Inhibition and control in depression

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It is a commonplace that psychiatric disorders such as depression and schizophrenia involve substantial disturbances to affectively-charged decision-making. Although our understanding of the latter has substantially advanced, with theoretical concepts drawn from reinforcement learning (RL) providing a normatively-sound framework within which to link psychological, neurobiological and pharmacological results, there have hitherto been only a few applications to psychiatry. Here, we use RL to identify components of decision-making that are key in depression, the psychiatric disease that is one of the world’s biggest scourges.

We focused on the central finding in depression of a vicious cycle, with impairments in decision-making apparently themselves contributing to the worsening of the disorder. For instance, stress is a main aetiological factor in the development of depression, but a significant fraction of the stress associated with depression is self-generated. Humans with depression self-select into high-risk environments, i.e. they fail to choose to avoid situations that control populations successfully avoid\textsuperscript{2}, and are frequently involved in aggressive acts\textsuperscript{5}, potentially because they fail to choose to terminate aggressive behaviour before escalation\textsuperscript{4}.

In RL terms, such vicious cycles can arise from forms of meta-learning, when moderately ineffective interactions in one environment (perhaps caused organically) lead to settings of expectations or priors that generalize to other environments, and make interactions there even worse. In the case of depression, we suggest the involvement of two such factors: variously associated with model-free, neuromodulatory, Pavlovian control, and model-based, instrumental control. With others\textsuperscript{1}, we argue that an important function of serotonin is reflexive, Pavlovian, behavioural inhibition in the face of anticipated punishment. Any lapse in this inhibitory crutch will lead to defective avoidance of negatively valenced (stressful) states. This will lead to excess punishment, and thus influence the environmental priors acquired by the model-based controller. Such priors will suggest that the subject is occupying environments that are more negative and less controllable than the norm, and therefore lead subjects to increasingly inefficient interactions.

We analyze this cycle, and use the deep understanding of controllability and learned helplessness in depression\textsuperscript{3} to make a connection to tonic levels of dopamine in the disease. We also present preliminary data from depressed and control subjects’ performance on a decision-making task developed to probe subjects’ prior beliefs about controllability and outcome bias along with their sensitivity to rewards and punishments.

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References