Disentangling the Role of Cortico-Basal Ganglia Loops in Top–Down and Bottom–Up Visual Attention: An Investigation of Attention Deficits in Parkinson Disease

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Abstract

■ It is solidly established that top–down (goal-driven) and bottom–up (stimulus-driven) attention mechanisms depend on distributed cortical networks, including prefrontal and fronto-parietal regions. On the other hand, it is less clear whether the BG also contribute to one or the other of these mechanisms, or to both. The current study was principally undertaken to clarify this issue. Parkinson disease (PD), a neurodegenerative disorder primarily affecting the BG, has proven to be an effective model for investigating the contribution of the BG to different brain functions; therefore, we set out to investigate deficits of top–down and bottom–up attention in a selected cohort of PD patients. With this objective in mind, we compared the performance on three computerized tasks of two groups of 12 parkinsonian patients (assessed without any treatment), one otherwise pharmacologically treated and the other also surgically treated, with that of a group of controls. The main behavioral tool for our study was an attentional

capture task, which enabled us to tap the competition between top–down and bottom–up mechanisms of visual attention. This task was suitably combined with a choice RT and a simple RT task to isolate any specific deficit of attention from deficits in motor response selection and initiation. In the two groups of patients, we found an equivalent increase of attentional capture but also comparable delays in target selection in the absence of any salient distractor (reflecting impaired top–down mechanisms) and movement initiation compared with controls. In contrast, motor response selection processes appeared to be prolonged only in the operated patients. Our results confirm that the BG are involved in both motor and cognitive domains. Specifically, damage to the BG, as it occurs in PD, leads to a distinct deficit of top–down control of visual attention, and this can account, albeit indirectly, for the enhancement of attentional capture, reflecting weakened ability of top–down mechanisms to antagonize bottom–up control. ■

INTRODUCTION

Visual selective attention refers to the ability to select and order the vast amount of retinal input that is presented to an individual at any given time. This cognitive process allows one to select the stimuli deemed more relevant for the task at hand while disregarding other stimuli and to prioritize the selected stimuli for further processing (Desimone & Duncan, 1995). Visual selective attention can be instantiated by two functionally separable but interacting control mechanisms, although such rigid distinction has recently been questioned (Awh, Belopolsky, & Theeuwes, 2012). Endogenous visual attention (EVA), reflecting top–down control, refers to a voluntary mode

of operation to allocate processing resources to locations or features designating relevant stimuli that are expected to occur before their actual occurrence (Posner, 1980). EVA is said to be goal-directed, because attentional priority is given to those events and objects that are in line with the current goals of the observer. In contrast, exogenous visual attention, reflecting bottom–up driven processing, refers to a largely automatic mechanism whereby salient stimuli receive priority, regardless of the current goals of the individual (Talsma, Coe, Munoz, & Theeuwes, 2009; Theeuwes, 1991b; Yantis & Jonides, 1984). Bottom–up mechanisms underlie attentional capture (AC), a phenomenon where salient objects or events command attentional priority regardless of the observer's goals, disrupting target search (Theeuwes & Godijn, 2002). AC can be considered as a measure of distractibility.

In spite of considerable progress in this domain, we are still lacking a complete understanding of the neural correlates of top–down and bottom–up mechanisms of visual attention and of the degree to which these mechanisms

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are sustained by shared or separable neural networks (Bisley, 2011; Talsma et al., 2009; Hahn, Ross, & Stein, 2006; Grosbras, Laird, & Paus, 2005; Serences et al., 2005; Peelen, Heslenfeld, & Theeuwes, 2004; Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999). However, a vast literature has provided converging evidence that two anatomically segregated, but interacting, networks subserve the two attention mechanisms (Shomstein, Lee, & Behrmann, 2010; Corbetta & Shulman, 2002; Rosen et al., 1999; Nobre et al., 1997). A more dorsal and largely bilateral frontoparietal system, including the intraparietal sulcus/superior parietal lobule, the FEF, and the supplementary eye field, is widely accepted to be the source of feedback exerting top–down control to modulate activity in posterior visual cortex (Corbetta & Shulman, 2002; Pessoa, Kastner, & Ungerleider, 2002; Gitelman et al., 1999; Rosen et al., 1999; Nobre et al., 1997; Corbetta, Miezin, Shulman, & Petersen, 1993). A time course analysis of fMRI signals revealed that there was an increase in activity in these frontal and parietal areas during the expectation period (in the absence of visual input), reflecting the engagement of an attentional set in anticipation of task relevant visual input, with no further increase evoked by the appearance of the attended stimulus (Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999). These results suggest that such activity pattern reflected signals for top–down attentional control and not the modulatory effects of attention on visual processing. This conclusion is further supported by the observation that, in an unattended condition, no appreciable visually evoked activity was detected in the same frontal and parietal regions (Kastner, Pinsk, Desimone, & Ungerleider, 2000).

Further results indicate that pFC, including dorsolateral pFC in humans, may be crucial in suppressing the response of more posterior regions to an irrelevant but salient stimulus, suggesting an important way through which top–down mechanisms can modulate AC effects (Bisley, Mirpour, Arcizet, & Ong, 2011; Talsma et al., 2009; de Fockert, Rees, Frith, & Lavie, 2004; Nobre et al., 1997). More generally, pFC is supposed to provide both inhibitory and excitatory input to distributed neural circuits required to support performance in diverse selective attention tasks (Knight, Staines, Swick, & Chao, 1999). Tract-tracing studies in monkeys have uncovered direct feedback projections from pFC to anterior inferior temporal cortex, as well as indirect feedback projections to areas V4 and the temporal-occipital areas via parietal cortex (Webster, Bachevalier, & Ungerleider, 1994; Ungerleider, Gaffan, & Pelak, 1989). Interestingly, the distractibility theory postulates that prefrontal patients are unable to suppress responses to irrelevant stimuli in a range of perceptual and cognitive tasks (Bartus & Levere, 1977). In particular, enhancement of primary auditory and somatosensory cortical responses to task-irrelevant distractors has been found in neurological patients with dorsolateral prefrontal damage (Yamaguchi & Knight, 1990) and in schizophrenic patients with prefrontal hypometabolism, as measured with PET scanning (Weinberger, Berman, & Zec, 1986). This suggests that prefrontal damage disrupts inhibitory modulation of inputs to primary sensory cortices, contributing to the attentional deficits observed in these patients.

A second, more ventral system, strongly lateralized to the right hemisphere and involving the TPJ (at the intersection of the inferior parietal lobule and the superior temporal gyrus) and the middle and inferior frontal gyri, has instead been proposed to detect salient and behaviorally relevant stimuli and to instantiate an alerting mechanism for the dorsal system when these stimuli are detected outside the focus of attention (Corbetta & Shulman, 2002; Corbetta et al., 2000). More specifically, the latter system could issue a control signal that terminates ongoing cognitive activity within the dorsal system, thus serving as a circuit breaker, when a behaviorally relevant or otherwise salient stimulus is presented (Serences et al., 2005; Corbetta & Shulman, 2002).

Available evidence suggests that, apart from the above cortical circuits, subcortical structures are also likely involved in determining attentional control, notably the BG (but also the superior colliculus and parts of the thalamus; e.g., see McNab & Klingberg, 2008; Grande et al., 2006; Muller, Philiastides, & Newsome, 2005; Weder et al., 1999). This may appear rather obvious, given the widespread interconnections linking the BG with vast sectors of the cortical mantle, including the aforementioned prefrontal and frontoparietal regions, and in line with the notion that the BG are part of articulated and diverse cortico-subcortical loops, which are involved in the control of motor, emotional, and cognitive processes (Yelnik, 2008; Mink, 1996; Parent & Hazrati, 1995; Alexander, DeLong, & Strick, 1986). Consequently, it should be expected that a normal functioning of the cortical networks mediating attentional control is not possible under conditions where the BG are not working properly.

Parkinson disease (PD), a neurodegenerative disorder of the BG, typically characterized by a progressive loss of dopaminergic neurons, predominantly in the substantia nigra pars compacta, which project to the striatum (Gibb & Lees, 1988), has proven to be a good model to investigate in humans the involvement of the BG not only in the selective gating and regulation of motor processes (Mink, 1996) but also in the modulation of behavioral and cognitive functions (Mallet et al., 2007; Cools, Ivry, & D'Esposito, 2006; Voon, Kubu, Krack, Houeto, & Troster, 2006; Funkiewiez et al., 2003). Mounting evidence indicates that PD, apart from the typical motor signs (Lang & Lozano, 1998; Gibb & Lees, 1988), is often accompanied by a variety of cognitive deficits (Caballol, Marti, & Tolosa, 2007; Pirozzolo, Hansch, Mortimer, Webster, & Kuskowski, 1982; Reitan & Boll, 1971), including rather subtle difficulties in visual-spatial perception (Boller et al., 1984), memory (Flowers & Robertson, 1985; Wilson, Kaszniak, Klawans, & Garron,

1980), language (Matison, Mayeux, Rosen, & Fahn, 1982), concept formation, and behavioral regulation (Flowers & Robertson, 1985; Cools, van den Bercken, Horstink, van Spaendonck, & Berger, 1984; Lees & Smith, 1983; Bowen, Kamienny, Burns, & Yahr, 1975), which suggests the involvement of the BG and the cortico-subcortical loops of which they are part in the regulation of these cognitive functions.

However, some caution is necessary here. According to the dual syndrome hypothesis (Robbins & Cools, 2014; Kehagia, Barker, & Robbins, 2013), the great variety and eterogeneity of cognitive deficits found in PD (Kehagia, Barker, & Robbins, 2010) may be explained not only in relation to the nigrostriatal dopaminergic depletion, with the resulting frontostriatal dysfunction, but also in relation to the impairment of neural pathways not involving the BG, notably the cholinergic and noradrenergic projection systems. In particular, the dysexecutive syndrome would be mainly related to a frontostriatal dysfunction, whereas the prodromal symptoms of dementia and the cognitive deficits observed in PD dementia would be mainly related to the involvement of pathways outside the BG, even if some degree of overlap in cognitive control between these different neural networks is plausible. It is therefore advisable to keep in mind the possibility that damage outside the BG might contribute to the constellation of cognitive deficits in these patients.

The PD model has enabled important observations on the involvement of the BG in the attentional domain. In particular, findings from several studies on parkinsonian patients hint at the existence of deficits of general attention, like, for example, reduced concentration (Bulpitt et al., 1985) and the inability to attend to more than one motor act at a time (Sanes, 1985). In addition, PD patients present difficulties in shifting from one cognitive set to another at the WCST (Lees & Smith, 1983; Bowen et al., 1975), and likewise, they are unable to maintain a set against competing alternatives at the odd-man-out choice discrimination task (Flowers & Robertson, 1985). Finally, they are more prone to interference in the presence of a distractor stimulus compared with normal controls, as measured on a dichotic listening task (Sharpe, 1992). Moreover, several behavioral studies indicate that parkinsonian patients with overall well-preserved cognitive functions may nevertheless be impaired at a variety of visual attention tasks (Filoteo et al., 1995; Wright, Burns, Geffen, & Geffen, 1990; Yamada, Izyuuinn, Schulzer, & Hirayama, 1990) and more specifically at tasks tapping selective attention mechanisms (Cools, Rogers, Barker, & Robbins, 2009; Henik, Singh, Beckley, & Rafal, 1993; Pillon et al., 1989).

The BG can be hypothesized to play a key role in the selective gating and regulation of response tendencies originating in specific cortical areas, facilitating and suppressing control signals that are competing for access to the respective neurofunctional system, according to task goals. If so, one should expect that a BG dysfunction may determine impairments in the ability to suppress conflicting responses, leading to exacerbated interference effects (Wylie, Ridderinkhof, Bashore, & van den Wildenberg, 2010; Wylie et al., 2009; Praamstra, Stegeman, Cools, & Horstink, 1998). In the realm of visual attention, a similar deficit could materialize in the form of a deficit of top–down control, which could be less effectively engaged to counteract the interference effect engendered by a distracting stimulus acting through bottom–up mechanisms. As of today, however, it is still unsettled to what extent the BG play a role in regulating either top–down or bottom–up mechanisms of attention, or a combination of both. This study was principally undertaken to provide clear-cut evidence bearing on these issues.

With this objective in mind, in our experimental approach, we decided to focus on PD patients evaluated in off-condition (without any antiparkinsonian treatment) and compare their performance on three computerized visual tasks with that of a group of healthy controls. Two groups of parkinsonian patients, of which one usually treated only with drugs and the other also with deep brain stimulation of the subthalamic nucleus (STN-DBS), participated in our study. We recruited these two groups of PD patients because in future work we plan to analyze and compare the therapeutic effects of dopaminergic versus STN-DBS treatments on any deficits of attention that may result from this study. Furthermore, the comparison between the performances of the two groups of parkinsonian patients, as evaluated by means of the present experimental protocol, enables us to ascertain whether surgery for electrode placement in the brain of some of the patients determines detectable deficits of visual selective attention. The interest for this issue stems from the fact that, although the STN-DBS is an established therapy in advanced stages of PD (Deuschl et al., 2006; Benabid, Koudsie, Benazzouz, Le Bas, & Pollak, 2002), there are some reports of a cognitive decline in relation to the surgical intervention (Witt et al., 2013; Okun et al., 2009; Pillon et al., 2000), including in the attentional domain (Morrison et al., 2004). Up to now, it is unclear whether surgery for PD can impact negatively on the control mechanisms of visual selective attention, and for this reason, a secondary goal of our study was to provide information bearing on this issue.

The main tool used in our experimental protocol was a computerized visual search task, known as the AC task, a tool especially suited for studying the exogenous capture of attention by comparing performance between conditions with versus without a salient task-irrelevant distractor (singleton). However, it should be noted that the degree of AC detected with this task also reflects the competition between top–down and bottom–up mechanisms of attentional control, so that any change in AC detected with the task may reflect a change in the efficacy of either control mechanism or of both. For example, an elevated level of AC can result from enhanced bottom–up mechanisms, or from weakened top–down control, or a combination

of both, and vice versa for a reduced level of AC. To overcome this ambiguity and better define the role of the BG in the mechanisms of visual attention, we suitably combined the AC task with a choice RT task, serving as a reference to assess perceptual decision (discriminatory) mechanisms as well as motor response selection mechanisms in isolation. By comparison, the AC task and the choice RT task enabled us to isolate any impairment of top–down control of attention in the patients relative to the controls. Specifically, any performance deficit in the no-distractor condition of the AC task, in the patients relative to the controls, above and beyond any deficit that might be revealed with the choice RT task, will attest to impaired top–down attention or EVA (see below, for a more detailed account of the logic). In turn, depending on whether or not we will identify a distinct deficit of top–down attentional control in our patients by the combined use of the two tasks, we would then be in a position to also establish whether any change in the degree of AC in the patients relative to the controls ought to be principally attributed to an alteration of bottom–up or top–down mechanisms of attention. According to the aforementioned hypothesis of BG function, we might expect that a dysfunction of the BG, as occurs in PD, determines a weakening of top–down control of attention with a consequent enhancement of the AC effect. However, this prediction can only be confirmed on the basis of solid empirical evidence.

Finally, given that the performance in our AC task not only reflected visual attention mechanisms but also other processes concerning motor response selection and motor response initiation, which are known to be altered in PD (Wylie et al., 2009; Frank, Samanta, Moustafa, & Sherman, 2007; Lang & Lozano, 1998), it was necessary to isolate these two components to better define their contribution to performance in the AC task. To this aim, in our experimental setting, we suitably complemented the choice RT task with a simple RT task, serving as a reference to assess motor response initiation mechanisms (see Methods).

METHODS

Participants

Each of the two groups of parkinsonian patients, as well as the group of healthy controls, consisted of 12 individuals, who were matched for age (±5 years), sex, and education across the three groups. The two patient groups were also matched for disease severity. Characteristics of all participants are provided in Table 1.

All participants were neurologically healthy, except for PD. Patients were clinically diagnosed as suffering from idiopathic PD according to the U.K. Parkinson Disease Society Brain Bank Criteria (Gibb & Lees, 1988) and, at an advanced stage of the disease, characterized by motor complications. Participants were not affected by mild/

severe dementia and/or dysexecutive syndrome, which might interfere with performance in the various paradigms. Moreover, the absence of dementia in our patients, even at an advanced stage of the disease, ensures that any attention deficit that might emerge in our study mainly reflects dysfunction within specific corticobasal ganglia loops (Robbins & Cools, 2014; Kehagia et al., 2013). Moreover, participants did not suffer from depression and apathy. Cognitive and behavioral profiles were assessed by a battery of neuropsychological tests (Table 1). Besides, participants did not manifest signs of psychosis, and they did not take psychotropic or neurotropic drugs (except for the L-dopa treatment; see below). Only short half-life benzodiazepines or similar drugs, but with the last intake occurring at least 12 hr before testing, were tolerated for the purposes of this study. Given the possibility that the neural networks underlying top–down and bottom–up attention are at least partly lateralized, for the sake of homogeneity all selected participants were right-handed and used the dominant hand for responding during the execution of the behavioral tasks. Because the visual tasks implied the perceptual processing of red and green stimuli displayed on a computer monitor, participants reported to have normal or corrected-to-normal vision, and they did not suffer from deficiencies in red–green color vision, as assessed by the desaturated D-15 Lanthony test (Luneau, Paris; Lanthony, 1978, 1986), a test that is widely used both in healthy participants and in parkinsonian patients (Diederich, Raman, Leurgans, & Goetz, 2002; Pieri, Diederich, Raman, & Goetz, 2000). Moreover, PD patients did not manifest any other appreciable medical or psychological problem, which might interfere with task performance (for instance, a marked tremor of the head and upper limbs).

STN-DBS-treated patients were selected among those who had undergone surgery at least 3 months before the experiment, because this is the time interval necessary for the disappearance of any microtraumatic effect due to the implantation procedure (Maltete et al., 2008; Tommasi et al., 2008; Deuschl et al., 2006), which in turn might affect the performance of surgically treated patients.

The surgical procedure for the implantation of the electrodes in the STN-DBS-treated patients was carried out as previously reported by the Grenoble team (Benabid et al., 2002). All patients were implanted bilaterally with quadripolar electrodes (DBS-3389, Medtronic, Minneapolis, MN) connected to a double-channel programmable pulse generator (Kinetra model 7428, Medtronic), placed in the subclavicular area. Only patients with correct placement of the electrodes in both STNs and in particular with at least one lead contact in the sensorimotor part and another contact in the associative part of the STN entered our protocol. This inclusion criterion was important because, in a future development of our line of research, we also plan to test and compare the effects produced with the selective stimulation of the sensorimotor and associative parts of the STN to assess for any

Table 1. Participant Characteristics

	Pharmacologically Treated PD Patients, Mean (±SE)	Surgically Treated PD Patients, Mean (±SE)	Controls, Mean (±SE)	p
Sex (male/female)	7/5	7/5	7/5	
Age (years)	57.1 (±2.3)	55.5 (±2.7)	56.1 (±2.6)	ns
Education (years)	13.6 (±1.1)	13.7 (±0.9)	13.7 (±1.0)	ns
Hand dominance	88.7 (±4.3)	86.3 (±5.1)	89.4 (±5.3)	ns
MMSE			29.4 (±0.3)	
MDRS	140.8 (±0.6)	139.4 (±0.8)		ns
FAB	16.7 (±0.3)	16.0 (±0.4)	16.9 (±0.3)	ns
BDI-II	8.0 (±1.5)	6.3 (±0.9)	5.8 (±0.9)	ns
SAS	6.8 (±1.2)	8.1 (±0.9)	7.6 (±1.0)	ns
Disease severity	37.5 (±2.4)	42.6 (±2.6)		ns
Disease duration (years)	13.9 (±2.1)	11.9 (±1.2)		ns
Levodopa therapy length (years)	7.7 (±1.5)	9.1 (±1.6)		ns
Elapse of time from surgery (months)		11.3 (±1.7)		
LEDD	804.4 (±81.1)	392.9 (±74.6)		.001

The global cognitive profile of patients was assessed by the Mattis Dementia Rating Scale (MDRS; maximum score = 144; Mattis, 1976), and that of healthy controls was assessed by the Mini-Mental State Examination (MMSE; maximum score = 30; Folstein, Folstein, & McHugh, 1975). A score of less than 130 and 24 in the MDRS and MMSE, respectively, is indicative of mild/severe dementia. The frontal lobe functions were assessed by the Frontal Assessment Battery (FAB; maximum score = 18), where a score below 13 is indicative of mild/severe dysexecutive syndrome (Dubois, Slachevsky, Litvan, & Pillon, 2000). Mood was rated with the Beck Depression Inventory-II (BDI-II), in which the maximum score is 63. A score above 20 corresponds to mild/severe depression (Beck, Steer, & Brown, 1996). Motivation was assessed by means of the Starkstein Apathy Scale (SAS; maximum score = 42, with higher levels indicative of more severe apathy). A cutoff at 14 points separates apathetic from nonapathetic participants (Starkstein et al., 1992). Hand dominance was assessed by the Edinburgh Handedness Inventory: A score above 40 indicates right-handedness (Oldfield, 1971). Disease severity was expressed as the motor score obtained in off-phase according to the Unified Parkinson's Disease Rating Scale part III (UPDRS III; Defer et al., 1999). The maximum score on the UPDRS III is 108, with a higher score denoting greater motor impairment. The motor scores were obtained by a trained neurologist. Disease duration was estimated on the basis of the patients' subjective estimate of the time of occurrence of the first symptoms of PD. Antiparkinsonian drugs were expressed as levodopa equivalent daily dose (LEDD) in mg/day (Deep-Brain-Stimulation-for-Parkinson's-Disease-Study-Group, 2001).

The listed variables were respectively analyzed by means of *t* tests for independent samples or by means of one-way ANOVAs, with Group as between-subject factor, depending on whether the comparison for a given variable was performed across two or more groups.

anatomo-functional specialization within the nucleus in relation to attentional control mechanisms. Electrode placement was assessed by fitting the images of a three-dimensional atlas of the BG to the postoperative MRIs of the patients (Bardinet et al., 2009; Yelnik et al., 2003, 2007).

All participants were naive as to the purpose of the experiment. All participants gave written informed consent according to the Declaration of Helsinki, and the research protocol was approved by the local ethical committee of the two universities (Grenoble and Verona) where the study took place.

Apparatus for the Three Computerized Tasks

The computerized tasks were created and run with the E-Prime software (Psychology Software Tools, Inc., Pittsburgh, PA) on a PC computer. The stimuli appeared on a 17-in. CRT monitor (Samsung SyncMaster 753DF-T/T, Samsung Electronics, UK; resolution 1024 × 768) and consisted of green (CIE x,y chromaticity coordinates of 0.288/0.609)

or red (coordinates of 0.633/0.334) geometrical shapes perfectly matched in luminance (18.4 cd/m^2). A fixation cross was presented in white (78.0 cd/m^2) on a black background (0.0 cd/m^2). The "1" and "2" adjacent keys (1.7 × 1.7 cm) of a numeric keypad (Manhattan model 176354 numeric keypad), connected to the computer via a USB port, were used as response devices.

Computerized Tasks

AC Task

Given the visual perception and cognitive abnormalities typical of PD (Bodis-Wollner & Paulus, 1999), we developed a variant of the classical AC task pioneered and validated by Theeuwes and colleagues (Deijen, Stoffers, Berendse, Wolters, & Theeuwes, 2006; Theeuwes, 1992, 1994), with some important changes to make it especially suitable for our current purposes, although we maintained its essential features (Theeuwes, 2010). As in the original task, participants received two conditions

(Figure 1A). In the so-called no-distractor condition (control condition), they were to search for a pentagon-shaped target, presented with the base at the top or bottom, embedded among five irrelevant diamond-shaped stimuli, according to previous instructions. The target resulted from the abrupt cut at the upper or lower corner of one of six diamond elements presented around fixation. Participants were instructed to focus their processing on the position (top or bottom) of the cut, responding to the orientation of the pentagon-shaped target by pressing key "1" of the numeric keypad if the base of the pentagon was at the top or key "2" if it was at the bottom, respectively, using their right-hand index and middle finger. In the so-called distractor condition, simultaneously with the target onset, one of the other five diamonds changed color (red instead of green, or vice versa), as well as orientation (45° rotation, becoming a square), therefore acting as a singleton distractor. This element represented an irrelevant but highly salient stimulus and was assumed to capture attention automatically and disrupt target search on the basis of bottom–up mechanisms. Participants were encouraged to focus only on the target while completely ignoring the distractor element.

A number of features of the AC task that we implemented should receive proper consideration. First, the top–down goal for the observers was very clear, in that throughout the experiment they consistently searched for the same target: the unique pentagon-shaped element among five diamonds. Second, the singleton distractor, an irrelevant yet salient object, was never the target, so that its interfering capability was solely determined by stimulus-driven, bottom–up mechanisms (and not any lingering

Figure 1. Graphic illustration of example trials for the three computerized tasks. (A) Example trials of the no-distractor and distractor conditions of the AC task. The sequence of events was as follows. Initially, a white fixation cross (0.5°) was presented at the center of the display against the black background, and it was accompanied by a warning sound for 300 msec. Participants were required to maintain gaze on the fixation cross for the entire duration of each trial. Then, a stimulus display consisting of six diamonds (1.2° on a side), all of the same color (green or red), equally spaced around the fixation cross on an imaginary circle whose radius was 3.6°, appeared on the monitor. After 700 msec, one of the six diamonds—the target—had its upper or lower corner abruptly cut (0.6° on a side), turning into a pentagon-shaped element, respectively with the base at the top or bottom. The target display lasted only 200 msec to discourage eye movements (Montagnini & Chelazzi, 2005). Following the disappearance of the target display, the screen went black, and participants had additional 2300 msec to provide their response (thus, the total time window to produce a response was 2500 msec). The intertrial interval was fixed at 1500 msec. (B) An example trial of the choice RT task is shown. (C) An example trial of the simple RT task. In all trials of this task, a diamond-target appeared on the monitor for 200 msec after a variable delay (delays between 400 and 2000 msec) from the onset of the fixation cross. Along the experiment, the orientation, color, and position of the target (for each computerized task) as well as the color and position of the singleton distractor (for the AC task) in the display were counterbalanced and randomly selected on each trial.
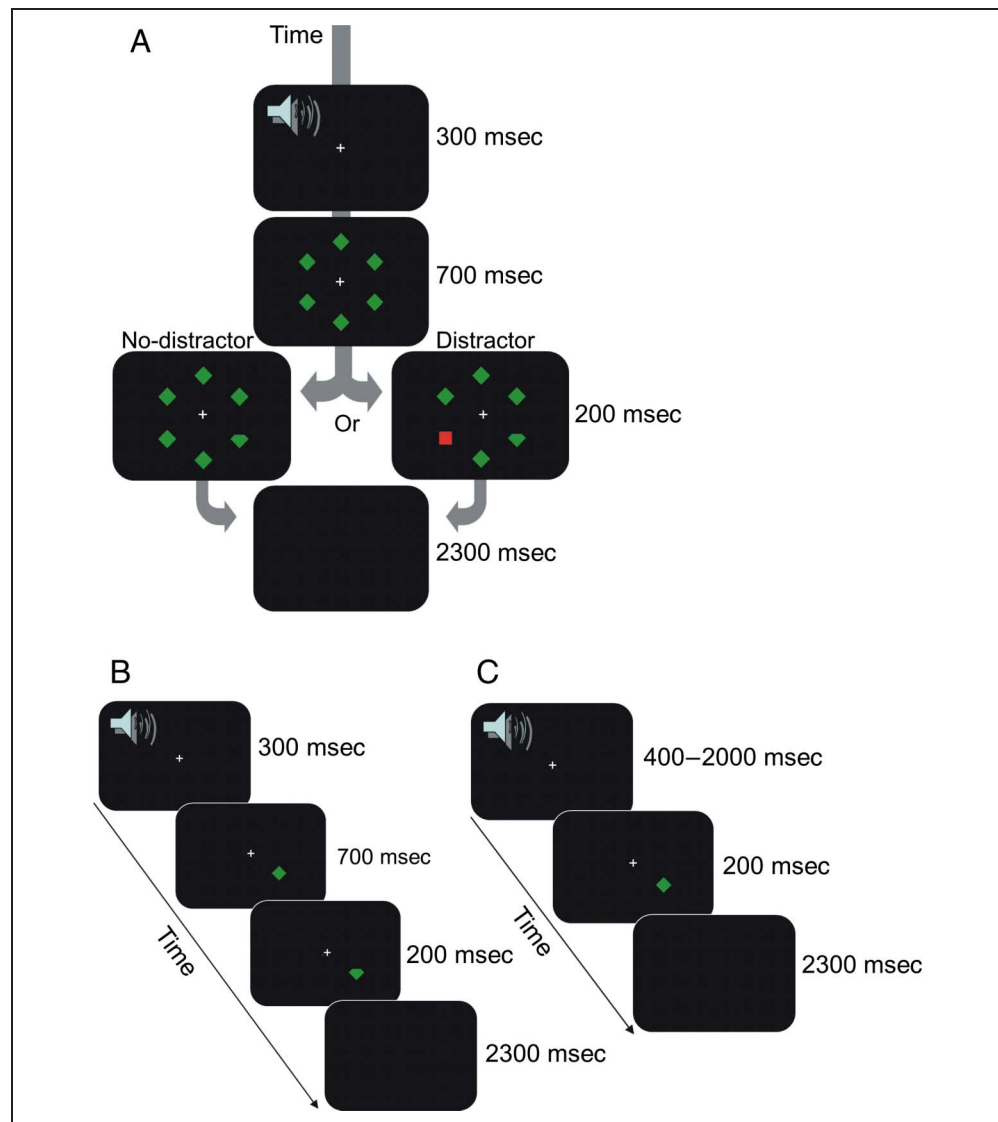
influence of past task relevance). Third, it should be noted that observers searched for the pentagon-shaped target but responded to its orientation in space. This is an example of so-called compound search task, which makes it possible to disentangle factors affecting the selection of the target within the stimulus array from those affecting response selection processes (Duncan, 1985). Importantly, when a compound search task is employed, the response requirements remain the same over the two conditions (no-distractor and distractor) to be compared, ensuring that any costs in terms of RT and error rate caused by the presence of the distractor can be safely attributed to perceptual-attentional interference and not to response conflict interference. Fourth, the target and distractor were simultaneously presented. This is important because when the two items are present simultaneously competition occurs strongly (Mathot, Hickey, & Theeuwes, 2010; Desimone & Duncan, 1995), in turn enabling one to measure relative control of bottom–up and top–down mechanisms of attention in trying to resolve this competition.

Procedure. In our AC task, on the whole, participants performed 360 randomly intermixed trials consisting of 240 no-distractor trials and 120 distractor trials. We included a low percentage of distractor trials in our AC task because it is known that the capture effect is stronger when the frequency of distractor trials is relatively low (Geyer, Muller, & Krummenacher, 2008).

To ensure an optimal level of attention throughout the whole experimental session while avoiding excessive fatigue, the total trials were presented in six blocks, each comprising 60 trials, separated by breaks, each one lasting no more than 3–4 min, at the participant's discretion. During stimulus presentation, participants were requested to maintain fixation at the center of the display, stressing that a steady fixation would reduce the RT and make the task easier. Both speed and accuracy were emphasized. In addition, participants were encouraged not to respond at random if they were unsure about the target orientation, which could reflect lack of attentional engagement onto the target item and insufficient perceptual analysis of the target shape.

Completion of the AC task as a whole took about 25 min (without breaks). Before the experimental session, participants practiced the task for at least two blocks, each of 60 trials, but practice continued, if necessary, until an accuracy of 70% or more was achieved.

Choice RT Task

Here we developed a version of the classical and validated choice RT task (Laming, 1968), adapted to the purposes of our study. A typical trial was similar to that described for the no-distractor trial of the AC task, except for only the presence in the display of a single diamond element (red or green, randomly) in one of the six eccentric positions occupied by the stimuli of the previous task. This element was abruptly replaced by a pentagon-shaped target (of the same color) with the base up or down (Figure 1B). Participants gave the response according to the instructions provided for the AC task.

Procedure. Overall, participants performed 72 trials in about 5 min. At the beginning of the experimental session, participants practiced the experimental task in one block of 36 trials. If an accuracy of 80% or more was achieved, the actual experiment was executed; otherwise, the practice block was repeated.

A typical trial of the choice RT task was characterized by a component of perceptual discrimination (which allowed identification of the target orientation), along with the resulting response selection stage (which key to press depending on the target orientation), followed by initiation of the motor response. From this point of view, a no-distractor trial of the AC task differed from the choice RT trial only for an additional component of perceptual analysis of the multi-item display and attentional selection, which supported extraction of the target element within an array of irrelevant stimuli in a top–down manner. Noteworthy, also bottom–up mechanisms contributed to target selection in this condition, owing to the fact that the target was defined by the abrupt shape change of one element in the array, which likely summoned attention to its location in a reflexive manner (Theeuwes, 2010; Egeth & Yantis, 1997). However, it is important to note that such transient event was present also in the choice RT task. Therefore, we argue that isolating the target selection subprocess in the no-distractor condition of the AC task mainly allowed us to measure the functioning of the EVA mechanisms (top–down control).

In an attempt to isolate the component process of attentional selection in a no-distractor trial of the AC task, we have adopted what we conceive as a conceptual version of the Donders subtraction approach (Donders, 1969; but see also Coltheart, 2011; Sternberg, 2011). The original approach is built upon the assumption that the incremental effect on RT, which is obtained by introducing a specific computational request into a task paradigm, is strictly additive in nature. For example, if an average RT of 300 msec is obtained in condition A and an average RT of 320 msec is obtained in condition B, and condition B differs from condition A solely because of a specific added computation, then the 20-msec difference in RT between the two conditions is thought to reflect the added computation. Although the strict principle of additivity that underlies this approach has been questioned on several grounds (Luce, 1986; Welford, 1980) and, as such, can hardly be maintained, a milder (conceptual) version of the same approach can instead provide valuable information concerning the nature and severity of a given cognitive deficit in a population of neurological patients. For example, the above subtraction

need not imply that the added computation takes (only) 20 msec to complete. This is, for example, because the added computation may partly overlap with other processes engaged by the given task. Nonetheless, it is still safe to assume that the 20-msec difference is a consequence and, thus, somehow reflects the added computation and can, therefore, be taken as an index (not as a direct measure) of that computation. Putting it simply, although it may be the case that the added computation takes longer than 20 msec to complete, still it is perfectly plausible to assume that the 20-msec difference is produced by and therefore reflects the added computation. A practical implementation of this method for our purposes is as follows. Let us assume that a given patient group displays no measurable deficit (e.g., no appreciable increase in RT) in condition A relative to a suitable control group, but it does display a deficit in condition B, which requires an additional computation. Under these circumstances, the approach allows one to infer that the deficit in the patient population is specifically due to an impairment concerning the added computation. This is what we had in mind by adopting a conceptual variant of the Donders method.

Our approach is comparable to more common approaches aimed at uncovering double dissociations in neuropsychology. Yet, the main difference is that in those approaches the ability to infer the specific role of a brain structure or circuit in a given function rests on the assessment of the deficit of two groups of patients in relation to two types of tasks, whereby one group will display a deficit in task A but not in task B and an opposite pattern will emerge in the other group. In our approach, instead, the ability to identify the impairments of specific computations in a single patient group (vs. a control group) relies on a comparative assessment of the deficit across a set of increasingly difficult tasks, which differ from one another for the incremental addition of a component process called into play to support task performance. With this approach, we compared performance of patients and controls to try and isolate the component process/es impaired in PD. In this vein, by comparing average RT between the no-distractor condition of the AC task and the choice RT task, we attempted to roughly estimate the contribution of the EVA mechanisms to the time needed to select the target within an array of irrelevant stimuli and therefore detect any deficit in EVA mechanisms (top–down control) in PD patients.

Simple RT Task

To assess whether our patients' performance in the AC task (and also in the choice RT task) was affected by possible deficits in motor response initiation, as one might expect considering the akinesia typical of PD, the overall experimental design also included a version of the classical simple RT task (Luce, 1986), adapted for the purposes of this study. In all trials, a diamond element (red or green) appeared on the monitor in one of the six eccentric positions occupied by the stimuli in the AC task (Figure 1C). Participants had to respond as fast as possible to the onset of the diamond, pressing the key "1."

Procedure. Overall, participants performed 60 trials, which were presented in two blocks, each consisting of 30 trials: In one block, the participant responded with the index finger, whereas in the other block, responses were provided with the middle finger. This task lasted about 5 min. At the beginning of the experimental session, participants practiced the task in one block of 30 trials. If an accuracy of 80% or more was achieved, the actual experiment was run; otherwise, the practice block was repeated. We did not include catch trials in our simple RT task, because preliminary evidence indicated that our version of the task did not lead to an appreciable fraction of anticipatory responses (responses emitted on the basis of rough timing information), probably because stimulus onset could occur within a broad range of time intervals after start of the trial.

This task enabled us to estimate the time required to initiate a simple motor response on the basis of very low level visual information (the simple detection of the stimulus onset). In this task, there were no components of perceptual discrimination and motor response selection, which were instead tapped by the choice RT task (likewise, there was no component of target selection within a multi-item display, which was instead tapped by the AC task). According to the logic discussed previously, the comparison of average RTs between the choice and simple RT tasks enabled us to roughly compute the time necessary to select the motor response (motor decision) on the basis of the discriminative visual analysis in the choice RT task. This component broadly reflects decision-making mechanisms. However, throughout the article, we will use the term "response selection" to designate this component. Therefore, the indexing of this component process in isolation allowed us to uncover whether our patients' performance was affected by possible deficits in response selection mechanisms.

General Experimental Procedure

Participants were tested in a quiet and dimly lit room, seated on a comfortable and adjustable armchair, with their head resting on a chinrest to hold the viewing centered on the monitor at a 57-cm constant distance. During the experimental session, each participant performed the three computerized tasks, which were presented in a counterbalanced order. As a whole, each evaluation session took about 1 hr.

Patients were evaluated in an off-treatment condition, 12 hr after withdrawal from antiparkinsonian drugs (medication-off condition [med-off]). In addition, the

surgically treated patients started the experimental evaluation after having the stimulation turned off for about 30 min (medication-off/stimulation-off condition [med-off/stim-off]). Therefore, in the med-off/stim-off condition, electrical stimulation was turned off as a whole for about 1 hr 30 min. Of course, these evaluation conditions entailed the reappearance of parkinsonian signs. Only patients who were able to tolerate these conditions and moreover could accept a mild level of discomfort were selected for participation. However, it should be noted that, in this condition, none of the patients showed an intensity of tremor, bradykinesia, and rigidity of the right hand that might compromise performance in the various tasks. It should also be considered that med-off and med-off/stim-off represent typical conditions for testing PD patients in both experimental and clinical contexts (Alberts et al., 2008; Funkiewiez et al., 2006; Schupbach et al., 2005; Moro, Esselink, Benabid, & Pollak, 2002).

To uncover possible changes in the patients' motor state during the experimental session, each session began and ended with the patients' global motor state evaluation scored by means of the Unified Parkinson Disease Rating Scale part III (Defer, Widner, Marie, Remy, & Levivier, 1999).

Data Handling

To pursue the objectives of this study, the main variables assessed were RT and error rate in performing the three computerized tasks. RT was the time in milliseconds between the presentation of the target display and the onset of the participants' response. Statistical analyses were performed on RTs from trials with correct responses. We excluded from further analysis trials on which the RT fell outside ±2.5 SDs from the mean value for each participant and trial type (Table 2). Error rate was computed as the percentage of omitted and wrong responses in the AC task and in the choice RT task and of omitted and anticipated responses (i.e., responses faster than 100 msec) in the simple RT task. To investigate and eliminate any potential speed–accuracy trade-off effect, we also calculated the inverse efficiency (IE) scores for the AC task. This was not necessary for the other tasks given the extremely low error rates in those tasks. IE scores were computed as mean RT divided by the proportion of correct trials for a given condition (no-distractor or distractor; Shore, Barnes, & Spence, 2006; Townsend & Ashby, 1983). Higher values correspond to worse performance. The AC effect was measured as the difference (Δ) between the distractor and no-distractor trials in RTs, error rates, and IE scores of the AC task.

The EVA component was isolated as the difference between the mean RTs in no-distractor trials of the AC task and in the choice RT task. Lower values of EVA index relatively more efficient mechanisms of target selection in a goal-directed manner, and therefore, they indicate relatively well-functioning top–down attention mecha-

Table 2. Percentage of Outlier Trials in Terms of RT for Each Group of Participants and for Each Computerized Task

	AC Task	Choice RT Task	Simple RT Task
Med-off	2.5	2.6	1.5
Med-off/stim-off	2.5	2.0	2.3
Controls	2.2	2.1	2.4

Med-off and med-off/stim-off = pharmacologically treated group and surgically treated group, respectively, both evaluated in off-treatment condition.

nisms. The response selection component was isolated as the difference between the mean RTs in the choice RT task and the simple RT task. Similar approaches were applied to error rates and IE scores.

Statistical Analysis

Collected data underwent statistical analyses using SPSS (version 12.0, SPSS, Inc., Chicago, IL). Normality of data distribution was checked with Shapiro–Wilk test, and the arcsine transformation was applied if normality was violated. As indicated below, data were evaluated by either paired or independent samples t tests, or repeated-measures ANOVAs. Post hoc analyses of significant effects were carried out by means of t tests, with Bonferroni's correction for multiple comparisons where necessary. Significant effects have been considered for $p \leq .05$.

RESULTS
Participants' Characteristics

We analyzed the demographic, epidemiological, and clinical variables listed in Table 1 to ascertain whether the two patient groups differed from each other for one or more of these variables and whether the patients, apart from the disease, differed from the controls. We did not find significant differences across the three groups (Table 1), except for the levodopa equivalent daily dose, which was half as much in the stimulated group compared with the one only treated pharmacologically [$t(22) = 3.73$, $p = .001$].

Furthermore, on average, we did not find significant differences in the patients' global motor state score (mean $\pm$ SE) between the beginning and end of the experimental session, respectively, 36.8 (±2.3) and 37.4 (±2.4) [$t(11) = -1.43$, $p = .179$] for the med-off group, and 42.0 (±2.6) and 42.6 (±2.6) [$t(11) = -1.85$, $p = .091$] for the med-off/stim-off group, as assessed by means of paired samples t tests.

Effectiveness of the Tasks

To assess the effectiveness of our main task in producing a reliable AC effect in healthy controls, we compared the

RT and error rate obtained in the distractor trials with those from the no-distractor trials by means of paired samples t tests. Analysis of RTs revealed a reliable effect of the type of trial, because of considerably longer RTs (mean $\pm$ SE) in the distractor condition (635.2 $\pm$ 18.6 msec) compared with the no-distractor condition (538.1 $\pm$ 16.6 msec) [$t(11) = -23.63, p < .001$]. Also the error rate was significantly greater in the distractor (4.0 $\pm$ 0.4%) compared with the no-distractor condition (1.0 $\pm$ 0.2%) [$t(11) = -7.43, p < .001$]. Thus, the results from healthy controls showed a robust AC effect in terms of both RT and error rate.

A first qualitative inspection of the mean RTs obtained in our three computerized tasks indicated that the more complex was the task, the longer was the RT. In the control group, we substantiated the increasing difficulty of the three tasks by analyzing the RTs obtained in each of them by means of a repeated-measures ANOVA with the Type of task as a within-subject factor. We found a significant effect of the Type of task [$F(2, 22) = 155.0, p < .001$], because of longer RTs in the no-distractor condition of the AC task compared with the choice RT task (439.6 $\pm$ 15.8 msec; $p < .001$) and in the latter task relative to the simple RT task (300.7 $\pm$ 8.9 msec; $p < .001$).

Effects of the Disease on the Mechanisms of Visual Attention

To pursue the principal objective of this study, that is, to investigate to what extent the BG play a distinct role in top–down and bottom–up control of visual selective attention, we compared the performance on the three tasks of both groups of parkinsonian patients evaluated in off-condition with that of the healthy controls.

At the qualitative level, PD patients displayed impaired performance in the AC task with respect to healthy controls, with slower RTs and higher error rates (comprising both omitted and wrong responses; see below; Figure 2A and B). In detail, analysis of RTs in the AC task revealed a significant effect of the Type of trial [$F(1, 33) = 479.3, p < .001$], because of longer RTs in the distractor condition (769.0 $\pm$ 18.7 msec) compared with the no-distractor condition (664.2 $\pm$ 16.3 msec). The factor Group was also significant [$F(2, 33) = 16.0, p < .001$], because of longer RTs in the med-off group (738.4 $\pm$ 30.2 msec) compared with healthy controls (586.6 $\pm$ 30.2 msec, $p = .003$) and in the med-off/stim-off group (824.8 $\pm$ 30.2 msec) compared with healthy controls ($p < .001$). Instead, there was no reliable difference between the med-off and med-off/stim-off groups ($p = .153$). Planned post hoc comparisons showed that, in the no-distractor condition and in the distractor condition likewise, both groups of patients were slower than healthy controls, whereas there was no significant difference between the two patient groups (Table 3). The interaction Type of trial $\times$ Group was not significant ($p = .127$), prima facie suggest-

ing that the BG are not principally involved in the mechanisms underlying the AC (but see below).

A different pattern of results emerged from the analysis of total error rates in the AC task (Figure 2B). Raw percentage of errors is reported in Table 4. Because error rates were not normally distributed (Shapiro–Wilk, $p < .050$), data were submitted to the arcsine transformation before entering into the analysis. Here we obtained a significant effect of the Type of trial [$F(1, 33) = 51.26, p < .001$] because of a higher proportion of errors in the distractor condition (arcsine-transformed values, mean $\pm$ SE: 0.369 $\pm$ 0.04) than in the no-distractor condition (0.084 $\pm$ 0.008). The factor Group was also significant [$F(2, 33) = 11.39, p < .001$)] because of higher error rates in the med-off group (0.302 $\pm$ 0.036) compared with healthy controls (0.085 $\pm$ 0.036, $p = .001$) and similarly in the med-off/stim-off group (0.293 $\pm$ 0.036) compared with healthy controls ($p = .001$). Instead, no significant difference in error rates ($p = 1.0$) was found between the two groups of patients. Planned post hoc comparisons showed that, in the no-distractor condition and in the distractor condition likewise, both groups of PD patients committed more errors than healthy controls, whereas there was no significant difference between the two groups of patients (Table 3). The interaction Type of trial $\times$ Group was also highly significant [$F(2, 33) = 5.41, p = .009$], and post hoc analyses revealed that the AC effect was larger in the med-off group (Δerror rate arcsine-transformed values: 0.392 $\pm$ 0.092) and in the med-off/stim-off group (0.362 $\pm$ 0.075) than in healthy controls (0.101 $\pm$ 0.014, respectively, $p = .016$ and $p = .034$), revealing enhanced AC in both groups of patients. The latter finding suggests that a dysfunction of the BG leads to a deficit in counteracting the interference caused by a distracting stimulus. Otherwise, no significant difference in Δerror rate was found between the two groups of parikinsonian patients (Table 3).

To better characterize the pattern of results in terms of error rates, we ran separate analyses for response omissions and wrong responses (arcsine transformed). Interestingly, we found that the main difference between patients and controls was not in the wrong responses, but in the omissions. More precisely, analysis of omitted responses revealed that the Type of trial was significant [$F(1, 33) = 25.41, p < .001$], because of a higher proportion of omissions committed by the participants in the distractor condition (arcsine-transformed values, mean $\pm$ SE: 0.33 $\pm$ 0.062) than in the no-distractor condition (0.04 $\pm$ 0.007). The factor Group was also significant [$F(2, 33) = 6.53, p = .004$)] because of a higher rate of omissions in the med-off group (0.26 $\pm$ 0.06) compared with healthy controls (0.02 $\pm$ 0.06, $p = .015$) and similarly in the med-off/stim-off group (0.28 $\pm$ 0.06) compared with healthy controls ($p = .008$). Instead, no significant difference in error rates ($p = 1.0$) was found between the two groups of patients. The interaction Type of trial $\times$ Group was also significant [$F(2, 33) = 5.2, p = .011$], and post hoc analyses revealed that the AC effect was larger in the med-off group (Δerror

Figure 2. Comparison across the two groups of parkinsonian patients evaluated in off-condition (in med-off for the pharmacologically treated group and in med-off/stim-off for the stimulation treated group) and the healthy controls in terms of RT (in A), total error rate (ER; including omitted and wrong responses; in B), and IE (in C), separately for the no-distractor and distractor conditions of the AC task. Δ = AC in terms of ΔRT (in A), ΔER (in B), and ΔIE (in C). Statistical comparison was performed by separate mixed design ANOVAs on RTs, ERs, and IEs of the AC task, with the Type of trial (no-distractor vs. distractor trials) as within-subject factor and Group as between-subject factor.
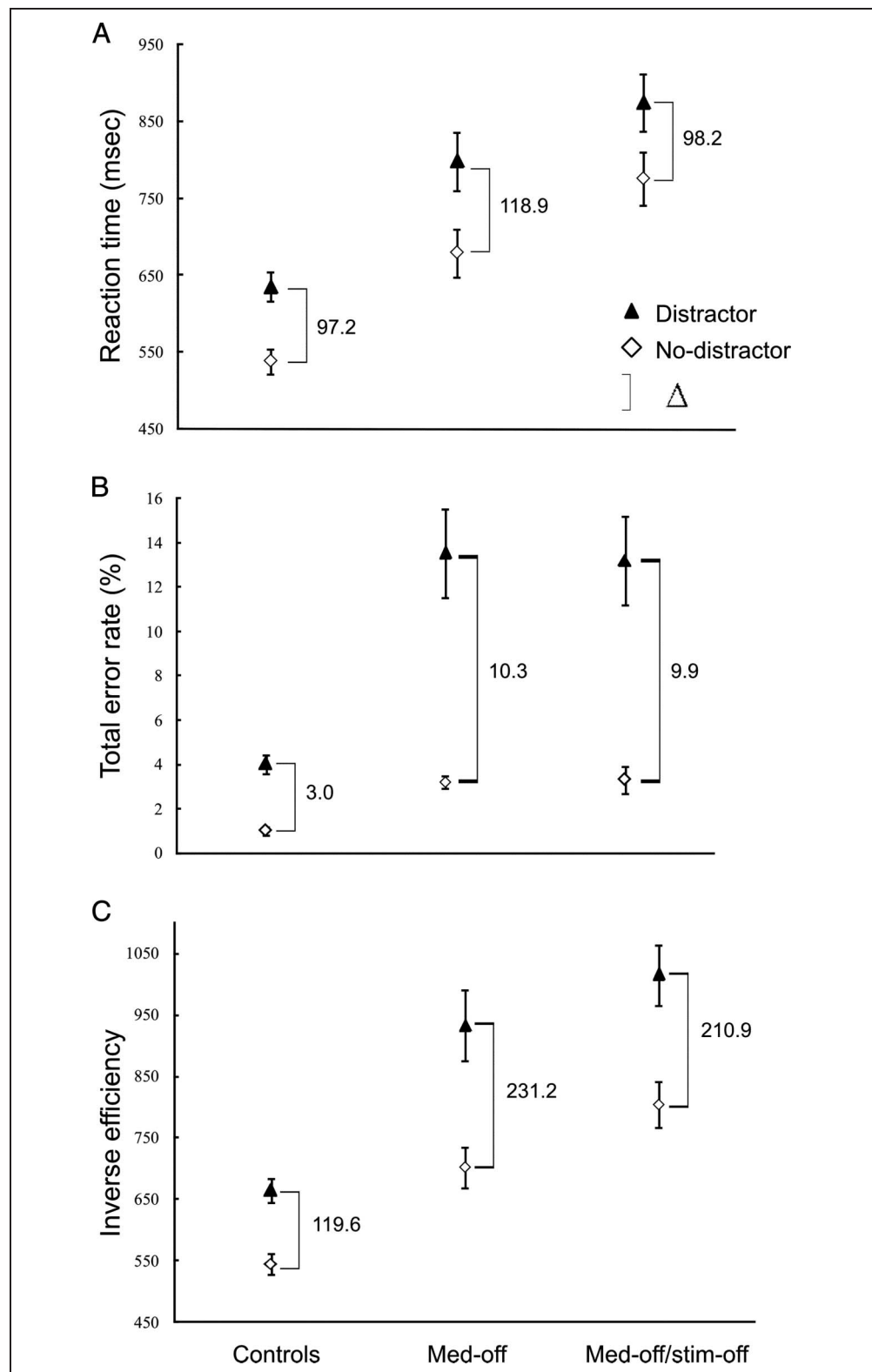
rate arcsine-transformed values: 0.41 ± 0.11) and in the med-off/stim-off group (0.45 ± 0.14) than in healthy controls (0.03 ± 0.01, $p < .038$ for both comparisons). Conversely, the analysis of wrong responses revealed only a significant effect of Type of trial [$F(1, 33) = 28.25, p < .001$] because of an overall higher proportion of wrong responses committed by the participants in the distractor condition (0.36 ± 0.05) than in the no-distractor condition (0.13 ± 0.02). The factor Group and the interaction Type of trial × Group were not significant ($p > .238$). Raw percentages of errors are reported in Table 5. These results concerning response errors indicate that the larger AC effect

Table 3. Post hoc Analyses across the Three Groups of Participants in the AC Task

	Med-off vs. Controls	Med-off/Stim-off vs. Controls	Med-off vs. Med-off/Stim-off
RT ND-trials	$p = .004$	$p < .001$	$p = .064$
RT D-trials	$p = .004$	$p < .001$	*ns*
ΔRT	*ns*	*ns*	*ns*
ER ND-trials	$p = .002$	$p = .001$	*ns*
ER D-trials	$p = .002$	$p = .005$	*ns*
ΔER	$p = .016$	$p = .034$	*ns*
IE scores ND-trials	$p = .002$	$p < .001$	$p = .070$
IE scores D-trials	$p = .001$	$p < .001$	*ns*
ΔIE	$p = .010$	$p = .044$	*ns*

Med-off and med-off/stim-off = pharmacologically treated group and surgically treated group, both evaluated in off-treatment condition; ER = error rate; ND-trials = no-distractor trials; D-trials = distractor trials; ΔRT, ΔER, ΔIE = AC in terms of ΔRT, ΔER and ΔIE.

in the patients relative to the controls is mainly reflecting omitted responses, likely because of a failure by the patients to properly engage attention onto the target stimulus in the presence of the salient distractor.

The above pattern of results reveals what might be seen as a discrepancy between the two measures of AC, that is, ΔRT and Δerror rate, likely reflecting a form of speed–accuracy trade-off. To clarify this discrepancy, we calculated the IE scores and compared these scores across conditions and groups (Figure 2C). First, this analysis revealed a significant effect of Group [$F(2, 33) = 18.6$, $p < .001$] because of higher IEs in the med-off group (817.2 ± 36.3 msec) than in healthy controls (603.6 ± 36.3 msec, $p = .001$) and in the med-off/stim-off group (909.1 ± 36.3 msec), again compared with the healthy controls ($p < .001$), confirming that PD impaired performance in the AC task. Instead, there was no reliable difference between the med-off and med-off/stim-off groups

($p = .248$). Planned post hoc comparisons showed that, in the no-distractor condition and in the distractor condition likewise, both groups of PD patients were characterized by worse performance relative to healthy controls, whereas there was no significant difference between the two groups of patients (Table 3). A significant effect of the Type of trial was also observed [$F(1, 33) = 167.6$, $p < .001$] because of overall massively higher IE scores in the distractor condition (870.3 ± 26 msec) than in the no-distractor condition (683.0 ± 17.5 msec). Most importantly, the interaction Type of trial × Group was highly significant [$F(2, 33) = 5.6$, $p = .008$]. In particular, post hoc analyses revealed that the AC effect was larger in both groups of patients compared with healthy controls, whereas no significant difference in ΔIE was found between the two groups of PD patients. These results indicate a remarkable behavioral consistency between the two groups of parkinsonian patients in terms of the AC effect, which appeared to be considerably enhanced by the pathological condition.

Table 4. Percentage of Errors (Raw Values, Mean ± SE) in the Three Computerized Tasks for the Three Groups of Participants

	Med-off	Med-off/Stim-off	Controls
AC task–distractor	13.5 ± 2%	13.2 ± 2%	4.0 ± 0.4%
AC task–no distractor	3.2 ± 0.3%	3.3 ± 0.6%	1.0 ± 0.2%
Choice RT task	0.8 ± 0.2%	0.5 ± 0.3%	0.4 ± 0.2%
Simple RT task	1.4 ± 0.6%	2.6 ± 0.9%	0.8 ± 0.2%

Med-off and med-off/stim-off = pharmacologically treated group and surgically treated group, respectively, both evaluated in off-treatment condition. The statistical comparisons of the error rates obtained in the AC task were performed by repeated-measures ANOVAs, with Type of trial as within-subject factor and Group as between-subject factor. Comparisons of the error rates obtained in the choice RT task and the simple RT task were performed by one-way ANOVAs, with Group as between-subject factor. Being error rates not normally distributed (Shapiro–Wilk test, $p < .050$), raw percentage of errors were arcsine-transformed before entering into the analysis.

Table 5. Percentage of Errors (Raw Values, Mean ± SE) in the AC Task, after Separating Response Omissions from Wrong Responses

	Med-off	Med-off/Stim-off	Controls
Response omissions			
Distractor	8.4 ± 1.9%	8.6 ± 2.1%	0.6 ± 0.2%
No distractor	1.3 ± 0.3%	1.2 ± 0.3%	0.04 ± 0.04%
Wrong responses			
Distractor	5.1 ± 0.8%	4.7 ± 1.2%	3.4 ± 0.5%
No distractor	1.9 ± 0.3%	2.1 ± 0.5%	1.0 ± 0.2%

Med-off and med-off/stim-off = pharmacologically treated group and surgically treated group, respectively, both evaluated in off-treatment condition.

This observation attests to an involvement of the BG in the mechanisms underlying AC and lends itself to two diverging interpretations. On the one hand, a dysfunction of the BG may determine an abnormal potentiation of the mechanisms of bottom–up attention, leading to exaggerated sensitivity to the salient singleton distractor. On the other hand, BG dysfunction may result in a weakening of top–down mechanisms, thus releasing the exogenous effect from any top–down antagonistic control, in line with the notion that top–down and bottom–up attentional control processes compete with one another to determine the overall pattern of attentional deployment at any point in time (Einhauser, Rutishauser, & Koch, 2008). In what follows, we will try to arbitrate between these diverging possibilities.

The analysis of RTs obtained in the choice RT task revealed a significant effect of the factor Group [$F(2, 33)$ = 12.0, $p < .001$]. In detail, we found longer RTs for the surgically treated patients (613.9 ± 30.8 msec) compared with healthy controls (439.6 ± 15.8 msec; $p < .001$), and we obtained a strong trend ($p = .059$) for a difference by comparing the pharmacologically treated parkinsonian patients (526.8 ± 26.4 msec) with healthy controls. We also found a trend for a reliable difference by directly comparing the two groups of patients with each other ($p = .059$).

Also the analysis of RTs in the simple RT task indicated a significant effect of the factor Group [$F(2, 33)$ = 10.4, $p < .001$] because of faster RTs in healthy controls (300.7 ± 8.9 msec) than in both groups of parkinsonian patients (med-off: 382.1 ± 18.3 msec, $p < .013$; med-off/stim-off: 421.2 ± 26.0 msec, $p < .001$), as one might expect given the typical akinesia of PD patients in off-phase. No significant differences ($p = .468$) emerged

by directly comparing the two groups of patients, consistent with a highly similar motor impairment in the two groups of patients (Figure 3).

Arcsine transformation was applied also to the error rates in the choice and simple RT tasks, because they were not normally distributed (Shapiro–Wilk, $p < .050$). The error rates were not significantly different across the three groups of participants in the choice RT task ($p = .420$) as well as in the simple RT task ($p = .140$). The raw percentage of errors is reported in Table 4. The error rates were generally lower in these two tasks than in the AC task, probably because the latter task was more demanding overall. Accordingly, when we consider the two simpler tasks, it is not surprising that differences in performance between parkinsonian patients and healthy controls emerged mainly in the form of longer RTs rather than higher error rates.

One might ask whether the larger increase of choice RTs observed for the PD patients was due only to a mere motor impairment or instead reflected a genuine impairment of the mechanisms of motor response selection. Analysis of the response selection component revealed that the factor group was significant [$F(2, 33)$ = 3.8, $p = .032$]. This effect was due to larger ΔRTs in the med-off/stim-off group (192.7 ± 16.8 msec) compared with healthy controls (138.9 ± 15.6 msec, $p = .050$; Figure 3). Conversely, in the med-off group, we found only a negligible increment in the response selection component (144.7 ± 12.5 msec) compared with healthy controls ($p = 1.0$). Finally, there was a slight tendency toward a significant difference between the med-off and med-off/stim-off groups ($p = .094$).

Of principal interest, the analysis of the EVA component revealed that the factor Group was significant [$F(2,$

Figure 3. Comparison across the two groups of parkinsonian patients evaluated in off-condition (in med-off for the pharmacologically treated group and in med-off/stim-off for the stimulation treated group) and the healthy controls in terms of mean times for movement initiation (simple RT, SRT), motor response selection (RS), and target selection (EVA). Note that, conceptually (not numerically) speaking, SRT + RS = choice RT, whereas SRT + RS + EVA = RT in the no-distractor condition of the AC task. The statistical comparisons of the RTs obtained in the choice RT task and the simple RT task, as well as the derived performance indices (EVA and RS), were performed by one-way ANOVAs, with Group as between-subject factor.
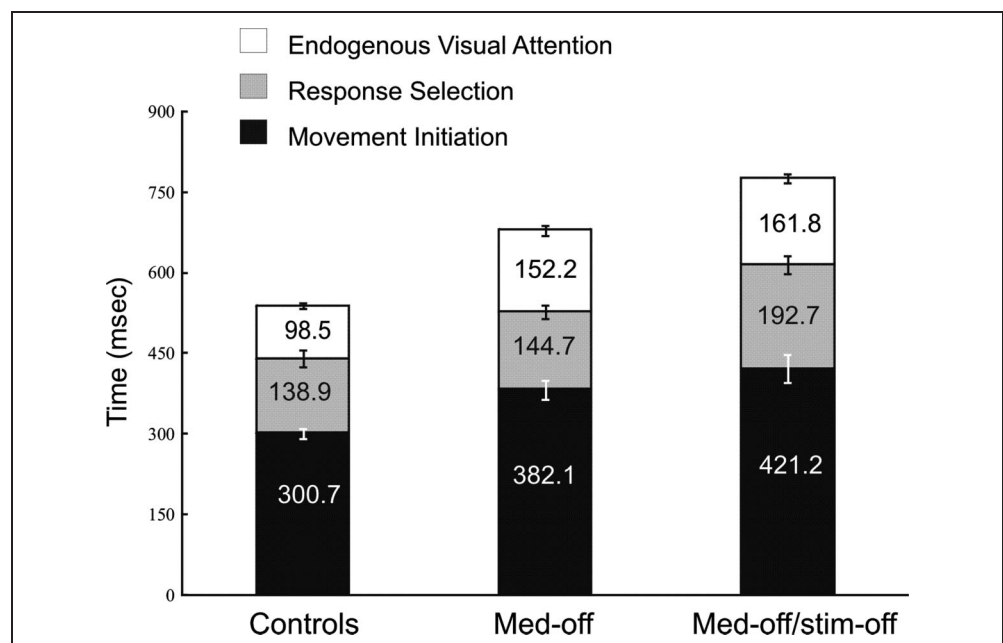
33) = 17.5, $p < .001$]. This effect was due to larger ΔRTs in the med-off group (152.2 ± 9.4 msec) compared with healthy controls (98.5 ± 5.7 msec, $p < .001$) and in the med-off/stim-off group (161.8 ± 8.8 msec) compared with healthy controls ($p < .001$), whereas no difference was found between the two parkinsonian groups ($p = 1.0$; Figure 3).

Therefore, the combined analysis of the results from all three tasks showed that, in both the med-off and med-off/stim-off groups, there was an impairment of the mechanisms underlying target selection and motor response initiation, whereas only in the med-off/stim-off group could we also detect a reliable deficit of the mechanisms underlying motor response selection. On the basis of these results and, in particular, the observation that target selection (EVA) was impaired in the patients, one may be led to hypothesize that the increased AC effect in PD, as we found, could be the indirect consequence of weakened top–down control of attention (see above).

DISCUSSION

We carried out the current study with the principal objective of elucidating the role of the BG in endogenous (top–down) and exogenous (bottom–up) mechanisms of visual attention, and we pursued this objective by characterizing deficits of attention in PD.

Our results indicated that parkinsonian patients showed increased AC/distractibility compared with healthy controls while performing an AC task, prima facie suggesting abnormally enhanced bottom–up attention mechanisms in the patients. However, the patients also showed weakened top–down mechanisms of attention, as reflected in a greater EVA index relative to the controls. These results are fully compatible with the view that a dysfunction of cortico-BG loops, such as occurs in PD, may result primarily in an impairment of top–down mechanisms, which could well account, albeit indirectly, for the enhancement of AC in the patients, owing to reduced or abolished antagonistic influence of top–down control on bottom–up attention.

More importantly, based on our attempt to isolate the different component processes underlying performance in the AC task, we were able to draw strong inferences about the true nature of the attention deficits in PD and therefore about the involvement of the cortico-BG loops in the mechanisms of visual attention. This was the case because our approach enabled us to separate any deficit of bottom–up and top–down attention from the accompanying deficits of other component processes, including movement initiation and response selection.

Effectiveness of the Tasks

Our main task proved to be an effective means to assess AC. In fact, in our AC task, presence of the distractor determined an RT cost of about 100 msec and a cost in terms of error rate of approximately 3% in the group of healthy controls. These results are in line with what was found previously with similar irrelevant singleton distractor paradigms, as developed by Theeuwes (1991a), in which the AC effect in terms of ΔRT amounted to 120–150 msec.

An important feature of the AC task used in this study is that attentional deployments to discrete locations within the stimulus array occurred without saccades (covert attention; Thompson & Bichot, 2005; Kinchla, 1992). Several findings have indicated that covert (or implicit) visuospatial attention and eye movements are implemented via at least partly shared circuits and neural signals (Thompson, Biscoe, & Sato, 2005; Moore, Armstrong, & Fallah, 2003; Corbetta & Shulman, 2002; Beauchamp, Petit, Ellmore, Ingeholm, & Haxby, 2001; Moore & Fallah, 2001; Rizzolatti, Riggio, Dascola, & Umilta, 1987), and this close relationship might afford the possibility to study the relative contribution of bottom–up and top–down control of visual selection by means of oculomotor variants of the AC task, such as the so-called "oculomotor capture" paradigm. In this paradigm, participants are asked to make a saccadic eye movement to the sought target while ignoring a salient singleton distractor, if present. The salient object, when present, not only captures attention but also sometimes triggers an exogenous saccade to its location (Theeuwes & Godijn, 2002; Theeuwes, Kramer, Hahn, Irwin, & Zelinsky, 1999; Theeuwes & Burger, 1998). In particular, an oculomotor capture task has been used before to assess the abnormal susceptibility to distractors in PD (Deijen et al., 2006). However, it remains to be established whether evidence provided by that prior study can be interpreted in terms of (covert) attentional processing per se or instead in terms of overt motor behavior, especially because PD patients are known to have a fundamental deficit in the motor domain, including in the control of saccades (Chan, Armstrong, Pari, Riopelle, & Munoz, 2005; Rascol et al., 1989). This is the principal reason why for our study we devised an AC task in which eye movements played no role.

One way to conceive the cognitive processes underlying visual selection in our AC task might be the serial deployment of attention to one or the other of the competing items presented (the target and the salient distractor). We can assume that at an early preattentive stage, when attention is spread across the whole display, the first sweep of information through the brain is predominantly characterized by stimulus-driven processing and is not penetrable by top–down control, as strongly argued by Theeuwes (2010). Preattentive analysis allows only to highlight the locations in salience maps where local visual features differ from the surrounding context (along perceptual dimensions such as color, shape, and orientation; Koch & Ullman, 1985), but it does not support detailed analysis of those features or any resulting response decision. Therefore, attention will be first and more potently captured by the most salient object in the display, as a result of bottom–up mechanisms. Only

after attention has been summoned to the location of the salient element, its identity becomes available, and top–down knowledge (such as the target defining features) determines whether attention will stay at that particular location (engagement) or should be quickly disengaged from that location. In other words, if the automatically selected singleton is the target the observer is looking for, then its orientation can be immediately determined and a response can be produced. If it is not, then top–down processing commands a quick disengagement of attention from the corresponding location, and attention will be shifted to the next most salient item in the array or the item, which is otherwise task-relevant owing to its feature composition (e.g., the target; Theeuwes & Godijn, 2004). It follows that the likelihood and size of the capture effect depends on a number of factors, including the relative salience of the singleton distractor with respect to that of the target and the other items, but also on the speed with which disengagement from the distractor can occur.

Another equally plausible scenario would be one wherein all items in the stimulus array compete with one another throughout stimulus processing, and the attentional priority conferred to each individual item depends on the combined influence of bottom–up factors (relative salience of each item) and top–down control (a match between the given item and the target template; Theeuwes, 2010; Burnham, 2007; Wolfe, Butcher, Lee, & Hyle, 2003; Wolfe, 1994; Folk, Remington, & Johnston, 1992; Yantis & Jonides, 1990). Even here the singleton distractor may have the highest attentional priority during early phases of processing after onset of the array, with the resulting capture effect, whereas the priority of the target item will increase with the passage of time because of progressively higher influence of top–down control (Mazza, Dallabona, Chelazzi, & Turatto, 2011; Theeuwes, 2010; Hickey, McDonald, & Theeuwes, 2006; Hochstein & Ahissar, 2002; Lamme & Roelfsema, 2000). It is within these conceptual frameworks that one should interpret the abnormal pattern of attentional performance reported in this study.

As previously pointed out, performance at our AC task not only reflected the competition between top–down and bottom–up mechanisms of visual attention but also other processes concerning response selection, as well as motor response initiation. This is especially relevant when considering the longer RT of the parkinsonian patients relative to the healthy controls in the no-distractor condition of the main task. The latter finding is compatible with a deficit affecting one or more of the processes mediating behavioral output. As such, our AC task did not enable us to ascertain to what extent slower responses in the no-distractor condition of the AC task depended on a weakening of selection (EVA) mechanisms, or an impairment of response selection mechanisms, or simply a deficit in motor response initiation, or any combination of them. From a methodological point of view the main novelty and fundamental contribution of our study consists in having attempted to isolate these three components by suitably complementing the AC task with two incrementally simpler paradigms.

Effects of the Disease and of Surgery for DBS Lead Implantation

In this study, PD patients showed increased AC in terms of Δerror rate, without any significant parallel increase of ΔRT, probably because of some sort of speed–accuracy trade-off effect (depending on the specific task paradigm, instructions, and context, participants may privilege speed of responding as opposed to accuracy). This discrepancy was overcome by calculating the IE scores, which unequivocally revealed that the pathological condition affects the mechanisms underlying AC, in turn ruling out an additional influence of DBS lead implantation on these mechanisms (see below).

The enhancement of AC observed in our patients is consistent with the increased distractibility manifested by PD patients in the presence of irrelevant but salient stimuli, as shown in prior studies (Uc et al., 2007; Henik et al., 1993; Sharpe, 1990; Wright et al., 1990; Pillon et al., 1989). In a controlled study carried out on medication-withdrawn PD patients performing a visuospatial memory task, behavioral and electroencephalographic measures indicated that patients were severely impaired at filtering out distractors (Lee et al., 2010). Moreover, Maddox, Filoteo, Delis, and Salmon (1996) found that a large proportion of nondemented parkinsonian patients, as compared with a group of healthy participants, was impaired at making perceptual judgments about a simple visual stimulus when this was presented together with competing, irrelevant visual information. However, this study is the first to try and go beyond the mere report of increased distractibility in PD, in that we could demonstrate that such effect likely reflects relative weakening of top–down attention mechanisms, thus leading to a better understanding of the role of cortico-BG loops in visual attention.

At first glance, the higher total error rates for the patients compared with the controls in both the no-distractor and distractor conditions of the AC task, with no significant differences in error rates across groups for the other two tasks, suggest that PD may affect top–down as well as bottom–up mechanisms of visual attention. In particular, the higher total error rate observed in PD in the no-distractor condition is compatible with a deficit in display analysis and target selection. Our take of the Donders approach highlighted that the component process underlying display analysis and target selection was impaired (prolonged) in both groups of patients, suggesting a weakening of top–down (EVA) mechanisms in PD relative to controls, which in turn could contribute to slowing down the overall response of the patients in the AC task. It is instead less likely that the deficit in display analysis and target selection stems from weakened bottom–up mechanisms,

aiding target selection on the basis of its salience, because we have already seen that these mechanisms, if any, are potentiated in the patients, as reflected in the enhanced AC effect. Importantly, the EVA deficit appears to be due to the disease and not to any consequence of DBS lead implantation, because there was no significant difference in the EVA component between the two groups of patients (see below).

On the other hand, the higher error rate committed by the patients relative to the controls in the distractor condition suggests a more potent summoning of attention toward the distractor, that is, an increased AC in terms of Δerror rate because of the pathological condition. As already alluded to, this could be because of an enhancement of bottom–up mechanisms of attention in PD, with the resulting increased effective salience of the distractor compared with the target. Otherwise, the increased capture effect in the patients could be mainly related to a deficit of top–down attention mechanisms, either because a weakening of EVA mechanisms determines a slower and less efficient disengagement of attention from the salient distractor or because bottom–up effects are less effectively antagonized and mitigated immediately after display onset if the growing influence of top–down mechanisms is temporally delayed or weaker altogether (Hickey et al., 2006). Both these accounts, together with the short duration of the target display in our AC task, likely explain why in our patients the AC effects mainly took the form of omitted responses. Interestingly, in complete agreement with our claim, Cools et al. (2009) maintained that in PD patients there was a failure of top–down mechanisms of attention, with a consequent disproportionate enhancement of bottom–up mechanisms.

Conversely, in another controlled experiment carried out in PD patients performing an oculomotor capture task (Deijen et al., 2006), untreated parkinsonian patients at an early stage of the disease (patients mean disease duration was 2.3 ± 1.9 years) presented an especially strong "capture effect," perhaps reflecting enhanced bottom–up attention in the patients, given that in the no-distractor condition the performance of the patients was similar to that of the controls, suggesting that top–down mechanisms of attention were spared. One possible explanation for the divergent findings between our study and that of Deijen et al. (2006) could be related to the different stage of the disease of the patients enrolled in the two studies. Namely, early stages of the disease might be mainly characterized by an increased susceptibility to distractors (Deijen et al., 2006), perhaps reflecting genuinely enhanced bottom–up mechanisms of attention, whereas more advanced stages of the disease might be dominated by an impairment of top–down mechanisms, as shown in this study. An alternative explanation for the divergent findings is simply that the two versions of the task—one measuring oculomotor behavior (Deijen et al., 2006) and the present one tapping covert attention mechanisms—might be differently effective

tools to uncover deficits of bottom–up versus top–down attention. Yet as a further alternative, one may conjecture that indeed any variation in the size of the capture effect is in fact a more sensitive index of altered top–down control, compared with the direct measure of search performance in the no-distractor condition.

Manifestations of enhanced distractibility in PD, similar to those observed in this study, could reflect impairments in the build-up and maintenance of inhibition of the irrelevant stimuli over time during task performance (Filoteo et al., 1997). A deficit of inhibitory mechanisms is compatible with the notion that PD leads to weakened top–down attention, given that the ability to suppress (potential) distraction is at the core of such form of control (Marini, Chelazzi, & Maravita, 2013). The idea that PD leads to a deficit of the specific mechanisms responsible for the inhibition of irrelevant stimuli has been also supported by studies on negative priming (Houghton & Tipper, 1994), which is held to directly reflect the intervention of inhibitory mechanisms of attention. Interestingly, several studies have revealed that parkinsonian patients show diminished negative priming, if any, suggesting that attention-related inhibitory mechanisms are severely impaired in PD patients (Filoteo, Rilling, & Strayer, 2002; Downes, Sharp, & Sagar, 1991; see also Grande et al., 2006).

Overall our results suggest that a dysfunction of the cortico-BG loops, such as occurs in PD, may have a negative impact mainly on the mechanisms of top–down attentional control, thus releasing stimulus-driven, bottom–up control mechanisms. In this regard, there is evidence for the direct involvement of the BG in the top–down guidance of visual attention. For instance, dopamine depletion in the caudate nucleus and the resulting consequences on circuits critical for top–down attentional control are thought to be one of the main causes of attentional sequelae in PD (Sawamoto et al., 2008; Owen, 2004). This view is further supported by data showing that working memory and attention deficits correlate with a specific decrease in dopaminergic innervation at the level of the caudate nucleus and not at the level of the putamen (Weder et al., 1999). Moreover, dopamine depletion in the caudate nucleus tends to be uneven, with the greatest loss in the anterodorsal extent of the head of the nucleus (Kish, Shannak, & Hornykiewicz, 1988), a subregion which receives massive projections from the dorsolateral pFC and posterior parietal cortex (Baizer, Desimone, & Ungerleider, 1993; Yeterian & Pandya, 1993), that is, from cortical regions that, as we have seen, are heavily implicated in the top–down control of attention.

In their work, Grande et al. (2006) postulated that the selective impairment of endogenously evoked inhibitory attentional mechanisms observed in PD patients might be related to a dysfunction of the globus pallidum internum because of dopamine depletion. Altered activity of this nucleus determined decreased activation of the intralaminar nuclei of the thalamus, specifically the centromedian parafascicular nucleus, which, by virtue of its

reciprocal connections with the frontal lobe, is in a position to play a critical role in selective attention (Van Der Werf et al., 1999; Mennemeier, Fennell, Valenstein, & Heilman, 1992). Therefore, it appears that the globus pallidum internum is a core structure within the neuronal network supporting top–down mechanisms of visual attention. This hypothesis is consistent with a recent fMRI study carried out on healthy participants, which showed greater activation in the left middle frontal gyri and the left BG (especially the globus pallidum) when participants attempted to disregard distracting stimuli (McNab & Klingberg, 2008).

Given the interconnections linking the BG with the dorsal frontoparietal system, responsible for top–down control of attention, and with cortical areas specifically involved in overcoming AC, one could expect that the disruption of the executive frontostriatal loop, following BG damage, may determine a dysfunction of these cortical areas. In turn, this should lead, on the one hand, to a deficit in goal-directed deployment of attention to the relevant target and, on the other, to diminished resistance to distraction, resulting in enhanced capture. For instance, PD patients presenting an impaired capability to suppress irrelevant stimuli showed a dysfunction of the dorsolateral pFC, especially at the level of the left inferior frontal gyrus, which was related to the disruption of the BG outflow (Bocquillon et al., 2012). Other cortical areas involved in attentional control and whose activity is modulated by the BG are the superior parietal lobule (which is part of the dorsal attention-control system) and the TPJ (which is part of the ventral system). In particular, the interactions between these two cortical areas seem to play a critical role in overcoming AC, as also supported by the analysis of patients with damage to one or the other of these distinct anatomical sites (Shomstein et al., 2010). In fact, patients with lesions encompassing the superior parietal lobule but a spared TPJ, in addition to the expected difficulties with goal-directed attentional orienting, also showed "hypercapture," or an exaggerated distraction effect by salient items, which should also be expected if the ventral system is no longer counteracted by a well-functioning dorsal attention-control system (Bisley et al., 2011; Talsma et al., 2009; Serences et al., 2005; Silver, Ress, & Heeger, 2005; Corbetta & Shulman, 2002).

Findings from an fMRI study with healthy participants performing a typical AC task (de Fockert et al., 2004) have highlighted a special role of the left lateral precentral gyrus (BA6; anterior, inferior, and lateral to the FEF) in the processes engaged to resolve the competition between a target and an irrelevant distractor. Indeed, the presence of a color singleton distractor also resulted in bilateral activations within the superior parietal cortex (BA 7), an activity that has previously been associated with spatial shifts of attention (Corbetta & Shulman, 2002). More importantly, the authors found a strong negative correlation between the neural signal in the frontal cortex and the magnitude of the distractor interference effect measured behaviorally. This means that the greater was the activity in the left lateral frontal cortex, the lower was the interference effect exerted by the irrelevant distractor, thus demonstrating that this frontal activity can modulate the AC effect. In further support of this hypothesis, a later study using rapid event-related fMRI showed that participants who were better able to suppress orienting to the color singleton showed greater middle frontal gyrus activation, and the degree of top–down control also correlated with left insular activity (Talsma et al., 2009). Of course, also the above cortical areas are subjected to modulation by the BG.

In addition to the notions elaborated so far, deficits of visual attention in PD might also result from dysfunction of the cortico-BG loops that control purposeful and reflexive saccades. For example, the superior colliculus in the midbrain, a nucleus that is part of these loops, has been implicated with both the execution of saccadic eye movements and the deployment of covert spatial attention (Muller et al., 2005). Moreover, the same structure receives projections from cortical areas involved in the top–down (the FEF, the supplementary eye field, the dorsolateral pFC) and bottom–up (sectors of posterior parietal cortex) mechanisms of visual attention (Hikosaka, 2007; Pierrot-Deseilligny, Milea, & Muri, 2004). It has been proved that the dorsolateral pFC can inhibit unwanted reflexive saccades by a direct influence on the superior colliculus (Pierrot-Deseilligny et al., 2004). Then, it has been supposed that a reduced dorsolateral pFC activity, because of a disruption of prefrontal BG-thalamo-cortical loops, such as occurs in PD, may result in a deficit in the ability to suppress reflexive saccades (Deijen et al., 2006). Similarly, one might suppose that the dopaminergic depletion in the striatum engenders a reduced inhibitory effect of the dorsolateral pFC on the superior colliculus, resulting in exaggerated susceptibility to distracting stimuli.

It could be argued that the current study is affected by a potential limitation, namely, having adopted a variant of the Donders subtraction approach, which we applied to the data obtained with three tasks of increasing difficulty and attentional demand, to try and isolate the different component processes underlying overall performance in the AC task. However, we emphasize that we conceived the Donders approach in conceptual or qualitative terms and not in its original meaning, which was strictly quantitative in nature. In fact we did not claim to accurately measure the exact duration of the different component processes contributing to task performance but rather to unveil the possible impairment of one or more of these components.

The combined use of a variety of task paradigms and our take of the Donders approach enabled us to appreciate that in both parkinsonian groups there was not only a deficit in the component processes of display analysis and target selection but also a significant impairment of the mechanism underlying motor response initiation, which might partly explain the longer RTs obtained in

the no-distractor condition of the AC task in both groups of patients relative to the controls. In addition and only in the group of stimulated patients (med-off/stim-off condition), we also detected a significant deficit of the mechanisms underlying motor response selection. The divergent pattern of motor response selection deficit found in the two groups of patients might simply reflect their heterogeneity in terms of decision-making skills (Gleichgerrcht, Ibanez, Roca, Torralva, & Manes, 2010). For example, on the basis of mere chance, one could hypothesize a more severe dopaminergic denervation in the group of stimulated patients relative to the medically treated ones, with a distinct impact on the response selection component. Otherwise and perhaps more plausibly, the differential deficit in this component could be explained as an effect of different treatments in the two PD groups. On the one hand, the selective decline in response selection observed in the surgically treated group might be related to the electrode placement, similar to what was previously reported in PD for verbal fluency and other executive functions (Okun et al., 2009; Morrison et al., 2004; Pillon et al., 2000). On the other hand, it might be related in part to differences in dopaminergic treatment, because the daily doses of dopaminergic drugs were higher in the pharmacologically treated patients than in the stimulated ones. This could imply a slight, residual dopaminergic effect in the former group even in the med-off condition, which in turn could better compensate for any underlying deficit in response selection in this condition (Cools, Barker, Sahakian, & Robbins, 2003).

More generally, a secondary, but still important, objective of this study was to assess whether surgery for DBS electrode placement, with the resulting unavoidable brain tissue damage, exerted any negative effects on a number of brain mechanisms. This objective was made viable by the direct comparison between the two patient groups, of which one was only treated pharmacologically and the other was additionally treated by means of STN-DBS, both tested after withdrawal of dopaminergic treatment and after turning off electrical stimulation. The similar magnitudes of AC and EVA obtained in the two patient groups further suggest that surgery for DBS electrode placement did not exert any appreciable impact on the mechanisms of visual selective attention in the surgically treated patients. This is important as it represents the basis for assessing in a future development of this line of research the differential impact of dopaminergic and electrical treatments on the described attentional deficits.

Conclusions

Our results are in line with the general notion that the BG are crucially engaged in gating and suppressing conflicting responses not only in the motor and emotional domains but also in the cognitive/attentional domain and more specifically in resolving the competition between top–down and bottom–up mechanisms of attentional control. Damage of the BG, such as occurs in PD, seems to compromise mainly the top–down control of visual attention, which could account, on the one hand, for the deficit in engaging attention onto a target stimulus and, on the other, for the deficit in disengaging attention from a distractor location (or otherwise resisting its impact on attentional control), thereby contributing to the observed pattern of "hypercapture." We have hypothesized that this failure of top–down mechanisms might be distinctly related to the striatal dopaminergic depletion, typical of PD, with a consequent dysfunction of the cortico-BG loops involving the dorsal frontoparietal attention network, especially the left frontal areas involved in overcoming AC, and the left globus pallidum internum. Finally, we have provided evidence to indicate that placement of the electrodes for DBS seems not to impact negatively on the neural networks supporting visual selective attention mechanisms.

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