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A neurocomputational account of cognitive deficits in Parkinson's disease

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ABSTRACT

Parkinson's disease (PD) is caused by the accelerated death of dopamine (DA) producing neurons. Numerous studies documenting cognitive deficits of PD patients have revealed impairments in a variety of tasks related to memory, learning, visuospatial skills, and attention. While there have been several studies documenting cognitive deficits of PD patients, very few computational models have been proposed. In this article, we use the COVIS model of category learning to simulate DA depletion and show that the model suffers from cognitive symptoms similar to those of human participants affected by PD. Specifically, DA depletion in COVIS produced deficits in rule-based categorization, non-linear information-integration categorization, probabilistic classification, rule maintenance, and rule switching. These were observed by simulating results from younger controls, older controls, PD patients, and severe PD patients in five well-known tasks. Differential performance among the different age groups and clinical populations was modeled simply by changing the amount of DA available in the model. This suggests that COVIS may not only be an adequate model of the simulated tasks and phenomena but also more generally of the role of DA in these tasks and phenomena.

1. Introduction

Parkinson's disease (PD) is caused by the accelerated death of dopamine (DA) producing neurons. The pattern of cell loss is opposite from and more severe than in normal aging. Within the substantia nigra pars compacta (SNpc), cell loss is predominately found in the ventral tier with less (but still extensive) damage in the dorsal tier (Fearnley & Lees, 1991; Gibb & Lees, 1991). In contrast, normal aging yields substantially less cell loss and in a dorsal-to-ventral pattern. Parkinsonian motor symptoms appear after a loss of 60–70% of SNpc cells and 70–80% of DA levels in striatal nuclei (Bernheimer, Birkmayer, Hornykiewicz, Jellinger, & Seitelberger, 1973; Gibb & Lees, 1991). Motor symptoms include tremor, rigidity, bradykinesia, and akinesia.

In addition to motor deficits, non-demented PD patients present cognitive symptoms that resemble those observed in patients with frontal damage. Numerous studies documenting cognitive deficits of PD patients have revealed impairment in a variety of tasks related to memory, learning, visuospatial skills, and attention (e.g., ignoring irrelevant and maintaining relevant information: Gotham, Brown & Marsden, 1988). While there are a plethora of studies documenting cognitive deficits of PD patients (for a review, see Price, Filoteo, & Maddox, 2009), very few computational models have been proposed to investigate the variegated landscape of deficits observed in those studies. In this article, we use the COVIS model of category learning (Ashby, Alfonso-Reese, Turken, & Waldron, 1998; Ashby, Paul, & Maddox, 2011) to simulate DA depletion and we show that the depleted model suffers from cognitive symptoms similar to those of human participants affected by PD.

2. The COVIS theory of category learning

COVIS (Ashby et al., 1998) is a neurobiologically detailed theory of category learning that postulates two systems that compete throughout learning—an explicit, hypothesis-testing system that uses logical reasoning and depends on working memory and executive attention, and an implicit system that uses procedural learning. The hypothesis-testing system of COVIS is thought to mediate *rule-based* category learning. Rule-based category-learning tasks are those in which the category structures can be learned via some explicit reasoning process. Frequently, the rule that maximizes accuracy (i.e., the optimal rule) is easy to describe verbally. In the most common applications, only one stimulus dimension is relevant, and the observer's task is to discover this relevant dimension and then to map the different dimensional values to the relevant categories. The Wisconsin Card

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Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993) is a well-known rule-based task. More complex rule-based tasks can require attention to multiple stimulus dimensions. For example, any task where the optimal strategy is to apply a logical conjunction or disjunction is rule-based. The key requirement is that the optimal strategy can be discovered by logical reasoning and is easy for humans to describe verbally.

The procedural system of COVIS is hypothesized to mediate *information-integration* category learning. Information-integration tasks are those in which accuracy is maximized only if information from two or more stimulus components (or dimensions) is integrated at some pre-decisional stage. Perceptual integration could take many forms—from treating the stimulus as a Gestalt to computing a weighted linear combination of the dimensional values. Typically, the optimal strategy in information-integration tasks is difficult or impossible to describe verbally. Rule-based strategies can be applied in information-integration tasks, but they generally lead to sub-optimal levels of accuracy because rule-based strategies make separate decisions about each stimulus component, rather than integrating this information.

3. Parkinson's disease and cognitive impairments

Many experiments have contributed to the identification of PD-related cognitive deficits. Although the diverse landscape of impairments may appear disparate, they can largely be attributed to failures in one of the two COVIS learning systems. Impairments in rule-based tasks will be considered first followed by impairments in procedural-learning tasks. The evidence presented here is by no means exhaustive, but instead has been selected as representative of learning failures that are amenable to exposition through model simulation without modifying the existing COVIS model architecture (Ashby et al., 1998, 2011). A fuller treatment of PD cognitive deficits can be found in Price et al. (2009).

3.1. *Rule-based learning*

PD patients display many of the same deficits in rule-learning tasks as patients with frontal lobe damage (Owen, Roberts, Hodges, & Robbins, 1993). These tasks demand attention, working memory, and logical reasoning to maximize performance. This section reviews empirical evidence for rule-related deficits in PD patients, with a focus on deficits in rule-based category learning, rule maintenance, and perseverative response tendencies. This focus is warranted considering that COVIS is a model of category learning that uses hypothesis-testing as a mechanism for rule learning, and that the goal here is not to design a specific computational model of PD deficits, but rather to simulate PD symptoms using an existing neurobiologically-detailed model (COVIS) without any modifications or additional assumptions. Evidence reviewed in Cools (2006) suggests that these impairments in 'executive functions' are DA related. More specifically, Price et al. (2009) reviewed evidence suggesting that rule shifting and rule selection impairments are DA related. Hence, rule-related cognitive symptoms will be simulated in COVIS by reducing DA levels (see Section 5).

Ashby and his colleagues (2003) tested PD patients, age-matched controls, and younger controls in a rule-based categorization task similar to the WCST, except that the stimuli varied on four dimensions instead of three. Like the WCST however, a simple one-dimensional rule could be used to categorize the stimuli perfectly. Each participant was classified as a learner if the rule was successfully learned (i.e., 10 consecutively correct responses) within 200 trials. Compared to controls, significantly more PD patients failed to learn in this task than both the young and age-matched controls.

The above experiment successfully identified a gross impairment in rule learning via simple rule-based categorization. More nuanced deficits have also been identified by using different kinds of rule-based tasks and performance metrics. For example, PD patients tend to demonstrate a failure of rule maintenance. Rule maintenance requires sustained attention to the relevant stimulus dimension (as determined by the rule) while ignoring variations in the other dimensions. Typically, rule maintenance is measured by set loss errors, which are defined as errors following several consecutively correct responses. In the WCST, PD patients exhibit significantly more set loss errors than controls (Beatty, Staton, Weir, Monson, & Whitaker, 1989). Similarly, Filoteo, Maddox, Ing, and Song (2007) observed more set loss errors in a rule-based categorization task when the irrelevant dimensions varied randomly than when there was no variability in the irrelevant dimension.

PD patients also appear to exhibit a perseverative tendency—patients often persist with the previous response strategy despite feedback suggesting a change in the relevant rule. Using a simplified version of the WCST (Nelson, 1976), Gotham et al. (1988) found PD patients to make significantly more perseverative errors than control participants. In addition, Beatty et al. (1989) found greater mean perseverative errors and responses than controls in the standard WCST. Finally, a meta-analysis of PD patient performances in WCST experiments found moderate effect sizes for both perseverative errors and perseverative responses, further supporting the hypothesis that PD patients exhibit perseverative tendencies (Zakzanis & Freedman, 1999).

3.2. *Procedural learning*

Using a different class of learning problems, some studies have identified a different pattern of learning deficits in PD patients. Procedural learning is important in categorization tasks in which optimal responding cannot be obtained via logical reasoning or by using any explicit rule-based strategy. Shohamy, Myers, Grossman, Sage, and Gluck (2005) reviewed evidence and collected data suggesting that at least some forms of procedural learning are DA-related. As such, procedural-learning deficits are simulated in COVIS by reducing DA levels in the model (see Section 5).

In a now classic study, Knowlton, Mangels, and Squire (1996) tested several patient groups in the Weather Prediction Task (WPT), a probabilistic classification task that requires participants to learn gradually to associate a number of stimuli with the correct outcome. Knowlton and her colleagues found that PD patients performed significantly worse than controls in this task, and PD patients with the most severe symptoms never performed above chance. Importantly, amnesic patients performed as well as controls, thus lending strong evidence that a failure of memorization was not the cause of the PD impairment and indirectly supporting the hypothesis that performance in this task depends on an intact mesostriatal dopamine system.

Ashby and his colleagues (2003) tested PD patients with an information-integration category-learning task that used the same stimuli as in the rule-based task described in Section 3.1. In the information-integration condition, the stimuli were separated into two categories in such a way that no easily verbalized rule would yield optimal performance. Interestingly, PD patients were unimpaired in this task compared to age-matched controls (although both groups were massively impaired relative to young controls). Similarly, PD patients showed no deficits in two other information-integration category-learning tasks that used two-dimensional continuous-valued stimuli when the categories