Basal Ganglia Play a Unique Role in Task Switching within the Frontal–Subcortical Circuits: Evidence from Patients with Focal Lesions

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Abstract

■ The performance of patients with lesions involving the basal ganglia (BG) was compared to that of patients with prefrontal (PFC) lesions, thalamic (TH) lesions, and age-matched controls in order to examine the specific role of the BG within the frontal–subcortical circuits (FSCC) in task switching. All the BG patients and none of the other participants showed a marked increase in error rate in incongruent trials where correct responses depended upon the choice of the correct task rule. Some BG patients erred in failing to switch tasks and others failed despite their attempt to switch tasks. Additionally, reaction time results indicate abnormal response repetition effects among the BG patients; failure in benefiting from advance task information among all the patients; and increased task mixing costs following PFC lesions. The authors conclude that although the frontal–subcortical circuits jointly determine some behaviors (such as benefiting from preparation), the BG play a unique role within the FSCC in action selection and/or the inhibition of irrelevant information. ■

INTRODUCTION

Cognitive flexibility is assumed to be one of the prominent markers for adaptive behavior in humans. In this sense, the ability to set new goals according to environmental changes and to act upon these goals seems to indicate intact executive functioning. The two major tools used by neuropsychologists for measuring cognitive flexibility are the Wisconsin Card Sorting Test (Heaton, Chelune, Talley, Kay, & Curtiss, 1993) and its derivatives (Intra/Extra Dimensional shift; Owen et al., 1993), and the task switching paradigm (e.g., Monsell, 2003, for a review). The major advantage of the latter is in its independence from rule learning and concept formation, which are involved in the Wisconsin Card Sorting Test. In a widely used version of the paradigm in which the tasks are randomly ordered and are cued in every trial, another advantage of the test is that conditions involving a switch and those without a switch are also equated in terms of working memory load.

Manifestations of cognitive flexibility deficit (measured primarily in slowed reaction time [RT] when a change of set was required) were well demonstrated among patients with prefrontal cortex (PFC) lesions (e.g., Keele & Rafal, 2000; Rogers et al., 1998) as well as among Parkinson's disease (PD) patients (e.g., Cools, Barker, Sahakian, & Robbins, 2001a; Hayes, Davidson, Keele, & Rafal, 1998, for review). The common switching deficit among the two populations is usually attributed to the frontal–subcortical circuits (FSCCs) connecting the PFC to subcortical regions including the basal ganglia (BG), which are impaired in PD, and to parts of the thalamus (TH) (Middleton & Strick, 2000; Mega & Cummings, 1994; Cummings, 1993; Alexander, Delong, & Strick, 1986). However, characterizing the functional contribution of these brain structures within these circuits to the shifting mechanism remains a challenging problem.

Several theories suggest unique roles for the BG within the FSCC in functions that are arguably related to task switching. According to one group of theories, the BG play a unique role in inhibiting competing action plans (cf. Mink, 2003) and filtering irrelevant information (Filoteo, Maddox, Ing, Zizak, & Song, 2005). Both filtering (Meiran, 2000a, 2000b, in press; Meiran & Marciano, 2002) and inhibition (Mayr, Diedrichsen, Ivry, & Keele, 2006; Masson, Bud, Woodward, & Chan, 2003; Mayr & Keele, 2000) have been shown to play a major role in task switching in normal participants. The other theories suggest that the BG are especially suited to select among competing action plans (Bogacz & Gurney, 2007; Gurney, Prescott, Wickens, & Redgrave, 2004; Redgrave, Prescott, & Gurney, 1999). A similar selection is described in task switching theory as ''goal setting'' (Rubinstein, Mayer, & Evans, 2001) or task decision (Fagot, 1994; see further Sohn & Anderson, 2001).

The only few studies that were conducted on patients with focal lesions in the BG indicated either rule

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abstraction deficits (Swainson & Robbins, 2001) or a deficit in switching attention to newly relevant stimulus features (Cools, Ivry, & D'Esposito, 2006). Most of what we know about the BG in task switching comes from studies on PD. Evidence for inhibition-related deficits comes, for example, from Fales, Vanek, and Knowlton (2006), who showed that PD patients exhibit extreme difficulty with executing a task that was inhibited beforehand. Along a similar line, Hayes et al. (1998) concluded that PD patients exhibit difficulty filtering out irrelevant information. Shook, Franz, Higginson, Wheelock, and Sigvardt (2005) interpreted their findings as evidence for dopamine-dependent inhibitory deficits in PD.

Other studies suggest that selection among responses (Ravizza & Ciranni, 2002) or actions is a prominent source of difficulty for PD patients in task switching. For example, it seems that PD patients show their most pronounced deficit under ''cross-talk'' conditions, in which the target stimulus contains attributes from both currently relevant and irrelevant tasks.[1] Cools et al. (2001a), who asked PD participants to switch between a digit naming task and a letter naming task every two trials, found increased RT performance switching cost (SC) under cross-talk conditions (e.g., ''8G''), compared to non-cross-talk conditions (e.g., ''7@''). A demonstration of the switching deficit in the similar paradigm was reported earlier by Rogers et al. (1998), who found a progressive increase in error switch cost for PD patients but only under conditions involving cross-talk stimuli. Similarly, Hayes et al. (1998) reported a high error rate for PD patients under cross-talk conditions relative to neutral conditions and conditions with univalent stimuli, containing information relevant only to the relevant task. A dramatic demonstration of error SC was also observed with cross-talk stimuli under experimental conditions involving only a single source of information regarding the currently relevant task. Brown and Marsden (1988) asked PD patients to switch between word naming and ink color naming of bivalent Stroop stimuli (such as the word RED printed in blue ink) every 10 trials. Under the cued conditions, when patients could retrieve the task identity from both the memory of the task sequence and the external cues, the proportion of errors (PE) in the immediate postswitch trials was low (0.03) compared to the noncued conditions when only the word ''ready'' signaled the switch and task identity information had to be retrieved from memory. These noncued conditions yielded an error rate of 0.25. Recently, Meiran, Friedman, and Yehene (2004) used a cueing task switching paradigm, in which memory for the task sequence was unhelpful because the tasks were ordered randomly. In their study, a dramatically high PE of about 0.50 was found among half of the PD patient sample, when the correct response depended on correct task identification, as opposed to a condition where the correct response could be made even when the wrong correct task rule was applied. The authors interpreted their finding as evidence for a goal setting deficit in PD in the absence of redundant task identity information. Despite that, Woodward, Bud, and Hunter (2002) showed that PD-related deficits were absent under cross-talk conditions that were not associated with increased attentional selection demand but were present with such demand. It is difficult to tell at present how general this finding is because the participants in this study were asked to switch between tasks of unequal difficulty, the Stroop task (requiring naming the ink color in which color words were written) and the reverse Stroop task (requiring reading the color words), and the literature on task switching suggests that this paradigm constitutes a special case (e.g., Yeung & Monsell, 2003).

In sum, results from previous studies on task switching and PD patients suggest, thus far, that the BG are involved in either inhibition-related functions (Fales et al., 2006; Shook et al., 2005; Hayes et al., 1998), or selection among actions or responses (Meiran et al., 2004; Ravizza & Ciranni, 2002; Cools et al., 2001a; Rogers et al., 1998; Brown & Marsden, 1988). The latter might be more pronounced in the absence of redundant information about the currently relevant task (Meiran et al., 2004; Brown & Marsden, 1988) or under increased attentional load (Woodward et al., 2002).

The present study aims to explore more fundamentally the unique role of the BG within the FSCC in task switching. To this end, we tested patients with (mostly ischemic) brain lesions. Critically, in order to demonstrate the unique role of the BG, we compared three groups of patients, whose lesions involved the major components of the FSCC described by Cummings (1993) and Alexander et al. (1986). All these circuits involve input from the entire association cortex, sent down to parts of the BG, then to the TH (mainly to the dorsomedial nucleus [DMN]), from which the information projects to selective parts of the PFC. Accordingly, in one group of patients, the lesion involved the TH (including the DMN). In another group, the lesion involved the association cortex (including the PFC). Finally, in the critical group, the lesion involved the BG. The performance of all groups of patients was compared to that of an age-matched control group. In the past, we studied a patient suffering from an extensive ischemic lesion involving the BG. In that study, the patient stopped to switch tasks after a few attempts to switch (Yehene, Meiran, & Soroker, 2005), thus suggesting that the BG might play a crucial role in task switching.

In evaluating task switching performance, we focused on the following behavioral indices. Following Yehene et al. (2005) and Meiran et al. (2004), we focused on the PE task rule congruency effect. This effect is based on a comparison between two types of cross-talk trials: trials in which the two task rules indicate different responses (incongruent trials) and trials in which both task rules indicate the same keypress as the correct response (congruent trials). Meiran and Daichman (2005), who

used a mathematical modeling approach to explain their error results, found that the best fitting model was one which explains the increased PE in incongruent (relative to congruent) trials as mostly due to the correct execution of the wrong task (''task errors''). These ''task errors'' could reflect one of two functions attributed to the BG, either poor release from inhibition of the relevant task (e.g., Fales et al., 2006) or a more pervasive impairment in action selection (Bogacz & Gurney, 2007; Gurney et al., 2004; Redgrave et al., 1999).

Although the current focus was on error rates, we also analyzed RTs. For these analyses, we focused on preparation effects and the influence of task switching. To examine preparation effects, we varied the task cue-to-target interval (CTI). To examine the influence of task switching, we focused on two comparisons. One comparison was between task-switch and task-repetition trials, both coming from blocks involving task switching. This effect is termed ''switching cost.'' The other comparison was between task repetition trials and a block involving a single task. This effect is termed ''task mixing cost'' (see Rubin & Meiran, 2005, and Los, 1996, for reviews).

Based on the literature on PD, we predicted that the BG patients would exhibit an increased PE in incongruent trials (Yehene et al., 2005; Meiran et al., 2004). We also predicted an increased task mixing cost (MC) in the PFC group based on Aron, Monsell, Sahakian, and Robbins (2004) and Keele and Rafal (2000). With respect to switch costs (switch vs. repeat), it was not possible to form clear predictions because of the mixed results in the literature. For example, Witt et al. (2006), Shook et al. (2005, the off-medication group), Pollux (2004), and Cools, Barker, Sahakian, and Robbins (2003) found increased switch costs in PD patients. Other studies suggest that this deficit is limited to specified conditions such as those involving cross talk (Cools et al., 2001a), a training phase (Werheid, Koch, Reichert, & Brass, 2007), or short preparation intervals (Meiran et al., 2004), and may not always be found (Fales et al., 2006). Finally, we predicted impaired task preparation (seen in lesser benefit by increasing the CTI) among the PFC group. This prediction is based on Brass and von Cramon (2004), who showed in an imaging study that the lateral PFC had increased oxygen consumption during task preparation.

METHODS

Participants

The participants were seven patients with focal lesions in the BG, four patients with focal lesions in the TH (including the territory of the DMN), and six patients with focal lesions including the PFC (see Table 1 for the patients' demographic, lesion, and neuropsychological data). In addition, seven participants who were matched to the BG patient group served as an age-matched control group. Patients were identified based on a radiological review indicating a single neurological injury that had occurred at least 3 months before testing. In all patients, except for Patient Y.H. who underwent a resection of an oligodendroglioma, the brain damage was caused by stroke. In all BG patients, the middle cerebral artery was involved. In all TH patients, the posterior cerebral artery was involved, whereas in the PFC patients, the middle cerebral artery territory (Patient G.T.), anterior cerebral artery territory (Patients A.H., S.T.), both these arteries (Patient N.E.), or the watershed area between the two vascular territories (Patient D.Y.) were involved. The difference in the mean age of the four groups of participants was significant [$F(3, 20) = 3.25$, $p < .05$]. Planned comparisons yielded a significant difference between the BG (mean age = 53.7) and the PFC groups (mean age = 41.3) [$F(1, 20) = 5.73$, $p < .05$], between the PFC and the age-matched groups (mean age = 56.5) [$F(1, 20) = 8.69$, $p < .01$], and only a marginally significant difference was found between the TH patients (mean age = 53.0) and the PFC patients [$F(1, 20) = 3.78$, $p = .06$]. The remaining comparisons among the different groups did not reach significance, $F < 1$. The mean years of education did not differ significantly among the groups of patients [$F(3, 20) < 1$].

The Paradigm

Participants were requested to determine the position of a target in a 2 × 2 grid according to one of two different task rules, up–down or right–left: specifically, whether the target stimulus is located in the upper or the lower part of the grid (up–down task) or whether it is located in the left–right part of the grid (right–left task). The relevant task rule was cued in every trial by arrows pointing to the sides or upward–downward, respectively (see Figure 1). Responses were given by pressing one of two keys, when Key 1 indicated both up and left responses, depending on the required task, and in the same manner, Key 2 indicated both down and right responses. For half of the participants, the responses to key mapping were reversed (Key 1 = up and right; Key 2 = down and left). To avoid relying on memory, we placed a directional arrow sticker on each response key indicating the meaning of the response key according to each task rule. In both response setups, there were target positions for which the correct response did not depend on the task rule (''congruent trials,'' e.g., if Key 1 = up and left and the target position is upper-left, then Key 1 is the correct response regardless of whether the required task decision is up–down or right–left. In other cases, the correct response depended upon the application of the correct task rule (''incongruent trials''). For example, if Key 1 = up and left and Key 2 = right and down, an upper–right target position requires a Key 1 response in the up–down task

Table 1. Patients' Demographic, Lesion, and Neuropsychological Data

Patient	*Age/Sex*	*YOE*	*Etiology*	*Time Post Lesion (Months)*	*Lesion Side and Site*	*LOTCA Scores*[a]					
						Orientation	*Visual Perception*	*Spatial Perception*	*Praxis*	*Visuomotor Perception*	*Categorization and Reasoning*
Basal Ganglia (BG) Group											
D.S.	67/m	8	I	4	Lt: GP–Pu	8/8	4/4	4/4	4/4	3/4	2/5
S.F.	65/m	12	H	3	Lt: GP–Pu, Ts, Pi, PVWM	8/8	3/4	2/4	3/4	3/4	3/5
M.O.	38/m	11	I	3	Lt: GP–Pu, PLIC, PVWM	8/8	4/4	4/4	4/4	4/4	2/5
N.Y.	56/m	11	I	4	Rt: GP–Pu, CN, ALIC, PLIC, PVWM, Insula, EC	8/8	4/4	4/4	3/4	2/4	4/5
H.Y.	51/m	11	I	3	Rt: CN, Fs, Fmed	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
H.K.	48/m	15	H	3.5	Rt: GP–Pu, Insula, EC	8/8	4/4	3/4	3/4	3/4	2/5
A.M.	51/f	11	I	3	Rt: GP–Pu, PLIC, Pi, Ts	7/8	4/4	3/4	3/4	3/4	3/5
Mean	53.7	11.2									
Thalamus (TH) Group											
M.Z.	62/m	15	I	4	Bi: Th (including the DMN), PLIC	8/8	4/4	4/4	4/4	4/4	4/5
H.M.	48/m	14	H	4	Lt: Th (including the DMN), PLIC, PVWM	8/8	4/4	4/4	4/4	3/4	4/5
R.M.	50/m	16	H	3	Lt: Th (including the DMN), PLIC	8/8	4/4	4/4	4/4	5/5	5/5
B.Y.	52/f	8	I	3	Rt: Th (including the DMN), PLIC, PVWM	7/8	4/4	4/4	4/4	3/4	4/5
Mean	53.0	13.2									
Prefrontal Cortex (PFC) Group											
G.T.	34/m	16	H	8	Lt: Fi, Ts, Pi, Insula	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Y.H.	44/m	15	Tu	12	Lt: Fi, Ts, Tm, Insula	8/8	4/4	4/4	4/4	4/4	5/5
D.Y.	28/f	11	I	3	Rt: Fs, Fm (watershed MCA/ACA)	6/8	4/4	3/4	4/4	3/4	2/5
S.T.	47/f	9	H	3	Rt: Fm, Fi	8/8	4/4	4/4	4/4	3/4	2/5
N.E.	56/f	12	I	3	Rt: Fm, Fmed	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
A.H.	39/f	8	H	3	Rt: Fmed, Anterior Cingulate	8/8	4/4	3/4	4/4	3/4	3/5
Mean	41.3	11.8									
Age-matched Control											
Mean	56.5	11.8									

YOE = years of education; I = ischemic infarction; H = intracerebral hemorrhage; Tu = tumor; GP–Pu = globus pallidus–putamen nuclei; CN = caudate nucleus; ALIC = anterior limb of internal capsule; PLIC = posterior limb of internal capsule; EC = external capsule; PVWM = periventricular white matter; Fi = inferior frontal gyrus; Fm = middle frontal gyrus; Fs = superior frontal gyrus; Fmed = medial frontal gyrus; Ts = superior temporal gyrus; Tm = middle temporal gyrus; Pi = inferior parietal lobule; Th = thalamus; DMN = dorsomedial nucleus; Lt = left; Rt = right; Bi = bilateral.

[a]LOTCA = Loewenstein Occupational Therapy Cognitive Assessment (Itzkovich, Averbuch, Elzar, & Katz, 1990). Scores in those categories represents a composition of the scores obtained in the several underlying subtests in this category.

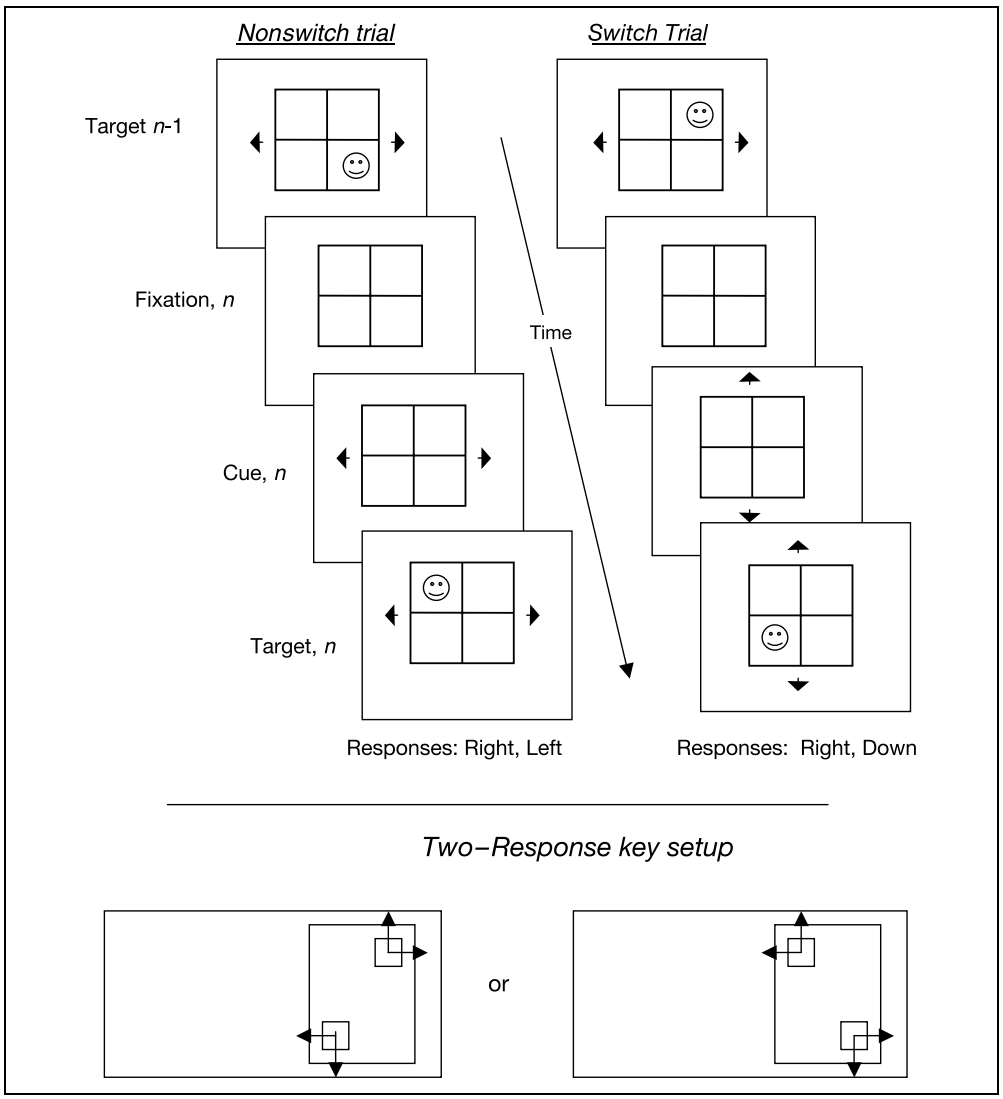

Figure 1. Schematic illustration of the paradigm. The left side of the figure displays the sequence of events for the nonswitch trials in which a right–left task trial was followed by another right–left task trial. The right side of the figure displays switch trials where a left–right task trial was followed by an up–down task trial.

(indicating up), whereas it requires a Key 2 response in the context of the right–left task (indicating right).

Procedure

The study involved the paradigm presented in Figure 1 and was run in one session lasting approximately 45 min. At the end of the experimental session, participants were tested under single-task conditions involving a single task without the need to switch tasks. Based on previous studies using this paradigm, we know that the two task rules produce very similar results. Therefore, the single-task block involved the up–down rule for one half of the patients in each group, whereas the remaining patients in the group received the right–left task. Given the performance observed in the BG group, this group of patients was invited for another session after 4 to 8 days, during which they were tested on the same paradigm but received the reversed task rule under single-task conditions. Thus, we tested each patient in the BG group on both task rules under single-task conditions.

Each experimental session began with 20 practice trials, followed by five experimental blocks (80 trials each). The first four blocks involved task switching and the last block was a single-task block. Participants were told to respond as quickly and as accurately as possible. After each experimental block (Blocks 1–4), participants were given a short break during which they were asked to explain the task and answer questions about the stimulus–response key mapping for each task. All participants were able to answer these questions correctly, indicating that they understood the instructions, the task, and the entire experiment. Before the transition, on the fifth block (single-task condition), participants were told that from now on they would be required to perform only one task and that the cues would not alternate.

Each experimental trial began after the response in the preceding trial (target, $n - 1$), with a response–cue interval of 2032 msec. An empty grid was presented during this interval [serving for fixation] (Fixation, n). The presentation of the instructional cue was either for

116 or 1016 msec (Cue, *n*) before the target stimulus appeared (Target, *n*). The target could appear in any one of the four positions on the grid. A 100-msec, 400-Hz beep was sounded after each error. The task rule (in Blocks 1–4), target location, and CTI were selected randomly for each trial. Thus, the sequence of the trials was unpredictable and the instructional cue did not therefore indicate the upcoming target location, keypress, or precise target onset. This led to an equal proportion of congruent and incongruent trials within each task. Additionally, 50% of the trials under mixed-task conditions involved immediate task switching, whereas the remaining trials involved immediate task repetition.

Under single-task conditions, because participants had to classify the target according to only one task rule, only the target location and CTI were selected randomly for each trial.

RESULTS

For RT analysis, responses immediately following an error and responses slower than 5000 msec or faster than 100 msec were discarded as outliers. This led us to exclude between 5% and 22% trials in the PFC group, 3% and 23% in the TH group, 41% and 52% in the BG group, and 8% and 32% in the age-matched control group. The rationale for excluding these trials was that once a patient kept applying the same task rule, even when a switch was required, the status of a given trial as ''real'' switch/repeat could not be ascertained. Critically, we acknowledge the fact that discarding those trials reduced the number of trials which were analyzed especially in the BG group. This might lead us to expect a compromise in the reliability of the results, but no change in the mean RTs. Moreover, because compromised reliability reduces the chances of getting significant effects, the significant effects that we report cannot be due to this procedure. Secondly and importantly, analyzing the results before and after excluding post-error trials yielded the same pattern of results.

PE as a Function of Congruency

The most revealing result concerns the proportion of correct responses (see Figure 2A for group means and Figure 2B for each participant's performance in each group under incongruent conditions). Interestingly, when a correct response could be made even when the wrong task rule was applied (congruent trials), accuracy was almost perfect and did not differ from the one observed under single-task conditions, when only one task rule was required, a finding which was true for all groups, all Fs < 1, for the comparison between congruent trials and single-task trials. Also, this performance pattern did not differ significantly among groups, Fs < 1. Note that the very high performance is consistent with the hypothesis that the choice of a response once task identity was known (e.g., choosing between left and right) was almost error free and that errors stemmed from the correct application of the wrong task rule (e.g., choosing correctly between right and left when the task was up–down). However, in incongruent trials, where the correct response depended on the execution of the correct task rule, accuracy was equally high in the PFC, TH, and age-matched control groups, Fs < 1, for all the pairwise group comparisons. However, the proportional accuracy for the BG group was dramatically lower than that seen among PFC patients [$F(1, 20) = 307.7$, $p < .0001$], TH patients [$F(1, 20) = 241.5, p < .0001$], and the age-matched control group [$F(1, 20) = 342.4, p < .0001$], and approximated guessing level. As can be seen in Figure 2B, the distribution of scores did not overlap among the groups so that the best BG performance was considerably worse than the worst performance seen in the other groups. Examining Table 1 shows that the large performance impairment observed among the BG patients is not due to age differences or their functioning on the neuropsychological tests because, for every BG patient who was older or who performed more poorly on the neuropsychological tests, there was at least one matched patient in the other groups.

In order to better characterize the performance profile of the BG patients, we analyzed the proportion of correct responses as a function of task and congruency.

Table 2 reveals two distinct performance profiles within the BG group. When task identification was essential in order to achieve a correct response (incongruent trials), three out of seven patients exhibited around 0.50 correct responses for both tasks. We call this profile ''task independent.'' The other group of patients exhibited almost zero correct responses for one task and a proportion of close to 1.00 correct responses for the other task. We call this profile ''task dependent.''

Although a proportion of 0.50 correct incongruent trials is to be expected if one simply ignores the task or guesses it, the results cannot be explained by guessing because the patients who exhibited this profile showed a significant task switch effect in RT (see below). Such switch effect may be taken as evidence that the task (Meiran, Chorev, & Sapir, 2000; Meiran, 1996, see also Arrington, Logan, & Schneider, 2007), or at least the task cue (Logan & Bundesen, 2003), was processed. Additionally, guessing can be ruled out because the very natural task cue was presented along with the target stimulus when the response was given.

The ''task-dependent'' profile is to be expected when one consistently applies only one task rule. This model predicts that in trials involving this task rule, performance will be relatively error free. In trials involving the alternative rule and not requiring knowledge of task identity, performance will still be relatively error free. Only in trials involving the alternative rule and requiring

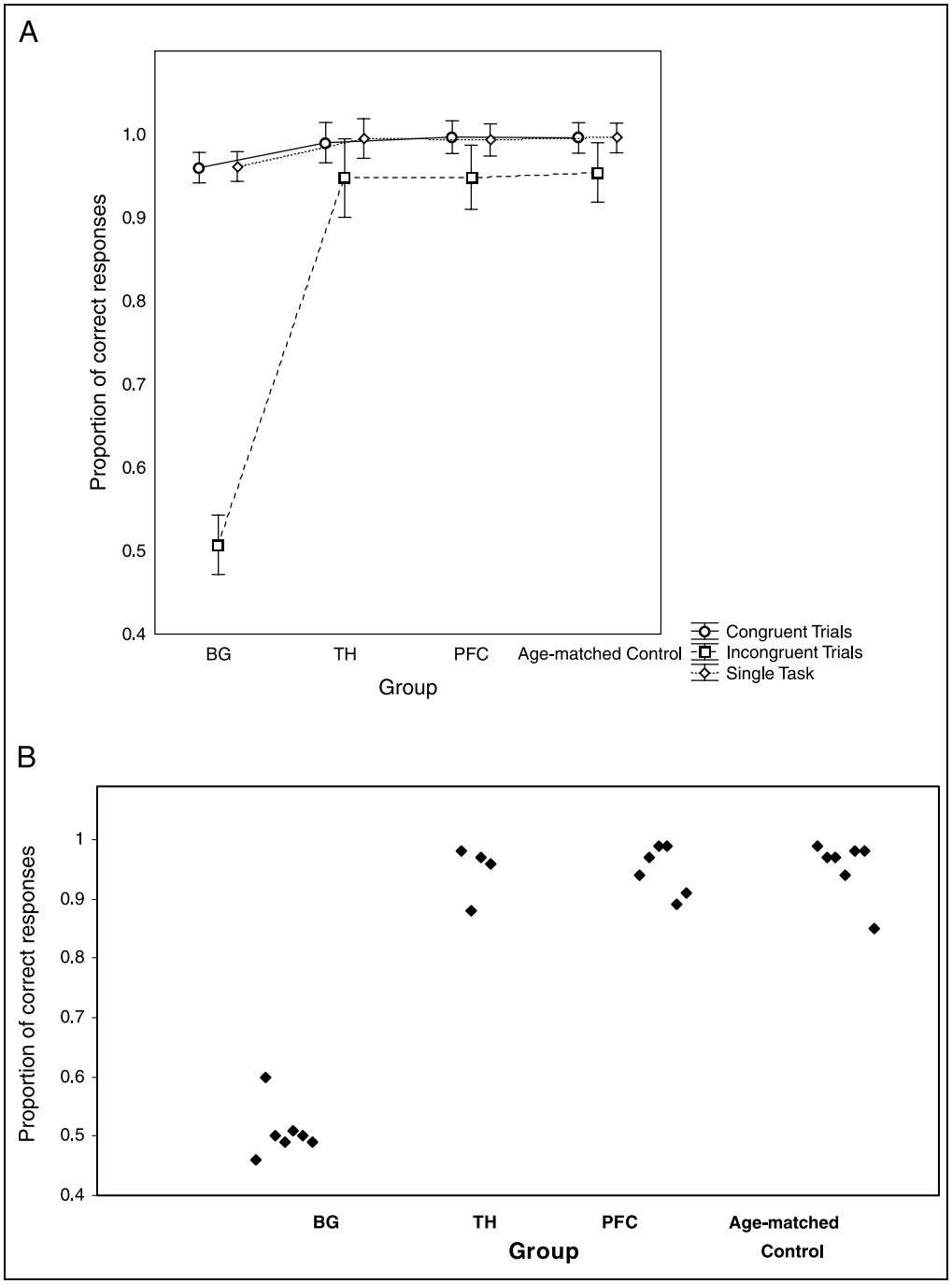

Figure 2. (A) Proportion of correct responses as a function of congruency and group. Vertical bars denote 0.95 confidence interval. (B) Proportion of correct responses for each participant in the incongruent condition as a function of group.

knowledge of task identity are nearly 100% errors expected (see Meiran & Daichman, 2005; Yehene et al., 2005, for details). Therefore, the results reflect a switching deficit among BG patients, with one group of patients who attempted to switch tasks and another group who did not switch tasks. This lack of task switching could be strategic to avoid the difficulty of switching, or could reflect a failed attempt to switch as some severe form of perseveration. For simplicity sake, we call the first group BG-switch and the other group BG-no-switch.

Interestingly, as can be seen in Table 1, two out of three patients in the BG-switch group had their lesion on the left side of the brain, whereas three out of four patients in the BG-no-switch group had the lesion on the right side of the brain. This distribution hints at the possibility that the spatial nature of the task, presumably involving the right hemisphere to a greater degree, contributed to switching difficulty. This interpretation is based on the assumption that the performance impairment was more severe in the BG-no-switch group because they apparently did not even attempt to switch tasks. In line with this speculation, another patient, A.F., as reported elsewhere (Yehene et al., 2005), exhibited a no-switch pattern in a nonspatial (or less spatial)

Table 2. Proportion of Correct Responses as a Function of Task, Congruency, and Session: BG Group

	Session 1				*Session 2*			
	Up–Down		*Right–Left*		*Up–Down*		*Right–Left*	
Patient	*Inc*	*Cong*	*Inc*	*Cong*	*Inc*	*Cong*	*Inc*	*Cong*
D.S.	**0.56**	1.00	**0.37**	0.98	**0.59**	0.99	**0.58**	0.99
S.F.	**0.65**	0.87	**0.55**	0.96	**0.42**	0.90	**0.58**	0.88
M.O.	**0.91**	0.94	**0.11**	0.93	**0.03**	1.00	**0.93**	0.97
N.Y.	**0.03**	0.98	**0.94**	1.00	**0.50**	0.99	**0.94**	1.00
H.Y.	**0.65**	0.98	**0.36**	0.96	**0.55**	0.88	**0.56**	0.91
H.K.	**0.01**	0.98	**0.97**	1.00	**0.01**	1.00	**1.00**	1.00
A.M.	**0.07**	0.92	**0.83**	0.88	**0.89**	0.95	**0.15**	0.97

Inc = incongruent (correct response requires correct task identification); Cong = congruent (correct response does not depend on correct task identification).

paradigm and her lesion was on the left side of the brain. Additionally, in three out of four patients in the BG-no-switch group, the lesion involved the posterior limb of the internal capsule; this region was spared among all the BG-switch patients. As can be seen in Table 2, the BG-no-switch included two patients who perseverated on the same task in both sessions (N.Y. and H.K.) and two patients who perseverated on one task in Session 1 and on another task in Session 2 (M.O. and A.M.). Interestingly, the two patients who perseverated on the same task are also the only BG patients whose lesion included the insula. It is important to note that insular lesions and lesions in the posterior limb of the internal capsule were insufficient to cause the drastically lowered accuracy in incongruent trials because two of the PFC patients had an insular lesion and did not show this behavioral impairment. Similarly, all the TH patients had a lesion which included the posterior limb of the internal capsule and none of them had a high error rate in incongruent trials. Of course, more work needs to be done to determine if the combination of a BG lesion and another lesion dictates the exact performance profile. Importantly, the classification of BG patients as ''switch'' and ''no-switch'' was the same for both sessions, suggesting its stability across time.

Characterizing BG-No-Switch Performance

Because we identified a subgroup of BG patients who always applied the same task rule, it seemed essential to further explore the possibility that the performance pattern within the BG group stems from a difficulty in switching between two task rules per se, rather than from a difficulty to perform one of the task rules. We therefore examined the results in order to address this concern. First, the aforementioned hypothesis cannot provide a unitary explanation for the patients' behavior because two of the patients who showed a task-dependent profile changed their task preference in Session 2. In other words, they did not show a preference for one of the tasks. The other two patients consistently executed the right–left task. The hypothesis can be examined by looking at their single-task performance, which seems to provide the best estimate for their ability to execute each task in isolation. For Patient N.Y., the mean single-task RT was 1766 msec (PE = 0.02) and 1626 msec (PE = 0) for the up–down and the right–left tasks, respectively. In this case, the right–left task was performed only slightly better than the up–down task, and this slight advantage could be entirely due to the differential practice because the single-task condition was tested after the mixed-task condition (in which the patient consistently applied the right–left task). Given these considerations, it seems implausible that the patient chose not to switch tasks because the right–left rule was easier. Only in Patient H.K. was the lack of switching perhaps due to the choice of the easier task. For this patient, the right–left task was considerably easier than the up–down task. Specifically, the mean single-task RT in the right–left task was 543 msec (PE = 0) as compared to 741 msec (PE = 0.12) for the up–down task.

Characterizing the BG-Switch Performance

We showed that two BG-no-switch patients reversed their task ''preference'' in Session 2. This opens the possibility that the performance pattern observed by the BG-switch patients reflects also a change in perseverative tendency within a block of trials, rather than a random switching between tasks. Namely, a patient could get stuck on Task A for a few trials then get stuck on Task B for a few trials, and so forth. We were especially interested to know whether this group exhibited a qualitatively different performance pattern rather than just changed their perseverative tendencies more frequently than the BG-no-switch patients. Such a distinction will help to elucidate the deficit observed in the BG group altogether by characterizing their different performance patterns. To this end, we divided the incongruent trials of Session 1 (the trials requiring knowledge of the task rule) into 16 mini-blocks, each containing 10 trials. Figure 3 depicts the proportion of correct responses for each task for each of the three patients.

In order to enable a quantitative description of each patient's performance, we classified the performance for each task as either high in accuracy (H, above 80%), low in accuracy (L, below 20%), or as in-between (IB) (see Table 3). The cutoff scores of 20% were chosen to be roughly twice the highest proportion presented among the perseverating BG patients (Patient O.M., 0.11). We chose to double this proportion to partly compensate for the lower reliability of the current scores due to the fewer trials which contributed to each proportion. We

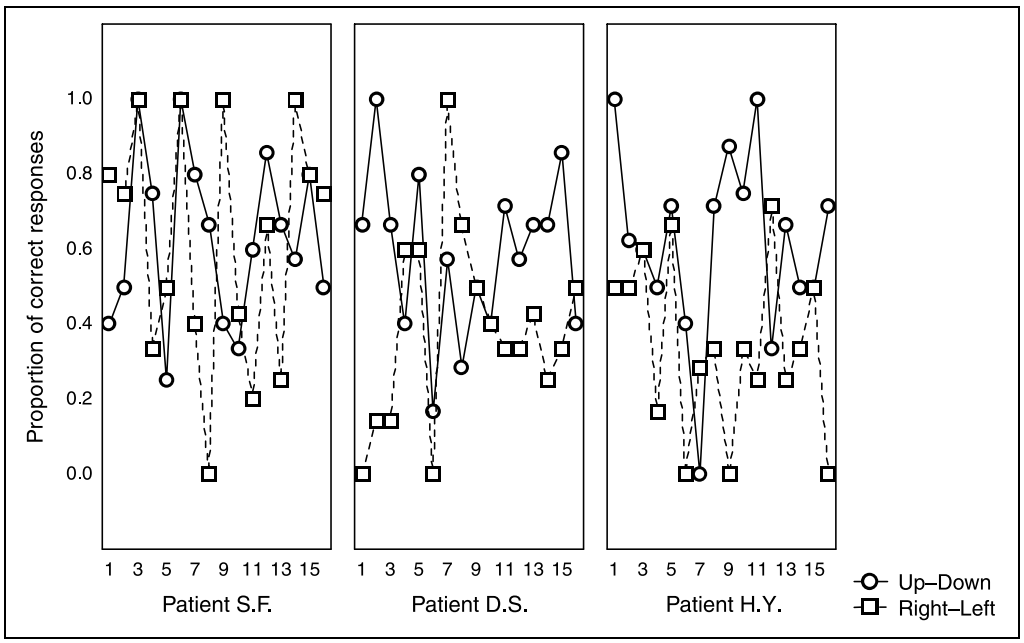

Figure 3. Proportion of correct responses in the incongruent condition as a function of mini-block, task, and patient. The numbers on the *x*-axis refer to the numbers of the mini-block (1–16). Each point of measurement was estimated for at least four trials.

were mostly concerned with combinations involving high accuracy in one task and low accuracy in the other task (H–L, Table 3). Such a combination indicates a perseveration or the performance of only one task, instead of switching between tasks. This combination was found only for Patients D.S. and H.Y., who demonstrated it in only 1 of the 16 mini-blocks. Based on the observed number of mini-blocks for each combination, we drew the expected value by chance for such a combination (H–L). The expected value by chance alone for such a combination was slightly less than one mini-block for both patients (0.81 mini-block for Patient D.S. and 0.75 mini-block for Patient H.Y.). Thus, the fact that there was one H–L mini-block could be explained by the chance combination of an H and L profile rather than by perseveration, at least as far as we can tell. However, this conclusion should be considered cautiously because of the low resolution of our analytic procedure. Therefore, we suggest that the task switching deficit observed in the BG patients resulted in either rule perseveration (''task dependent'') or random switching (''task independent'') pattern. We do not offer an elaborate explanation for this apparently random switching. A reasonable conjecture is that the patients, despite being able to describe the task and the meaning of the task cues in words when we asked them to do so, were unable to integrate and utilize this information when performing. As a result, they attempted (but failed) to take the cue information into account.

Reaction Time

Although the primary finding in the present study concerns the high proportion of errors found in the BG group in the incongruent conditions, for completeness sake, we report here the analyses of RTs as well. Although not very innovative, this set of analyses is important to show that we were able to demonstrate most of the effects already documented in the literature in our paradigm.

Congruency Effects

Because our core result refers to PE as a function of the congruency variable (incongruent trials RT minus congruent trials RT), it was important to examine this effect in RT as well. There was a significant congruency effect [$F(1, 19) = 18.94$, $p < .001$], which was not accompanied by a significant Congruency × Group interaction [$F(4, 19) = 1.25$, $p = .33$]. The mean RT congruency effect was 363, 54, 209, 265, and 123 msec among BG-switch, BG-no-switch, TH, PFC, and age-matched control, respectively. A focused comparison between patients who switched tasks (all patients, excluding BG-no-switch) and age-matched control did not reach statistical significance [$F(1, 19) = 2.39$, $p = .14$]. A contrast which

Table 3. Number of Mini-blocks (Out of 16) as a Function of Patient and Performance Pattern (Each Letter Refers to One of the Two Tasks): Session 1

Patient	*H–H*	*H–IB/IB–H*	***H–L/L–H***	*IB–IB*	*IB–L/L–IB*	*L–L*
S.F.	3	5	**0**	6	2	0
D.S.	0	3	**1**	9	2	1
H.Y.	0	2	**1**	9	4	0

H = high accuracy rate, over 80%; L = low accuracy, below 20%; IB = in between, 20–80%. Each letter in a given combination refers to one task.

tested for the significance of the smaller congruency effect in BG-no-switch compared to other patients only approached significance [$F(1, 19) = 3.21$, $p = .09$]. These findings further support the dissociation between the congruency effect in PE and in RT. Meiran and Kessler (in press) argued that the congruency effect in RT represents the activated long-term memory representations of the task rules or the task-related response categories (such as up or left). In contrast, the PE congruency effect reflects task selection or task inhibition difficulties.

Switching Costs, Mixing Costs, and Preparation

In examining task switching effects, we focused on switching cost (SC: switch RT minus repeat RT) and mixing cost (MC: repeat RT minus single task RT). Descriptively, SC represents the cost associated with immediate task switching, or the benefit associated with immediate task repetition. MC reflects the cost associated with needing to switch within the given block of trials. These costs may reflect strategic readiness for a switch (e.g., Braver, Reynolds, & Donaldson, 2003; Los, 1996) or the need to make a decision as to which task is required for the given trial (Rubin & Meiran, 2005), among other things.

Switching Costs and Preparation

The first ANOVA focused on switch costs. It involved group (BG-switch, BG-no-switch, TH, PFC, and control), CTI (short vs. long), and switch (switch vs. nonswitch). This analysis yielded significant main effects for group, CTI, and switch, respectively [$F(4, 19) = 4.36$, $MSE = 1{,}081{,}652.23$, $p < .05$, $F(1, 19) = 11.53$, $MSE = 20{,}623.79$, $p < .005$, and $F(1, 19) = 51.79$, $MSE = 13{,}564.28$, $p < .0001$]. In addition, there was a significant interaction between switch and group [$F(4, 19) = 3.08$, $MSE = 13{,}564.28$], and a marginally significant interaction between CTI and group [$F(1, 19) = 2.22$, $MSE = 20{,}623.79$, $p = .10$]. The slowest groups were the BG-switch (2166 msec) and the PFC (2092 msec). TH was in between (1571 msec) and the BG-no-switch and age-matched control participants were the quickest (1189 and 1117 msec, respectively). Switch costs were 239, 274, 182, and 195 msec for the BG-switch, TH, PFC, and control participants, respectively (all $p < .005$). They did not differ significantly from one another ($F < 1$). Switch cost was only 7 msec (*ns*) for the BG-no-switch group. This switch cost was significantly smaller than for the remaining groups [$F(1, 19) = 11.38$, $p < .005$]. CTI effects (short minus long CTI) were 135, 31, 88, and 29 msec for the BG-switch, BG-no-switch, TH, and PFC groups. None of these effects reached significance. The $F(1, 19) = 2.64$ and 1.67 for the BG-switch and TH groups, and $F < 1$ for the PFC and BG-no-switch. The patient groups did not differ significantly from one another ($F < 1$). In contrast, there was a significant CTI effect of 238 msec in the control group ($p < .001$). Moreover, the CTI effect in the age-matched control group was significantly different from that observed among the patient groups [$F(1, 19) = 6.63$, $p < .05$]. The fact that the preparation effect was observed in the age-matched control group who also had the fastest RT cannot be explained by general nonspecific slowing because such an account predicts an increase in effects with slowing, not a decrease as we have found (see the Appendix in Meiran, 1996 for a short proof).

Mixing Cost and Preparation

The next (nonindependent) analysis was performed using group, mixing (repeat vs. single task), and CTI as independent variables. Here we had to make decisions regarding which single-task data to use for the BG-no-switch group. Our choice was to take the single-task data which involved the same task on which they perseverated in Session 1 (the one being analyzed here) to hold task constant in this comparison. There were significant main effects for group, CTI, and mix, respectively [$F(4, 19) = 4.68$, $MSE = 476{,}282.68$, $p < .01$, $F(1, 19) = 9.18$, $MSE = 10{,}528.77$, $p < .05$, and $F(1, 19) = 41.33$, $MSE = 148{,}149.87$, $p < .0001$]. In addition, there was a significant interaction between mixing and group [$F(4, 19) = 3.48$, $MSE = 148{,}149.87$, $p < .05$]. All the remaining effects did not even approach significance and had $F < 1.01$. The novel finding here, relative to the preceding analysis, is the interaction. MC (repeat RT minus single task RT) was 735, 122, 496, 945, and 348 msec for BG-switch, BG-no-switch, TH, PFC, and age-matched control group, respectively. It was significant for all the groups ($p < .05$), except for BG-no-switch ($F = 0.40$). Nonetheless, MC was positive among all four patients in this group and ranged between 59 and 246 msec. We ran a series of planned contrast analyses to compare the MCs for each of the patients' groups to that of the age-matched control group. The only significant difference was found for the PFC group [$F(1, 19) = 7.77$, $p < .05$]. As before, the difference could not be only due to general slowing because the TH group, for example, had mean single-task RT that was quite similar to that of the PFC group (938 vs. 1057 msec, respectively), yet their MC was about half that of the PFC group. In order to completely rule out the possibility that general slowing was the reason for the increased MC for the PFC group, we computed normalized MCs by dividing them by the mean RT for the given participant. The proportional MC was 0.94 in the PFC group and only 0.64 in the age-matched control group, although this difference fell short of significance [$t(11) = 1.68$, $p = .06$, one-sided test].

Switching Cost and Response Repetition

Aron et al. (2003) related BG dysfunction to elevated RTs and errors on switch trials for repeated responses. In

their experiment, Huntington's disease patients, who were also at a more progressed stage of the disease, showed increased repetition effect, as evidenced by elevated RT on switch trials for repeated responses relative to controls. The authors assumed this to indicate excessive response-related inhibition on the previous trial resulting in a bias to respond with the other hand for the next trial. Shook et al. (2005) reported a similar result for PD patients who were off medication but not for L-Dopa-medicated patients. Cools et al. (2006) tested patients with focal BG lesions. They reported normal response repetition effects in errors but did not report the switching by repetition effects in RT. Moreover, their paradigm was very different from the task switching paradigms in which response repetition effects are usually studied.

We therefore ran an ANOVA on the RT data according to task switch (switch vs. repeat), response repetition, and group. In the literature on healthy young adults, the usual trend of the interaction between task switch and response repetition indicates a more pronounced switch effect for repeated responses (Rogers & Monsell, 1995; see also Mayr & Bryck, 2005; Meiran, 2000a; Kleinsorge & Heuer, 1999). As can be seen in Figure 4A, in the present results, this trend was most pronounced in the TH group but was also observed in the PFC and the age-matched control groups. Notably, it was absent (BG-no-switch) or reversed (BG-switch) in the BG groups. The triple interaction among group, switch, and response repetition was significant [$F(4, 19) = 4.14$, $MSE = 10{,}228.57$, $p < .05$]. Follow-up planned contrasts indicated that the simple interaction between switch and response repetition was significant only for the TH group [$F(1, 19) = 20.80$, $p < .0005$], and did not approach significance for any of the other groups.

A similar analysis of the PE data (see Figure 4B) confirmed the conclusions drawn from the RT results. Specifically, there was a marginally significant triple interaction among group, switch (switch vs. repeat), and response repetition [$F(4, 19) = 2.87$, $MSE = 0.0004$, $p = .051$]. It resulted from a significant simple interaction between switch and response repetition for the two BG groups [$F(1, 19) = 8.39$ and 3.67, $p < .01$, for BG-switch and BG-no-switch, respectively], which yielded results opposite to the predicted pattern. The same interaction contrast did not approach significance for any of the other groups. To summarize, looking at all the groups except for the BG groups, shows the usual trend of the interaction in the RT data, although this trend reached significance only within the TH group. The RT data showed the predicted numerical pattern of interaction between switch and response repetition for all the groups except for the BG groups. Future studies should explain why PD and Huntington's Disease cause a different form of abnormal response repetition effects (Shook et al., 2005; Aron et al., 2003) than do BG lesions that were caused by cerebrovascular disease such as those studied here. These studies should also clarify why the TH group in the present study showed an increased interaction, which resembles that seen in nonmedicated PD patients, for example (Shook et al., 2005). The difference relative to Cools et al.'s study on focal BG lesions is likely due to the very different paradigms that were used. The small sample size in this group makes it necessary to also replicate the findings in larger samples in the future.

DISCUSSION

The present study aimed at better characterizing the specific role of the BG within the FSCC in task switching. To this end, we tested patients with lesions occupying the three major components of the FSCC including the PFC, the BG, and the DMN of the TH, as well as a group of age-matched controls. Our main results concern accuracy. Specifically, all the BG patients and none of the other participants showed a marked reduction in accuracy in incongruent trials. These marked differences in accuracy (or PE) were coupled with lack of parallel RT differences. Additionally, we identified two subgroups of BG patients. One group showed a PE of around 0.50 for both tasks. Based on our previous modeling work (Meiran & Daichman, 2005), we argue that this performance profile indicates that these patients switched tasks. The fact that there was a significant SC and MC in this group supports this interpretation. The other group of BG patients showed near-zero PE for one task and near 1.00 PE for the other task. Again, based on our previous modeling work (Meiran & Daichman, 2005), we argued that these patients did not switch tasks. The nonsignificant and numerically negligible SC in this group supports this interpretation. The fact that all of them had a positive MC may be taken as evidence for their attempt to switch tasks (see Yehene et al., 2005).

Aside from these main findings, there are other interesting findings in the RT data. First, none of the patients' groups showed a significant preparation-related gain in RT in blocks involving task switching. This contrasts with what we observed among the age-matched control participants whose RT shortened following a long CTI. This result suggests that the FSCC is important for task preparation and mirrors a similar finding by Pollux (2004) on PD. We acknowledge the fact that the present results do not allow us to rule out the possibility that any brain damage would compromise the ability to prepare toward a new task because we did not include a group whose lesion did not occupy the FSCC. Second, there was an increased MC following PFC lesions in line with previous findings in the literature (e.g., Aron et al., 2004; Keele & Rafal, 2000; Rogers et al., 1998). Finally, BG lesions resulted in abnormal response repetition effects under conditions involving task switching. The fact that abnormalities were found agrees with the literature on PD (Shook et al., 2005) and

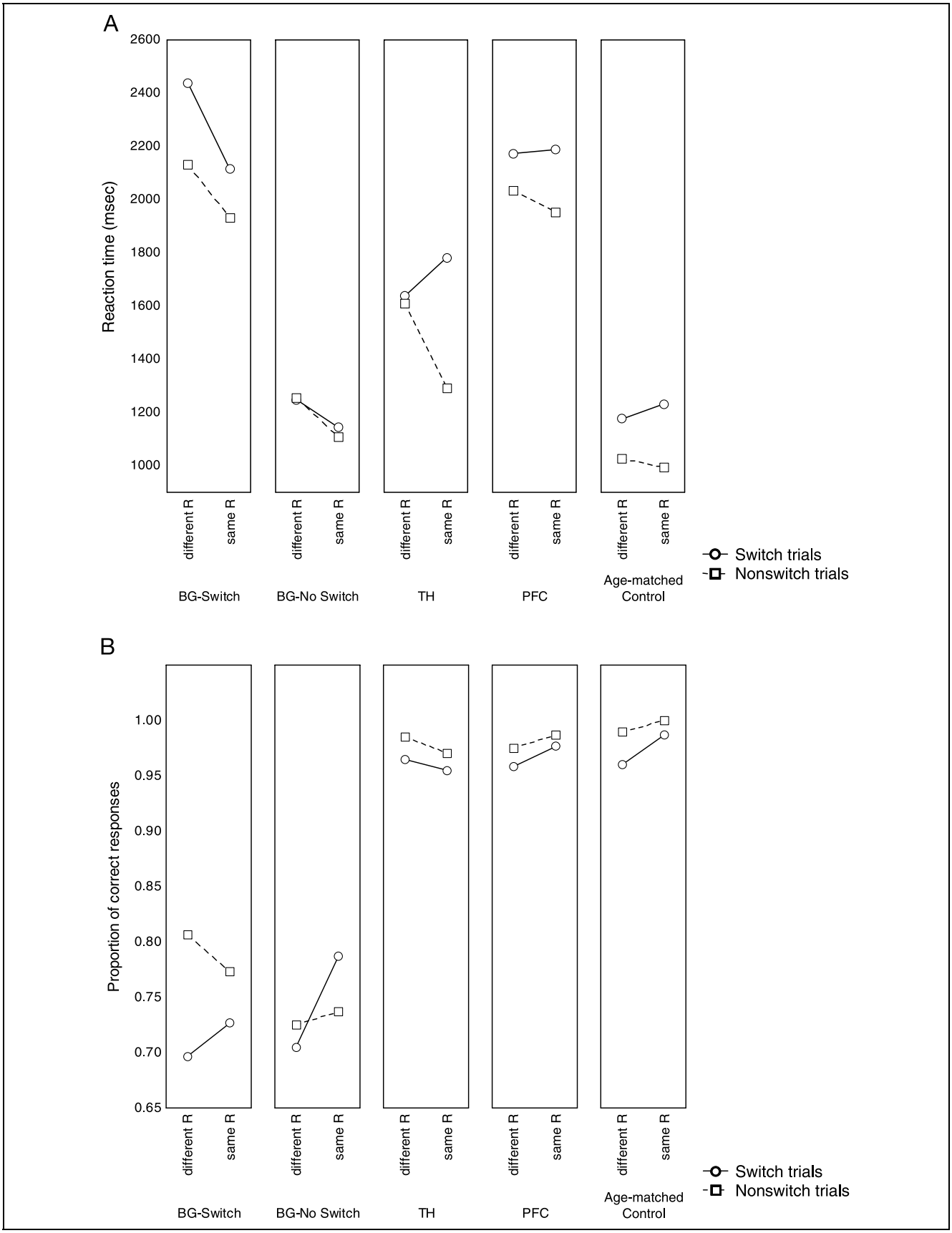

Figure 4. (A) RT as a function of group, task switch, and response repetition. (B) Proportion of correct responses as a function of group, task switch, and response repetition. Different R = different response; same R = same response.

Huntington's disease (Aron et al., 2003). However, the abnormality that we found following ischemic brain lesions was different from the abnormalities in PD, which are possibly due to dopamine deficiency, as seen in the effects of L-Dopa medication (Shook et al., 2005) and different from those seen following Huntington's related pathology.

Put in a larger context, our major conclusion regarding the role of the BG in task set schema and choice selection also accords with the two classes of theories upon which we based our predictions. These theories suggest a special role for the BG in action selection (Graybiel & Rauch, 2000; Redgrave et al., 1999; Mink, 1996; Graybiel & Kimura, 1995; Jackson & Houghton, 1995) and in the inhibition of irrelevant information (Filoteo et al., 2005).

Previous investigations of the switching deficit among PD patient attributed the deficit to dopamine depletions within the striatum and even demonstrated the enhancement of switching ability caused by dopaminergic medication (e.g., Shook et al., 2005; Cools, Barker, Sahakian, & Robbins, 2001b; see also Owen et al., 1993). Nonetheless, the deficits observed in the present study were considerably larger than the equivalent deficits observed in studies on PD and dopamine. Although dopamine depletion has very significant impact on performance in general, its specific impact on BG functioning is likely to be less than that of a lesion which may not only compromise BG functioning but may eliminate it altogether. Additionally, the fact that we have used a spatial paradigm for both studies (Meiran et al., 2004 and the current one), as opposed to previous studies, might also bear relevance. Notably, only 50% of the PD patients in Meiran et al.'s (2004) study showed the deficit demonstrated by all the BG patients studied here.

The contribution of task content has been recently demonstrated in a study on healthy young adults. We (Yehene & Meiran, 2007) examined the correlations between equivalent indices of executive functioning taken from two logically and structurally similar paradigms, the spatial one used here and a shape–size paradigm that was used by Yehene et al. (2005). The results of that study show that task content contributes significantly to executive functioning. A hint that the spatial content of the paradigm contributed to the increased error rate in incongruent trials comes from the distribution of left-sided and right-sided lesions. Whereas three out of four patients in the (arguably more impaired) BG-no-switch group had a right-sided lesion, two out of three patients in the (arguably less impaired) group had their lesion on the left side of the brain.

Although our results support the hypothesis concerning the specific role of the BG within the FSCC, there are alternative explanations to rule out. First, one could argue that the lack of switch-related deficits among the PFC group is due to the fact that four out of the six PFC patients had a lesion on the right side of the brain and that right-sided lesions do not produce a switch deficit (Rogers et al., 1998; see also Bédard & Richer, 1999). However, Mayr et al. (2006) have recently shown that right-sided PFC lesions eliminate task set inhibition. Moreover, Arbuthnott (2005) has recently shown that conditions in which task set inhibition is low produce large congruency effects and vice versa. Therefore, if anything, our sample of PFC patients was more likely to show increased congruency effect. Finally, in the two PFC patients with left-sided lesions, the lesion occupied the inferior frontal gyrus, a region that plays a major role in imaging work on task switching (Derrfuss, Brass, Neumann, & von Cramon, 2005). Neither one of them exhibited the deficit shown by the BG patients.

Another argument that is based on the theory concerning FSCC is that lesions positioned in lower components of the circuits are likely to produce more pervasive deficits because the different circuits show more overlap or occupy smaller amounts of tissue in deeper structures (Cummings, 1993). According to this line of reasoning, lesions in the BG should produce more pronounced deficits (in the sense of involving more circuits and therefore more functions) than PFC lesions. However, if this argument was true, one would predict that the most impaired group would be the TH. Our results therefore clearly refute this argument.

Finally, in the Introduction, we described two classes of theories, both of which predict BG-specific functioning in task switching. According to some theories, the primary role of the BG is action selection (Bogacz & Gurney, 2007; Gurney et al., 2004; Redgrave et al., 1999). According to other theories, it is inhibition (Filoteo et al., 2005; Mink, 2003). Although the present results cannot decide between these possibilities, we would like to point out the fact that selection often uses inhibition as its mechanism. Two prominent theories agree on this issue. One is the classical theory of Norman and Shallice (1986), which describes a mechanism to select among competing actions (the contention scheduling) by lateral inhibition. The other is Mayr and Keele's (2000) theory of sequential inhibition. According to this theory, the successful selection of the next task is made possible by the inhibition of the just-abandoned task set. In fact, Schuch and Koch (2003) and Yeung and Monsell (2003) both make the case that the inhibition of the competing task set is accomplished as a part of response selection.

To conclude, the present work demonstrated a specific role for the BG within the FSCC in task switching. Our major finding shows that BG patients showed marked elevation of error rates in incongruent trials. We argue that these elevated error rates reflect the involvement of the BG in action selection and/or in the inhibition of irrelevant information. In contrast to this finding suggesting a specific role of the BG within the FSCC, lack of benefit from task preparation seems to demark the integrity of the circuits as a whole.

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Note

1. It is important to distinguish between the terms ''cross talk'' (Rogers & Monsell, 1995) and ''congruence'' (Sudevan & Tylor, 1987). Cross talk refers to the presence of information which is related to the irrelevant task rule. Congruence is defined only for cross-talk trials, and it refers to whether the information related to the irrelevant task indicates the same response as in the relevant task (congruent) or a different response (incongruent).

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