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Review article

Transdiagnostic impairment of cognitive control in mental illness

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ABSTRACT

Intact cognitive control or executive function has characteristic patterns in both behavior and functional neurocircuitry. Functional neuroimaging studies have shown that a frontal-cingulate-parietal-insular (i.e., "multiple demand") network forms a common functional substrate undergirding successful adaptation to diverse cognitive processing demands. Separate work on intact neurocognitive performance implicates a higher order factor that largely explains performance across domains and may reflect trait cognitive control capacity. In the current review we highlight findings from respective psychiatric disorders (i.e., psychotic, bipolar and unipolar depressive, anxiety, and substance use disorders) suggesting that cognitive control perturbations amidst psychopathology are most pronounced within these common brain and behavioral indices of adaptive cognitive functioning and moreover, are evident across disorders (i.e., transdiagnostically). Specifically, within each of the disorder classes impairments are consistent in the multiple demand network across a wide range of cognitive tasks. While severity varies between disorders, broad as opposed to domain-specific impairments consistently emerge in neurocognitive performance. Accumulating findings have revealed that phenotypically diverse psychiatric disorders share a common factor or vulnerability to dysfunction that is in turn related to broad neurocognitive deficits. Furthermore, we have observed that regions of the multiple demand network, which overlap with the salience network (dorsal anterior cingulate and bilateral anterior insula) are characterized by reduced gray matter transdiagnostically and predict weaker neurocognitive performance. In summary, transdiagnostic (as opposed to disorder-specific) patterns of symptomatic distress and neurocognitive performance deficits, concurrent with parallel anomalies of brain structure and function may largely contribute to the real-world socio-occupational impairment common across disorders.

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Cognitive control or executive functions refer to those processes integral to the effortful deployment of cognitive resources for flexible, adaptive responding to shifting contingencies. As such, cognitive control undergirds the self-regulation imperative for successful, dynamic accommodation to the demands of daily life (cf. Diamond, 2013 for review). Even among healthy individuals, cognitive control capacity predicts endeavors and success in educational performance and attainment (Duncan et al., 2007), occupational stability and advancement (Foxall, 2014), health promotion (McClernon et al., 2015; Riggs et al., 2010), as well as broader measures of overall quality of life (Davis et al., 2010). Given the influence on functional status among healthy individuals, cognitive control/executive functions are likely integral to the development, resistance to, maintenance, and remediation of psychopathology. That is, as phasic (or prolonged) distress manifests in the context of mental health or illness, cognitive control neurocircuits are likely recruited in the service of symptom regulation. In fact, meta-analysis of functional neuroimaging studies of adaptive emotion regulation demonstrate the recruitment of neural networks characteristic of cognitive control—a frontoparietal network containing the dorsolateral prefrontal and posterior parietal cortices, and a cingulo-opercular network containing the dorsal anterior cingulate cortex (dACC), anterior insula, and the anterior prefrontal cortex (Kohn et al., 2014).

The foundation of intact cognitive control has characteristic patterns in both behavior and functional neurocircuitry. As such, cognitive control perturbations amidst psychopathology are potentially most pronounced within indices of these processes common to adaptive functioning and moreover, evident across disorders (i.e., transdiagnostically). In this review we first discuss behavioral evidence of cognitive dyscontrol transdiagnostically, focusing on psychotic, bipolar and unipolar depressive, anxiety, and substance use disorders. Second, to contextualize behavioral correlates of cognitive control anomalies in mental illness relative to underlying structure, we discuss our recent findings from a meta-analysis (Goodkind et al., 2015) demonstrating transdiagnostic gray matter reductions in a dorsal anterior cingulate-anterior insula-based network. We also highlight the demonstrated functional relevance of this network in terms of impaired cognitive control performance. Next, we focus on the neurocircuitry implicated across psychotic, bipolar and unipolar depressive, anxiety, and substance use disorders in functional neuroimaging studies of cognitive dyscontrol. Finally, we briefly discuss the implications for future research and the potential to leverage cognitive control and its neurocircuitry for innovating powerful and broadly applicable transdiagnostic interventions to ameliorate distress and improve daily real-world functioning.

1. Clues to core cognitive control dysfunction common across psychiatric disorders

1.1. A common underlying cognitive control factor: behavior

Latent variable analysis of performance on a wide array of neuropsychological tasks has shown that intact cognition has a characteristic pattern of interrelated executive functions throughout the lifespan from childhood (Lehto et al., 2003) through middle (Miyake et al., 2000) and older adulthood (Adrover-Roig et al., 2012). For example, Miyake and colleagues (2000, 2012) have demonstrated that updating (i.e., monitoring and refreshing working memory store), inhibition (resisting prepotent responses), and shifting (switching between mental sets) largely explain cognitive processes. Alternatively, Alvarez and Emory (2006) have highlighted the synergy of working memory, inhibition, and selective attention. The fact that diverse functions show coherence suggests that these heterogeneous processes may work in tandem to promote cognitive wellbeing, but may also share a vulnerability to dysfunction.

In fact, latent variable analysis of task batteries spanning multiple domains of cognitive control suggest that hallmark executive functions are explained not only as subprocesses such as updating, inhibition, and shifting, but also an underlying common factor reflecting general cognitive control capacity (Miyake and Friedman, 2012). The extent of impairment in this common factor has yet to be examined in most psychiatric disorders. Historically, hallmark symptoms of individual disorders have prompted hypotheses about domain-specific impairments in neuropsychological profiles per disorder (e.g., poor resistance to interference in PTSD due to intrusions). As such, investigations on respective disorders have typically focused on one or two exemplar tasks of a given domain, precluding latent variable analysis to discern contributions of a common cognitive control factor. However, taken together the extant literature on neuropsychological performance shows broad (i.e., domain non-specific) rather than distinct performance impairments in studies of individual psychiatric disorders.

Evidence of broad impairments for respective disorders and classes of related disorders, albeit with variations in severity, was clearly demonstrated by Snyder et al. (2015). The authors summarized the effect sizes of meta-analyses of cognitive control/executive functions by individual disorder. For consistency with prevailing latent variable models, results for individual tasks were aggregated into domains of shifting, inhibition, updating, and working memory manipulation and maintenance. Measures of planning and verbal fluency, which typically recruit multiple executive functions and thus do not clearly load one of the other factors, were also summarized across studies as they have been examined frequently in clinical samples. Schizophrenia showed the most pronounced and consistently cross-domain deficits, aligned with the severe functional impairment characteristic of the disorder (Harvey and Strassnig, 2012). Specifically, aggregating across eight meta-analyses, schizophrenia demonstrated impairments with large effect sizes on all measures except the relatively less demanding process of working memory maintenance, for which a medium effect sized impairment emerged. Slightly less severe, but nonetheless consistent cross-domain deficits were observed in the average of ten meta-analyses of bipolar disorder. Notably, eight of the ten meta-analyses examined euthymic bipolar disorder, suggesting that cognitive control deficits are present regardless of mood state but are likely more pronounced during acute depression or mania. Unipolar depression showed the same pattern but marked by medium effect sized deficits across all domains with the exception of a lesser impairment on working memory maintenance, a pattern that was similar to, but less severe than in schizophrenia. Aggregating across three meta-analyses of obsessive-compulsive disorder (OCD) and one of posttraumatic stress disorder (PTSD) showed medium to small effect sizes across all domains. Neurocognitive functioning in other (DSM-IV-defined) anxiety disorders (i.e., specific phobia, social anxiety, generalized anxiety, and panic disorders) have been the subject of few published investigations, possibly reflecting the file drawer problem (i.e., hurdles to publishing null results) or a presumption on the part of investigators that cognitive control is uninterrupted in these presentations and thus not examined. Finally, multiple substance use disorders demonstrated deficits foremost in inhibition, but also shifting and working memory. Notably, Stavro et al. (2013) revealed that deficits were typically moderate up to one year of abstinence, and lessened for samples abstinent for at least one year. Despite the paucity of work directly comparing different disorders, taken together these findings have prompted a growing appreciation of the likelihood of shared deficits in cognitive control capacity across