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A model-based quantification of action control deficits in Parkinson's disease

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ABSTRACT

Basal ganglia dysfunction in Parkinson's disease (PD) is thought to generate deficits in action control, but the characterization of these deficits have been qualitative rather than quantitative. Patients with PD typically show prolonged response times on tasks that instantiate a conflict between goal-directed processing and automatic response tendencies. In the Simon task, for example, the irrelevant location of the stimulus automatically activates a corresponding lateralized response, generating a potential conflict with goal-directed choices. We applied a new computational model of conflict processing to two sets of behavioral data from the Simon task to quantify the effects of PD and dopaminergic (DA) medication on action control mechanisms. Compared to healthy controls (HC) matched in age gender and education, patients with PD showed a deficit in goal-directed processing, and the magnitude of this deficit positively correlated with cognitive symptoms. Analyses of the time-course of the location-based automatic activation yielded mixed findings. In both datasets, we found that the peak amplitude of the automatic activation was similar between PD and HC, demonstrating a similar degree of response capture. However, PD patients showed a prolonged automatic activation in only one dataset. This discrepancy was resolved by theoretical analyses of conflict resolution in the Simon task. The reduction of interference generated by the automatic activation appears to be driven by a mixture of passive decay and top-down inhibitory control, the contribution of each component being modulated by task demands. Our results suggest that PD selectively impairs the inhibitory control component, a deficit likely remediated by DA medication. This work advances our understanding of action control deficits in PD, and illustrates the benefit of using computational models to quantitatively measure cognitive processes in clinical populations.

1. Introduction

Computational models of cognition provide a quantitative account of behavioral data, and decompose performance into psychologically meaningful processes. These models force researchers to be explicit about underlying assumptions, and are increasingly used in clinical research to isolate impaired cognitive processes associated with disorders (Aschenbrenner et al., 2016; Frank, 2005; Frank et al., 2004; Ho et al., 2014; Lee et al., 2015; Ratcliff et al., 2004; Shankle et al., 2013; White et al., 2015, 2010a, 2010b). A growing body of evidence suggests that basal ganglia dysfunction in Parkinson's disease (PD) is associated with deficits in action control mechanisms, particularly in times of response conflict (e.g., Chan et al., 2005; Praamstra et al., 1999; Praamstra and Plat, 2001; Praamstra et al., 1998; Wylie et al., 2010; Wylie et al., 2005). Interpretation of data has been driven primarily by qualitative theories. The present study uses a new computational model of conflict tasks (Ulrich et al., 2015) to shed light on the nature of action control deficits in PD.

1.1. The effect of PD on action control mechanisms

Learning complex motor skills such as driving a car or playing the violin is a slow and effortful process that engages goal-directed systems. Motor plans become increasingly automatic with extensive training (Logan, 1988; Shiffrin and Schneider, 1977; Servant et al., 2017). Although automatic response tendencies are an important component of adaptive behavior, they can sometimes conflict with goal-directed actions (Kornblum et al., 1990). Theories of conflict processing generally assume that top-down inhibitory mechanisms are engaged to suppress automatic response tendencies and achieve goals (Ridderinkhof, 2002; Van den Wildenberg et al., 2010; but see Hommel, 1993, 1994).

Patients with PD typically show prolonged response times (RT) compared to healthy controls (HC) on tasks that instantiate a conflict between automatic response tendencies and goal-directed actions (e.g., Chan et al., 2005; Praamstra and Plat, 2001; Praamstra et al., 1998; van Wouwe et al., 2016; van Wouwe et al., 2014; Wylie et al., 2012; Wylie et al., 2010; Wylie et al., 2005; Wylie et al., 2009a, 2009b). This finding

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has been interpreted as reflecting a deficit in inhibitory control, resulting in a greater sensitivity to interference. Recent studies, however, suggest that goal-directed processing is also impaired in PD (de Wit et al., 2011; Sharp et al., 2016).

Both goal-directed and inhibitory processes are mediated by basal ganglia circuits, and by dopaminergic (DA) projections in those circuits (Aron, 2007; Aron and Poldrack, 2006; Balleine and O'Doherty, 2010; Frank, 2006; Jahanshahi et al., 2015; Yin and Knowlton, 2006). PD severely compromises the brain's DA system, leading to altered processing in the basal ganglia (Bernheimer et al., 1973; Kordower et al., 2013; Redgrave et al., 2010; Robbins and Cools, 2014). Understanding the nature of these alterations is critical for developing efficient therapeutics. In the present work, we use a computational model of conflict tasks to decompose cognitive processes involved in action control, and quantify the effects of PD and DA medication.

1.2. Simon task: measuring response conflict

The Simon task offers one of the most sensitive experimental measures of conflict between goal-directed and automatic actions (Hommel, 2011; Kornblum et al., 1990). Participants are instructed to issue a left or right hand button press response to an attribute (e.g., the color) of a spatially lateralized stimulus. Responses are typically slower and less accurate when the location of the stimulus and the response signaled by the imperative attribute do not correspond (e.g., a left hand response to a stimulus presented to the right visual half-field) than when they do, a phenomenon known as the Simon effect (Simon and Small, 1969). Theories of this effect assume that the irrelevant location of the stimulus automatically primes a corresponding lateralized response (De Jong et al., 1994; Hommel, 1993; Kornblum et al., 1990; Ridderinkhof, 2002). Plots of accuracy data as a function of RT quantiles (i.e., conditional accuracy functions, or CAFs) provide support in favor of this hypothesis (Gratton et al., 1988; Ridderinkhof, 2002; Servant et al., 2014). For corresponding trials, accuracy is high and relatively constant over the distribution of RTs. By contrast, non-corresponding trials are associated with an early reduction of accuracy (Fig. 2A, upper panel), betraying a fast response capture by the location of the stimulus. Electrophysiological recordings have provided converging findings. Early electrical activations of the motor cortex and response agonist muscles associated with the spatially-driven response hand have been observed in non-corresponding trials (Coles et al., 1985; C. W. Eriksen et al., 1985; Leuthold, 2011; Servant et al., 2015, 2016).

Theories explaining the Simon effect differ with respect to the evolution of the location-based automatic response priming. Distributional analyses of RT have revealed that the magnitude of the Simon effect decreases as processing time increases. This dynamic is best appreciated with the delta plot technique (De Jong et al., 1994). Delta plots represent the difference (y-axis) against the average (x-axis) of equivalent RT quantiles between non-corresponding and corresponding conditions (Fig. 2A, lower panel). Decreasing delta plots have consistently been observed for healthy subjects, showing that the Simon effect is maximal early in the course of processing and decreases for higher RT quantiles (Pratte et al., 2010; Proctor et al., 2011; Schwarz and Miller, 2012). Ridderinkhof (2002) activation-suppression theory asserts that the location-based automatic response priming is actively suppressed by a top-down inhibitory process that takes time to build (see also Van den Wildenberg et al., 2010). Other theories propose that the automatic response priming passively decays over time (e.g., Hommel, 1993, 1994, 2011). Our model-based analyses offer quantitative estimates of the buildup and reduction of automatic response priming, providing insight into these theoretical alternatives.

Comparisons of CAFs and delta plots from PD patients and HC matched in age, gender and education in the Simon task have revealed consistent patterns. The early dip of accuracy observed on CAFs in the non-corresponding condition does not generally differ between PD and HC, suggesting that the strength of automatic response capture by the location of the stimulus is similar (van Wouwe et al., 2016, 2014; Wylie et al., 2010). Delta plots, however, show an effect of disease, with a less negative-going delta plot slope for PD than HC. This effect has been interpreted in the context of the activation-suppression model (Ridderinkhof, 2002). Specifically, the shallower delta plot observed for PD is thought to reflect a deficit in top-down inhibitory response control (Wylie et al., 2010). Interestingly, delta plots are normalized by DA medication, suggesting that the deficit in inhibitory control is linked to basal ganglia dysfunction induced by DA depletion (van Wouwe et al., 2016).

It should be emphasized that theories of the Simon effect introduced so far are qualitative. In the present work, we sought to provide a quantitative account of behavioral data from PD patients and HC using a computational model of conflict tasks (Ulrich et al., 2015). This model, introduced below, has proven to account for RT distributions and accuracy data observed in the Simon task, and corresponding neurophysiological dynamics (Servant et al., 2016).

1.3. The diffusion model of conflict tasks (DMC)

The DMC (Ulrich et al., 2015) is an extension of the diffusion model for decision-making (Ratcliff, 1978). The diffusion model has been widely employed in basic and clinical research to decompose behavioral performance from two-choice RT tasks into psychologically interpretable processes (Ratcliff and McKoon, 2008; Ratcliff et al., 2016; White et al., 2010b). The model assumes that task-relevant sensory information is continuously accumulated until it reaches a threshold level, and then the decision terminates in a choice and the response is executed. Noise in physical stimulations and sensory systems makes the process stochastic, potentially leading to an incorrect choice (Brunton et al., 2013; Ratcliff, 1978). The diffusion model has four main parameters (Fig. 1, left). The rate of task-relevant sensory information accumulation is called the drift rate (v); it is determined by the quality of the sensory information and the efficiency of attentional processes. Decision thresholds (b: correct choice; $-b$: incorrect choice) regulate the speed/accuracy strategy. Lower thresholds produce faster but less accurate responding. The starting point (z) of the accumulation process indexes response bias. The process is biased toward the response associated with the nearest threshold. The decision time is the latency between the onset of the accumulation process and the first crossing of a decision threshold. A residual processing latency (*Ter*), comprising sensory encoding and motor execution components, is added to the decision time to produce a RT. The model predicts the shape of RT distributions for correct and incorrect responses, which can be specified by the probability density function or from computer simulations. These predictions can be fit to data to extract underlying parameters (Ratcliff and Tuerlinckx, 2002).

The DMC extends the diffusion model framework by incorporating components of automatic processing. Performance is determined by the sum of automatic and goal-directed decision activations, an architecture reminiscent of a model of automaticity proposed by Logan (Logan, 1980). Contrary to its predecessor, however, the DMC assumes that the contribution of automatic processes is short-lived in conflict tasks such as the Simon task (Ellinghaus et al., 2017; Lu and Proctor, 1995; Simon et al., 1976). The automatic decision activation $X_a(t)$ is modeled as a pulse-like gamma function that favors the correct response in corresponding trials and the incorrect response in non-corresponding trials (Fig. 1, middle). Its expected mean as a function of time is described by the following equation:

$$E[X_a(t)] = Ae^{-t/\tau}\left[\frac{te}{(a-1)\tau}\right]^{(a-1)}$$

Where a, τ and A are the shape, characteristic time and peak amplitude of the gamma function respectively. The peak amplitude A quantifies the strength of the automatic activation: the higher the peak amplitude,