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Response preparation in Parkinson's disease: Automatic vs. controlled processing

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ABSTRACT

Using a finger cuing paradigm, we investigated response preparation in Parkinson's disease (PD). The central question was whether PD individuals are differentially affected by preparatory cues that specify a more automatic response set configuration (that induces within-hand preparation) as opposed to a more controlled one (that induces between-hands preparation). Reaction times (RTs) and error rates were measured in 20 non-demented individuals with PD and 20 healthy control participants with a long and short preparation interval (500 ms and 2000 ms). RT benefits and/or costs were measured for cues indicating a within- and between-hands motor preparatory set. Overall, RTs were significantly longer, and errors more frequent, for PD participants than for control participants. More importantly, in comparison with control subjects, PD individuals showed a significant deficit in between-hands preparation but not in within-hand preparation. Furthermore, longer preparation intervals slowed down cued RTs of the control participants, but not those of the PD individuals. Together, these findings suggest that whereas automatic response preparation processes are spared in PD, controlled response preparation processes operate at a slower rate and/or are delayed in time.

1. Introduction

The purpose of this article is to investigate how PD affects the configuration and activation of a selective motor set. The process of establishing links between stimuli and their corresponding motor responses is believed to be implemented by a network of circuits interconnecting the prefrontal cortex, motor cortex and basal ganglia (the frontostriatal system, Alexander & Crutcher, 1990). More specifically, a circuit connecting the supplementary motor area with the basal ganglia has been repeatedly associated to the planning of complex motor functions such as bimanual coordination, movement planning, or self generated motor set activation (e.g., Cunnington, Bradshaw, & Iansek, 1996; Hoshi & Tanji, 2004).

PD is a neurodegenerative syndrome linked to selective loss of dopaminergic neurons in the substantia nigra pars compacta, one of the subcortical nuclei that compose the basal ganglia. This type of lesion produces a number of clinical symptoms including slow movements, tremors, and rigidity. More importantly for our purposes is that voluntary movement initiation is difficult (akinesia), but substantially improved by external cues (Siegert, Harper, Cameron, & Abernethy, 2002), even producing an over-reliance on visual information to guide movements (Praamstra & Plat, 2001; Praamstra, Stegeman, Cools, & Horstink, 1998). This condition is commonly attributed to a deficit in the selective control of perceptual information, which may lead to incorrect response activation (Mari-Beffa, Hayes, Machado, & Hindle, 2005; Seiss & Praamstra, 2006). In addition, it has also been found that PD individuals have difficulty maintaining a state of readiness before motor execution (Spencer, 2007). Although some explanations for this difficulty focus on the rapid decay of the activated motor program (Berardelli, Rothwell, Thompson, & Hallett, 2001), it could also reflect a difficulty in maintaining an appropriate task set. While most of the research has used response conflict tasks to study response selection processes, relatively little is known about how PD affects the ability to establish a selective motor set based on spatial cues (for an early exception, see Jahanshahi, Brown, & Marsen, 1992). Hence, one of the aims of this study was to gain information on the ability of PD individuals to adaptively implement a selective motor set based on visual cues. To this end we used the finger cuing task (Miller, 1982).

In this task, a visual cue temporally precedes the target signal. The cue specifies a subset of two out of four possible (keypress) responses (implemented by the index and middle fingers of both hands), thus allowing a process of selective response preparation. Four cue or preparation conditions can be distinguished (see Fig. 1). In the hand-cued condition, the cue specifies two fingers on the same hand

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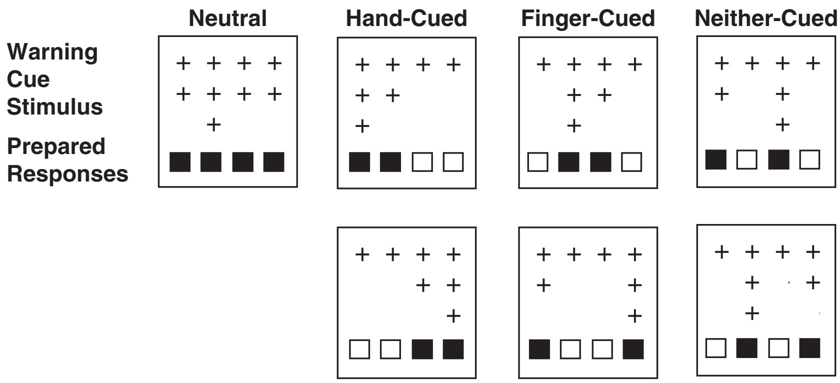

Fig. 1. The four cue types in the finger-cuing task developed by Miller (1982). The black squares specify the possible responses indicated by the cue, and thus reflect the number and type of prepared (not executed) responses. Thus, in all conditions only one response was executed, namely the response triggered by the single target stimulus.

(e.g., the left-index finger and the left-middle finger). In the finger-cued condition, the cue specifies the same fingers on different hands (e.g., the two index fingers). In the neither-cued condition, the cue specifies different fingers on different hands (e.g., the left-middle and right-index fingers). Also, a neutral condition is included, which provides no advance information, and thus precludes selective preparation of any combination of two finger responses. This condition is a control condition because it leaves the basic, four-choice task unaltered. Cue effectiveness is inferred from a significant reaction time (RT) advantage for the informative cue conditions (i.e., hand-cued, finger-cued, and neither-cued) over the control, uninformative (neutral) cue condition.

The consistent finding from the finger cuing paradigm is a pattern of differential cuing benefits: RTs are shortest for the hand-cued condition and longest for the neither-cued condition, with RTs for the finger-cued condition being intermediate. This pattern of differential cuing benefits is apparent primarily at short preparation intervals (i.e., intervals shorter than about 2 s), with longer preparation intervals producing a pattern of equivalent cuing benefits (Reeve & Proctor, 1990).

A recent account of the pattern of differential cuing benefits in the finger cuing paradigm is the Grouping Model (Adam, Hommel, & Umiltà, 2003, 2005). The key idea of the Grouping Model is that the individual elements of multi-element visual displays and multi-element response arrays are not processed independently but are pre-attentively organized or “grouped” according to low-level grouping factors that depend on stimulus driven factors (e.g., Gestalt principles) and on response-related factors (e.g., inter-response tendencies). Each stimulus set and each response set has a default organization established pre-attentively by the bottom-up computation of perceptual and motor units or subgroups; this process is relatively fast and automatic. With additional, top-down processing, however, alternative organizations can be attained; this process is slow and effortful. Thus, the pattern of cuing effects that emerge in the finger cuing task critically depends on the nature of these default groupings and on the time available to reorganize these representations, if necessary.

According to the Grouping Model, the processing advantage of hand-cues simply reflects the natural, strong grouping of the two leftmost and two rightmost stimulus–response elements that leads to a fast, automatic priming or activation of fingers on the same hand. The co-activation of adjacent areas of the motor cortex corresponding to fingers from the same hand could be at the basis of this grouping. Finger- and neither-cues, on the other hand, are more difficult to process because they require slow, controlled modulation to break-up the default, left-right spatial organization and to create a new organization based on the characteristics of the cue. Hence, according to the Grouping Model, hand-cues are “easy” cues, inducing automatic, bottom-up control, whereas finger- and neither-cues are “difficult” cues, requiring slower, effortful, top-down processes to select and prepare the cued responses (Adam et al., 2005; Moresi et al., 2008; Posner, 1980).

The aim of the present study was to investigate the integrity of response preparation in individuals with PD in comparison to a group of healthy control subjects, matched for age, sex, and education. Of particular interest was whether PD would affect preparation efficiency differentially for cues prompting (automatic) within-hand preparatory processes vs. cues prompting (controlled) between-hands preparatory processes. Based on the processing assumption of the Grouping Model, we expected relatively small effects of PD on the more automatic preparatory effects associated with hand-cues (within-hand preparation), but a strong negative effect of PD on the more controlled preparatory effects associated with finger- and neither-cues (between-hands preparation). To investigate the temporal aspects of response preparation, we used a short (500 ms) and a long (2000 ms) preparation interval.

2. Method

2.1. Participants

The study was approved by the Institutional Review Board of Maastricht University Hospital. Participants gave written informed consent. Twenty PD patients were included. They were recruited from the neurological outpatient departments of the Maastricht University Hospital and the Atrium Medical Center. All patients were diagnosed with PD, according to the United Kingdom Parkinson's Disease Society Brain Bank criteria. Patients who were diagnosed with any neurological disease other than PD, or with any psychiatric disorder, including depression, as defined by the criteria of the Diagnostic and Statistical Manual (DSM-IV) of the American Psychiatric Association, were excluded from participation. The presence of any psychiatric disorder, notably major depressive disorder, was established in an unstructured psychiatric interview assessing DSM-IV criteria. Other exclusion criteria were the use of psychoactive medication, such as antidepressants and antipsychotics; the use of l-dopa (direct dopaminergic effect); the abuse of alcohol or drugs; and dementia, which was operationally defined by a short psychiatric interview checking for the DSM-IV criteria and a score on the Mini-Mental State Examination (MMSE) of less than 23. Both patients and controls had an average MMSE score well above 23 (27.7 ± 1.5 vs. 28.6 ± 1.4, respectively), indicating no clinically relevant cognitive impairments. A prior personal or family history of depression was also reason for exclusion. Patients had a low mean HAMD score of 0.85 (± 0.9), indicating no clinically relevant signs of depression. Patients were tested on medication. For further clinical features of these patients and their individual medications see Table 1.