motor programs to be coactive (Mink 1996). In the context of real time inhibitory control such interactions could instantiate the computational architecture of the countermanding and redirect paradigms that suppose a race between a GO and a STOP process. The striatum to GPi pathway may implement the GO process while the STN to GPi pathway may implement the STOP process. Any disturbance in the balance of these two pathways as a result of PD may produce deficits in inhibitory control.

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