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Cognitive control in depression and anxiety: out of control?

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The recent literature on cognitive control dysfunctions in depression and anxiety is reviewed with particular emphasis on evidence for proactive and reactive control deficits. Individuals with depression and anxiety show few, if any, specific control deficits, however, there is evidence for non-specific interference that can be related to problems with rumination, worrying, attention and inhibition. Moreover, both electrophysiological and neuroimaging studies provide strong evidence for altered processing during cognitive control paradigms in depression and anxiety. Thus a layered model of control deficits is proposed, which presumes that agent-specific, task-irrelevant factors contribute to cognitive control processing alterations in anxiety and depression. A Bayesian Ideal Observer model is suggested as a possible approach to better disambiguate the dysfunctional processes in depression and anxiety.

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Introduction

Mood [1] and anxiety [2] disorders will account for approximate $\$16 \times 10^9$ lost productivity or 25% of global GDP over the next 20 years [3] and are among the most common and devastating mental health conditions worldwide. Both disorders affect a variety of different behavioral, cognitive and affective processes that extend beyond changes in mood and anxiety. In particular, investigators have focused on examining alterations in cognitive processing among individuals with these disorders. The basic notion underlying these approaches is that a better delineation of these dysfunctional processes can help to quantify the severity of these disorders, predict impact on daily functioning, and develop new interventions that are targeted more specifically to remedy these specific processes. These investigations have focused on executive functions [4] in general and cognitive control [5••] in particular. This review summarizes the findings from recent studies examining cognitive control dysfunctions in depression and anxiety with particular emphasis on the notion of proactive and reactive cognitive control [6•]. It is proposed that a computational approach within a Bayesian framework, which focuses on the trial-by-trial adjustments of control but acknowledges a specific agent, may be helpful to advance the field toward a deeper understanding of the processing dysfunctions of these disorders.

Experimental and theoretical approaches to cognitive control

Whether to work on a manuscript or updating ones Facebook page, cognitive control [7] refers to processes that support the ability of individuals to regulate, coordinate, and sequence thoughts and actions according to internally maintained behavioral goals [6•]. Control processes help to optimize behavior in situations when conflicting action tendencies have to be modified based on contextual information. Experimentally, the influence of competing information or the preceding trial characteristics on response accuracy and speed are used to determine levels of control. Several behavioral tasks have been developed to probe these situations. For example, meaning and color of a written word are used to examine interference in the Stroop Task. In comparison, the congruent or incongruent directions of flanking arrows interfere with the response to a center target arrow in the Erikson Task. These tasks have been extended to include emotional stimuli such as affectively valenced words or images both as task-relevant or task-irrelevant stimuli.

A dual mechanisms of control framework has been proposed [6•] to explain a number of recent behavioral and neural processing findings. Two modes are thought to modulate levels of cognitive control, i.e. a proactive control mode, which comprises a sustained process using goal-relevant information to optimally bias attention and a reactive control mode, which consists of a corrective mechanism that is mobilized on a just-in-time basis to optimize behavioral performance in a high conflict situation. In a recent study [8•], two additional factors affecting control have been identified that have thus far been less well appreciated. First, there are sequential expectation

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effects generated by the subject looking *forward* in time, e.g. how likely it is that stimuli will occur on one side of the screen. Second, the subjective awareness of a conflict, i.e. the ability to explicitly verbalize that there is a discrepancy between the expectation and the observed stimulus, which can influence the selection of optimized action. Therefore, levels of cognitive control are modulated proactively by context, expectations of the trial-by-trial likelihood of conflict, and the self-related sense of agency and reactively by trial-by-trial adjustments. Given an increasingly more sophisticated understanding of cognitive control and the ability to assess these processes with thoughtful experimental paradigms, it is reasonable to question how depression and anxiety influence these processes and whether there is a consistent dysfunction emerging that can be linked to underlying neural processing deficits.

Before reviewing the literature on cognitive control in depression and anxiety, it is useful to consider several constructs that are important for these disorders and may have a non-specific influence on cognitive control processes. In a framework elaborated below these constructs are labeled agent-specific, task-irrelevant processes, which provide a different layer of monitoring ongoing control processes. First, rumination can be conceived as a repetitive internal cognitive process of thoughts that often deal with negative past events and focus on the origin, causes, and consequences of negative emotions [9]. Similarly, worrying focuses on possible negative events in the future and strategies to prevent such events from occurring [10]. Both constructs rely heavily on self-relevant processing [11], which has been related to excessive engagement of particular brain systems such as cortical midline structures. The anterior cingulate and medial prefrontal cortex [12] have been considered a dynamic hub providing an interface of affect and cognition. The function of these structures is moderated by anxiety and these brain regions integrate information about conflict and punishment in the face of uncertainty to select and maintain 'options' that are learned through a process of hierarchical reinforcement learning [13]. Second, alterations in attention engagement and disengagement have been proposed as dysfunctional processes in anxiety and depression [14], respectively. An inability to disengage attention from negatively valenced information has been proposed to be a depression specific processing abnormality [15], whereas an increased attentional bias toward threat-related stimuli has been at center of cognitive processing abnormalities in anxiety [16]. It has been proposed that these difficulties in attentional engagement and disengagement from negatively valenced material with tendencies to interpret information in a negative manner interferes with cognitive control [17]. Third, deficits in inhibition, i.e. the ability to hold back or stop an action based on contextual information as measured by go/no-go or stop signal tasks, have been suggested in both depression [18] and anxiety [19]. Therefore, differences between groups of depressed or anxious individuals and comparison subjects may not be due to control-specific dysfunctions but may be due to these agent-specific, task-irrelevant constructs that may have a general effect on cognitive control processes.

Cognitive control and depression

Evidence for cognitive control deficits in depression comes from several studies that have used cued task designs to modulate the extent to which one has to engage control processes. This approach is based on the idea that a cue signaling an increased frequency of trials with high cognitive control demands will strategically result in activating proactive control, i.e. increase the brain's ability in a particular context to employ control processes. One such task is the Cued Emotional Control Task [20], which provides the individual with a cue whether to respond with the key mapped onto the facial emotion that is displayed on the screen or whether to press the key that is mapped onto the opposite facial emotion. This task presumes that individuals need to engage control processes when asked to press the opposite key to withhold the prepotent response to press the key mapped to the emotion displayed on the screen. Emphasizing focus on speed or accuracy during a standard or emotional Stroop task [21] is another approach to examine differences in proactive control. Here higher sustained cognitive control will be exerted during the accuracy relative to the speed instruction. Reactive control is primarily measured by examining speed or accuracy following a trial where a pre-potent response had to be inhibited versus a trial without such control properties. A third way of assessing cognitive control in depressed individuals is the use of the Internal Shift Task [22]. In this task, individuals are asked to complete a non-emotional or gender condition and an emotional condition. In the gender condition, participants had to focus on the 'gender' dimension of the face in the emotion condition; they had to focus on the 'emotion' dimension of the face. The participant's task is to keep a silent mental count of the number of faces in each category presented within a block of trials. Due to the sequence of the faces, there are switch and no-switch trials in each block of items. Switch costs are calculated as the difference in reaction time between switch and non-switch trials within the blocks and serve as the main dependent variable in the analyses.

Individuals with Major Depressive Disorder (MDD) showed evidence of abnormal proactive control while performing the Cued Emotional Control Task [23••] as indicated by increased response latency, longer duration of dominant ERP topopgraphy in dorsal anterior cingulate, and slower responses to the incongruent happy condition. Although measures of brooding, an aspect of rumination, were not associated with different performance levels, they were positively correlated with