

## Neuroscience: Decision-making in Parkinson's disease and cherry-picking dilemmas

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### Summary:

When making decisions we combine our previously acquired knowledge with the available current information to optimize our choices. A study shows that Parkinson patients are impaired in using their prior knowledge leading to suboptimal decisions when current information is ambiguous.

### Main text:

Parkinson's disease (PD) is a common neurological disorder affecting several million people worldwide [1]. PD is considered a 'movement disorder' causing – amongst other symptoms - an abnormal slowing of movements, which has been largely related to deficiency of the neurotransmitter dopamine [2]. In recent years, it has become increasingly clear that PD patients do not only exhibit problems executing movements, but also show marked impairments when deciding which movement to perform [3]. A new study by *Basso et al.* [4] sheds new light on this impairment by demonstrating that patients with PD have great difficulties in using prior, i.e. previously learned, information to guide their decisions during perceptual decision-making.

### What is perceptual decision-making?

Consider picking cherries to eat. In sunlight the decision whether or not to pick a cherry is relatively simple, because you can clearly see the colour of the fruit. However, once dusk has fallen, this decision becomes more challenging. You need more time to deliberate and are more likely to make a mistake. It turns out that this behaviour can be described by a relatively simple model [5,6]. For ease we consider decisions between two alternatives (figure 1A). If choice A and choice B are equally likely, evidence starts to accumulate exactly from the middle between boundary A (indicating the decision for A) and boundary B (decision for B) and drifts towards choice A or choice B over time depending on the cues received. If these are clearly in favour of A the evidence will quickly drift towards boundary

A (high drift rate) resulting in fast and accurate decisions. However, if the cues are less clear, evidence will only drift slowly towards A or B (low drift rate) leading to slower and, because the evidence accumulation process is noisy, less accurate choices.

In the study by *Basso et al.* PD patients and healthy, age-matched participants had to judge whether the orientation of a presented stimulus was leftwards or rightwards. In some trials, the orientation was clearly visible, while there was no clear orientation in other trials. Overall, patients performed the task well indicating that they understood the task instructions, were able to discriminate leftwards from rightwards orientations, and perform the movement to indicate their choice. Thus, both patients and healthy people chose the correct response with high accuracy when the orientation of the stimuli was clear, and performed at around chance level when the stimuli were unclear. A strong difference between the two groups became only evident when the authors assessed how participants made use of any prior knowledge about which choice was more likely to be correct when stimuli were unreliable.

How can prior knowledge guide our choices during uncertainty?

When we have to make a decision, but are faced with ambiguous information it often makes sense to rely on our previous experiences, i.e. prior knowledge. For example, cherries are more likely to be ripe during their peak season. This 'prior' will bias our choices: We are more likely to pick a cherry at that time even if its ripeness is difficult to judge based on its colour. In the article by *Basso et al.* the use of priors was studied by making one of the responses (either left or right) more likely to be correct than the alternative response. Participants had to learn that this was the case for a subset of the stimuli (experiment 1 and 2), or were explicitly made aware of the unequal distribution (experiment 3). As expected, when the orientation of the presented stimulus was unclear healthy participants made use of these priors so that they were more likely to choose correctly. In contrast, patients with PD failed to implement such a bias for the more likely answer (figure 1B). They simply chose "left" 50 % of the time when the stimuli did not show a clear orientation, even if "right" was a-priori more likely to be the correct answer. Importantly, they still failed to properly bias their decisions even when they were explicitly made aware of the unequal distributions in experiment 3.

In order to better understand this novel finding, the authors then modelled the latent decision-making processes underlying the participants' choices using a model similar to the one shown in figure 1A.

What mechanisms can bias our decisions?

When faced with decisions in which one option is more likely to be correct than the alternative option an optimal observer, i.e. a person performing the task in an ideal way, could adjust their behaviour by means of two mechanisms. The first mechanism involves preparing the more frequent response to a larger extent even before presentation of the stimulus, which in the model corresponds to a bias in a starting point of evidence accumulation [5,7]. The evidence does not start in the middle between boundary A and B, but more closely to the more frequent option. The second mechanism is an increased drift rate towards the boundary corresponding to the more likely option [5,8]. As time progresses without arriving at a decision, the observer may also infer that the current stimulus conveys ambiguous information and thus increase their reliance on priors rather than the current stimulus [5,9].

In the study by *Basso et al.* healthy participants behaved according to these predictions. They adjusted the starting point of evidence accumulation as well as the drift rate in order to bias their responses to the choice which was more likely to be correct (figure 1C). PD patients, on the other hand, did not properly adjust their starting point. They did, however, adjust the drift rate even more than healthy people (figure 1D). The authors interpret this as a putative compensational mechanism, which might be used in PD to compensate for the inability to move the starting point of evidence accumulation closer to boundary for the more likely response.

Why are Parkinson patients impaired in using prior knowledge during decision-making?

The pathophysiological hallmark of Parkinson's disease is a progressive loss of cells in the midbrain producing the neurotransmitter dopamine. Physiologically, the controlled release of dopamine into synapses connecting the cerebral cortex and the basal ganglia plays a central role during the selection and reinforcement of actions as well as motivational

enhancement of motor vigour [10,11]. Furthermore, the basal ganglia are thought to be involved in setting decision boundaries determining how much evidence needs to be integrated before committing to a choice [12,13] (see Figure 1A). Previous neuroimaging and electrophysiological studies have provided converging evidence that biases implemented through adjustments of the starting point are related to activity in the basal ganglia and fronto-parietal cortical networks [14,15]. Interestingly, the activation of exactly these areas seems to be most severely affected in PD [16]. Conversely, bias implemented through drift rate adjustments has been related to activity in the temporal cortex in a previous functional neuroimaging study [17]. Thus, the failure to use prior knowledge in order to adjust the starting point and the increased use of drift rate adjustments in PD might reflect a shift from activation of more severely to less affected neural networks in PD.

Is the observed behavioural deficit related to dopamine deficiency? PD is a heterogeneous disorder comprising alterations in multiple neurotransmitters and neural networks [2]. Furthermore, dopamine replacement therapy, rather than dopamine deficiency, can affect decision-making by impairing patients' abilities to learn, to express learned information or both [3,18,19]. Since in the study by *Basso et al.* all patients were taking their normal dopaminergic medication, it remains to be elucidated whether dopamine itself affects how people bias their decisions using prior knowledge.

Together, the results by *Basso et al.* showing that PD patients are impaired in using prior information during choice uncertainty are an important new lead in understanding decision-making deficits in PD. It remains an open question for future studies to what extent this contributes to the clinical symptoms of PD, particularly the increased reliance on external stimuli during movement [20].

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Figure 1. Biased decision-making.

A: The drift diffusion model [6] can explain behaviour (reaction times and accuracy rates) during simple decisions between two alternatives. Evidence accumulates from a starting point (SP) towards the boundary for choice A where the sensory evidence favours choice A over choice B. Once one of the boundaries is crossed, the decision process is terminated and the respective choice is executed. B: When there is no clear sensory evidence for either of the choices and no prior knowledge of one of the choices being more likely to be correct, participants chose option A or B with equal probability. When past experience dictates that one choice is more likely to be correct, healthy participants chose this option more frequently, even if the presented stimulus is not informative. PD patients, on the other hand, fail to implement such a bias. C: Applying the drift diffusion model indicated that healthy persons both adjusted their starting point and drift rate in order to bias their response towards the choice which was more likely to be correct. D: PD patients only adjusted their drift rate, which was insufficient to properly bias decisions according to prior knowledge when clear sensory evidence was lacking.