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Cognitive control in pediatric obsessive compulsive and anxiety disorders: Brain-behavioral targets for early intervention

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Abstract

The DSM provides distinct criteria for obsessive compulsive and various types of anxiety disorders, but phenomenological overlap, high rates of comorbidity, and early onset suggest common underlying mechanisms. This notion is further supported by use of the same treatments – cognitive behavioral therapy (CBT) and serotonin reuptake inhibitor medication – for managing both obsessive compulsive disorder (OCD) and non-OCD anxiety disorders in clinical settings. While early intervention with these gold standard treatments is recommended for pediatric OCD and anxiety disorders, young patients often remain symptomatic even after treatment. To guide the development of novel, mechanistically targeted treatments to better resolve OCD and anxiety symptoms, the identification of neural circuits underlying psychological constructs with relevance *across disorders* has been recommended. One construct that may be relevant for understanding pediatric OCD and anxiety disorders is cognitive control, given the difficulty that young patients experience in dismissing obsessions, compulsions and worry despite recognition that these symptoms are excessive and unreasonable. In this review, we examine findings from a growing body of literature implicating brain-behavioral markers of cognitive control in pediatric OCD and anxiety disorders, including before and after treatment. We conclude by suggesting that interventions designed to enhance the functioning of the task control circuits underlying cognitive control may facilitate brain maturation to help affected youth overcome symptoms.

Keywords

OCD; anxiety disorders; cognitive control; task control circuits; default mode network; triple network model; review

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1. Introduction

1.1. Obsessive compulsive and anxiety symptoms: Relevance of cognitive control?

Distinctions between obsessive compulsive disorder (OCD) and non-OCD anxiety disorders are codified by categorical diagnostic systems, but common underlying mechanisms are suggested by repetitive, distressing thoughts (i.e., obsessions, worries and fears) and related avoidance behaviors across presentations. The obsessions of OCD tend to be more intrusive, bizarre and ego-dystonic than the worries and fears of anxiety disorders which are typically provoked by a triggering stimulus or situation and involve more ego-syntonic, everyday concerns (1). However, these distinctions fall along a continuum in real-life patients, particularly children, complicating differentiation between OCD and non-OCD in clinical settings (2). Across this continuum, patients typically recognize obsessions, fears and worries as unreasonable and/or excessive (1), even at young ages (3). Yet, despite this recognition, patients find the repetitive thoughts of both OCD and non-OCD anxiety difficult to dismiss, leading to illness-related *avoidance behaviors*. In OCD, avoidance takes the form of compulsions or mental ritualizing to reduce obsession-related distress (e.g., hand-washing to alleviate anxiety about contamination, thinking a 'good' thought to counteract a bad one). In anxiety disorders, avoidance can take the form of physically avoiding a feared stimulus as in specific or social phobias, or deliberately engaging in worry to attain a sense of control over possible negative outcomes in generalized anxiety (4–7). Avoidance is driven by a desire to alleviate anxiety but, over the long term, reinforces repetitive negative thinking and associated distress (8). To interrupt this cycle, patients must *resist* the urge to avoid until obsession-, fear- and worry-related distress naturally decreases (9). Here, we suggest that *cognitive control* – the ability to flexibly adapt thoughts and behaviors – is the key mechanism by which patients resist avoidance behaviors to break the vicious cycle of illness (see Figure 1).

1.2. Cognitive Control: Definition, development, and focus on relevant subcomponents

Cognitive control is a set of capacities that support goal-directed behaviors in the face of difficulties (10). Common control processes include inhibitory control (withholding prepotent, but task-irrelevant responses), conflict processing (resolving competition between response options), task switching (flexibly adjusting between tasks), and working memory (holding information in mind while carrying out a task). In addition, error monitoring (detecting and adjusting to response errors) supports the adaptation of behavior to optimize performance across the various component processes that contribute to cognitive control. Factor analyses indicate these capacities are interrelated but separable (11). Among the sub-processes of cognitive control, inhibitory control and error-monitoring have been a focus of research into mechanisms underlying OCD (12) and have also received some attention in mechanistic studies of non-OCD anxiety disorders (13). Inhibitory control is invoked by tasks that require response inhibition or conflict processing (12), whereas error-monitoring occurs in tasks in which mistakes are made. Importantly, these processes interact to support cognitive control, with error-monitoring signaling for inhibitory control to optimize subsequent task performance (10).

Many neurofunctional models of cognitive control exist (10, 11, 14), and most implicate frontoparietal and cingulo-opercular networks (FPN, CON). These 'task control (TC)' networks have been identified and segregated through analysis of task-based and resting-state fMRI datasets from healthy individuals (15–18) (Figure 2). The FPN (sometimes referred to as the central executive network) consists of dorsolateral prefrontal cortex (dlPFC), intraparietal sulcus, midcingulate, and intraparietal lobe, whereas the CON (sometimes referred to as the salience network) consists of dorsal anterior cingulate cortex (dACC), anterior insula (frontal operculum), thalamus, and anterior prefrontal cortex (17). Both networks are engaged during cognitive control processes, including inhibitory control and error monitoring. However, these networks operate on dissociable timescales, with CON performing sustained monitoring of performance across the task, and FPN enlisted during specific instances of adjusting control (17, 19, 20).

Importantly, the CON and FPN interact reciprocally with the task-negative default mode network (DMN). DMN is comprised of posterior cingulate and ventromedial prefrontal cortices that are typically engaged during rest, mind wandering, and self-referential processes, and deactivated during tasks demanding cognitive control (21–24). Deficient recruitment of TC networks appears to couple with atypical engagement of DMN during cognitive control processing, leading to impaired performance (25).

Healthy development from early childhood through adolescence is characterized by improvements in cognitive control performance (faster reaction times, higher accuracy) that parallel the maturation of task control networks (26). Resting-state fMRI data indicate control networks are organized and stably integrated (i.e., functionally coupled) with other networks before adolescence but that integration involving the CON continues into adulthood (20, 27). Further, cross-sectional and longitudinal data suggest regions within the DMN become increasingly integrated (28–30) and segregated from TC regions over development (31, 32). Thus, the continued enhancement of CON integration as well as increasing segregation between TC and default mode regions may support the maturation of cognitive control processes over healthy development.

An electrophysiological marker of CON function sensitive to development is the error-related negativity (ERN, 33) an index of dACC-based error-monitoring functions (34, 35). The ERN is observed in children as young as 3 years old (36), and increases in amplitude with age, being largest among healthy adults (37, 38), consistent with the gradual development of neural substrates of cognitive control (26). Larger ERN is typically associated with better performance on cognitive control tasks (39, 40), consistent with improvements in behavioral performance with development (41). Longitudinal data suggest increasing dACC-indexed CON activation to errors mediates improvements in inhibitory control performance from 8 to 26 years (42) while activation of FPN regions remains unchanged or decreases with age, suggesting developmental changes in the control functions of the FPN and CON. Thus, age-related increases in ERN magnitude may track the increasing sophistication of CON performance-monitoring functions in relation to FPN capacity for adjusting control (17, 27). Indeed, the dACC – a critical hub within adult CON and one of the main generators of the ERN (33) – is more integrated in the FPN in young

children, but gradually segregates from FPN and consolidates within CON by adulthood (29).

1.3. Cognitive Control in youth OCD and anxiety disorders: A frame for reviewing the evidence

Here, we focus on the inhibitory control and error-monitoring subcomponents of cognitive control that have received the most attention in the broader literature and our own work on pediatric OCD and anxiety disorders. Further, we consider OCD across symptom clusters and the pediatric anxiety disorders across diagnostic categories (i.e., social, separation and generalized anxiety disorders), consistent with other clinical (43, 44) and neuroimaging research (45) and the commingling of OCD and anxiety symptoms in early development (i.e., 60% of children with OCD have a comorbid anxiety disorder; 2, 46–48). Finally, we focus our review on pediatric samples. Building from evidence linking brain-behavioral markers of cognitive control with pediatric OCD and non-OCD anxiety disorders, we suggest that altered development of TC networks may contribute to the emergence and early course of illness and could be targeted to help young patients overcome symptoms.

2. Brain-behavioral markers of cognitive control in pediatric OCD and anxiety disorders

2.1 Behavioral indices of cognitive control studies

Pediatric OCD.—Deficient response inhibition has long been posited in OCD, given patients' inability to suppress inappropriate thoughts and compulsive behaviors (49). Indeed, longer reaction times and more errors on tasks requiring inhibitory control are noted in affected youth and adults (12). In pediatric OCD, deficient response inhibition is most consistently evident on anti-saccades tasks (50, 51). By contrast, a meta-analysis of performance across a wider variety of cognitive control sub-processes revealed largely equivalent performance between OCD and healthy children (52).

Pediatric anxiety disorders.—Problems with executive functions (distractibility, difficulties concentrating) are included in the symptom criteria of many anxiety disorders, suggesting deficits in cognitive control. However, findings from behavioral studies of "cold" cognitive tasks in pediatric anxiety disorders are mixed. In contrast to OCD, some theorists even propose that anxiety may be associated with *enhanced* response inhibition, consistent with the behavioral inhibition risk factor (53). Despite some evidence for enhanced response inhibition in pediatric anxiety disorders (54, 55), other work shows no behavioral differences compared to healthy children (56–60). On the other hand, performance deficits during other cognitive control sub-processes (e.g., working memory and set shifting) have been demonstrated (61). Methodological (e.g., sampling, task parameters), analytic (e.g., covariates such as ADHD symptoms), and developmental processes likely contribute to discrepant findings in the literature (62).

2.2. Task control network function

Accumulating research demonstrates alterations of CON and FPN function in adults with OCD (12, 63–67) and non-OCD anxiety disorders (13, 68, 69) that may couple with a failure to deactivate the DMN during cognitive control processes (68–73). Given the role of the DMN in self-referential, emotive processes, atypical engagement of this network could underlie the intrusive, distressing thoughts and worries experienced by patients, while failure to engage CON and FPN may associate with their inability to dismiss these thoughts and related avoidance behaviors as contextually inappropriate. Altered balance among these networks is consistent with the triple network model (74) whereby the CON interfaces between the DMN and FPN, acting like a switch modulating the attention and cognitive resources between self-referential thoughts, internal processes (i.e., DMN processes) and external goal-directed behavior (i.e., TC processes). While most of these findings come from studies of adult patients, research from our labs and others suggest the involvement of TC and default mode networks in pediatric patients. Acknowledging the need for longitudinal research directly comparing children with OCD and non-OCD anxiety disorders, we review cross-sectional evidence suggesting that the triple network model may be relevant for understanding the mechanisms underlying both illnesses from the earliest stages.

2.2.1. OCD—FMRI findings from adults with OCD demonstrate alterations in TC networks (64, 67, 75, 76), with meta-analysis providing strong evidence of CON hyperactivation during error-processing, and hypoactivation during inhibitory control (12). In pediatric OCD, varied findings across studies (77–80) may be due to the component control process studied, methodological choices (MRI acquisition parameters, data processing procedures) and samples (included ages, medication status, OCD severity, comorbidities). Indeed, we have demonstrated greater pMFC response to errors with older age (8–18 years, replicating prior report (77)) and lower OCD severity in pediatric patients, and with better performance in healthy, but not OCD-affected youth (78). Collectively, these findings raise the possibility that “hyperactive” CON response to errors may represent an adaptive response that normally facilitates task performance and, in pediatric OCD, develops with age to help patients control symptoms. Other fMRI data suggest atypical involvement of FPN and DMN during the engagement of control processes in pediatric OCD. In OCD-affected compared to healthy youth, evidence suggests FPN hypo-activation during error-processing (79, 81), cognitive conflict (77, 79), task switching (79, 82) and planning (83). Consistent with research in adult OCD, failure to deactivate the vmPFC region of the DMN during cognitive conflict is also reported in pediatric patients (80). Thus, pediatric patients seem to exhibit hypoactivation of FPN regions during cognitive control demands (both error processing and inhibitory control), and may also show DMN hyperactivation. By contrast, hypo- versus hyper-activation of CON during error-processing may relate to patient age, with hypoactivation more likely at younger ages and hyperactivation emerging from adolescence into adulthood.

2.2.2. Anxiety disorders—Deficient recruitment of prefrontal cortex during control processes may also relate to non-OCD anxiety in children and adults (13, 81, 84, 85) (Figure 2). Hypoactive dlPFC response to errors in pediatric patients with separation, social and/or generalized anxiety disorders, as well as those with OCD, suggests deficient recruitment

of FPN for behavioral adaptation across these diagnostic boundaries (81). Other work in pediatric anxiety disorders suggests differential associations between age (8–18 years) and error-related activation of CON and FPN regions (positive for anxious, negative for healthy youth) (45). These findings follow the same pattern as those from pediatric OCD (78) and could thus reflect an age-associated compensatory mechanism by which maturing task control networks are enlisted to mitigate symptoms in older OCD- and anxiety-affected youth. By contrast, in younger children (8–12 years), greater "overcontrol", an anxiety-related phenotype defined by cognitive inflexibility, perfectionism and an aversion to making mistakes, associates with less error-related dACC activation (86). Thus, *less* CON activation may relate to heightened levels of overcontrol in younger children, supporting a developmental model in which less error-related engagement of TC networks associates with greater propensity for anxiety at younger ages.

The bulk of neuroimaging research in pediatric anxiety disorders has examined the processing and regulation of response to emotional and/or threatening stimuli. While not designed to examine TC function, this work suggests an important role of TC networks in regulating threat responses. When studied categorically, patients with pediatric anxiety disorders, relative to healthy youth, exhibit altered recruitment of TC regions, such as vlPFC (87–91) and ACC (91–93). Reviewed elsewhere (94), this work suggests heightened amygdala reactivity to threat detection, reduced prefrontal cortical regulation of threat-related signals from amygdala and, depending on task, compensatory prefrontal cortical regulation of the amygdala when anxiety is less severe. Relatedly, when attention is directed away from threat, greater connectivity of task control regions such as vlPFC and ACC with limbic and/or subcortical regions (e.g., amygdala, parahippocampus/hippocampus, basal ganglia) associates with lower levels of anxiety (91, 93, 95). Collectively, these findings suggest that greater prefrontal-mediated regulatory control over threat processing may aid the suppression of anxiety symptoms.

2.2.3. Error monitoring and the ERN in OCD and anxiety disorders—Larger ERN is demonstrated in adults with OCD and anxiety disorders compared to healthy individuals (96–98); however, the direction of ERN-anxiety associations may shift at younger ages. When studied dimensionally, a *smaller* ERN was marginally (trend-level) associated with higher levels of anxiety in younger children (8–10 years) whereas the more adult-like pattern of larger ERN was demonstrated in older anxious children (11–13 years; 99). This pattern is consistent with evidence from a community sample of 5–7 year-olds in which a smaller ERN was associated with greater separation anxiety symptoms (58). Other work found a smaller ERN with more anxiety at 4–7 years of age, and a larger ERN with more anxiety (i.e., adult-like pattern) at 7–9 years of age, but only among girls (57). The possible shift of ERN-anxiety relations in childhood is further supported by longitudinal work showing more fearful temperament at age 3 to associate with smaller ERN among 6-year-old children, but with larger ERN when children were re-assessed at aged 9 (40). By contrast, when anxiety was examined categorically, six-year-olds who met criteria for one or more anxiety disorders exhibited larger ERN compared to healthy children (i.e., adult-like pattern; 99).

The functional significance of developmentally-sensitive ERN-anxiety associations remains poorly understood. We hypothesize that low levels of ERN-indexed cognitive control in younger children may leave early anxiety symptoms unchecked, whereas the reversal of this relationship at older ages may reflect a compensatory process by which increasing neural capacity for cognitive control is leveraged to maintain adequate performance on task (100) and/or reduce anxiety symptom severity (101). The latter possibility aligns with the insight that is characteristic in patients with pediatric OCD and anxiety disorders, and tends to increase with age (102). That is, patients may correctly detect obsessions, worries and fears as "thinking errors" but, due to immature neural substrate for cognitive control, are unable to dismiss these to move on to more adaptive, contextually appropriate behaviors. As patients age, maturation of CON-based error-signaling could help to mitigate symptoms, as suggested by fMRI research in pediatric OCD (78), but not fully resolve illness due to residual deficits of neural substrate for inhibitory control (12). Alternatively, given evidence that worry/anxious apprehension rather than fear symptoms drive associations of larger ERN with greater anxiety in adults (97), the reversal of ERN-anxiety associations in children may stem from the greater prevalence of fear symptoms (e.g., phobias) at younger ages (103). Thus, extant literature raises the possibility that ERN-anxiety associations may shift with age, gender, symptom severity and symptom type.

2.2.4. Atypical TC development in OCD and anxiety disorders?—In general, children with less mature task control networks seem to have less capacity for cognitive control and are therefore more likely to find a given task more difficult (lower accuracy, slower reaction times at younger ages). Moreover, clinically affected patients may be more likely to exhibit TC network hypoactivation at younger ages, when TC networks are less developed, possibly in association with the emergence of symptoms. By contrast, adolescent patients may be more likely to show a different pattern of CON and FPN alterations relative to healthy youth. Based on the literature reviewed, we suggest that brain maturation enables compensatory error-related CON engagement relative to persistent FPN hypoactvation during inhibitory control in the presence of persistent illness. We thus recommend that future, longitudinal fMRI research assess both error- and inhibitory control-related functioning of TC networks in youth with OCD and anxiety over time, considering main effects and interactions between age, performance and symptom severity on these brain functions. Ultimately, such work may pave the way for developmentally sensitive therapies to modulate TC circuits and reduce or prevent childhood onset illness.

2.2.5. TC networks as predictors of treatment response—Brain-behavioral deficits in cognitive control in pediatric OCD and anxiety disorders raise the possibility that clinical trial research incorporating measures of TC function may generate clinically useful predictors of treatment response and elucidate mechanisms underlying treatment-induced symptom reduction. Much of this work has been conducted in adult patients, with some evidence of increased activity after CBT and pharmacological treatment in TC networks during cognitive processing in OCD (104) and during the regulation of threat response in non-OCD anxiety disorders (105). Below, we focus on task-based fMRI, resting-state connectivity and structural findings from treatment studies that implicate TC networks in pediatric patients.. Collectively, the findings reviewed suggest that, in young patients, more

'mature' TC function may predict better treatment response and that these circuits might become more efficient when treatment is most effective.

OCD.: In pediatric OCD, better CBT response associates with increased pre- to post-CBT activation of dlPFC, dACC/pre-supplementary motor area and premotor cortex during cognitive conflict (77) and dlPFC and parietal cortex during planning (83), suggesting that CBT may reduce symptoms by increasing TC capacity for cognitive control. In adolescent and adult patients, pre-CBT engagement of the CON (ACC node) during cognitive conflict predicted better CBT outcomes across age groups (106). Other findings from adults with OCD show that greater conflict-related CON and DMN activation during the resolution of cognitive conflict on a Simon task predicts better response to CBT (107). Collectively, these data suggest greater TC network responsivity to cognitive control demands may identify patients who are able to benefit from CBT. Moreover, given that TC activation typically couples with DMN deactivation during cognitive control (21–24), patients who are better able to engage the CON and FPN may require less DMN suppression to meet the cognitive control demands required by CBT (i.e., resisting performing rituals when exposed to OCD-triggering stimuli; 107). Further, reduced FPN-DMN resting-state connectivity was detected in OCD-affected compared to healthy youth, with less altered (i.e., less reduced) connectivity predicting better CBT response in patients (108). In the same sample, reduced cortical thickness in FPN regions and fewer diffusion-weighted MRI streamline counts (less anatomical connectivity) between CON regions predicted CBT response (107). Given the synaptic pruning of these regions with advancing age (109), these data suggest that more advanced structural maturation of TC networks may underlie the capacity of young patients to benefit from CBT.

Anxiety.: A growing body of work suggests that treatment outcomes in the pediatric anxiety disorders also depend on the engagement of TC networks, albeit during tasks designed to test the regulation of emotion. For example, when directly attending to threatening faces (explicit threat processing), greater activation in dlPFC and vlPFC predicted greater response to CBT and SSRI treatment in patients with mixed pediatric anxiety disorders (110). By contrast, when diverting attention from threatening faces to attend to other, non-emotional stimuli (implicit threat processing), *less* activation of the dorsal ACC and dorsomedial PFC predicted better treatment outcomes (111). Other work has shown pre- to post-treatment with CBT and/or SSRI increases of activation in the rostral ACC (112) and vlPFC during explicit threat processing in anxiety-affected adolescents (113). These converging lines of evidence in youth with clinically-significant anxiety suggest that those with greater TC engagement during direct appraisal of threat may be most likely to benefit from treatment, whereas those with pre-existing functional deficits of TC networks during implicit fear processing may have more to gain from treatment, presumably via increased treatment-related TC engagement to regulate response to indirect threat.

3. Future Directions

3.1. Opportunities for clinical translation

Collectively, the extant literature suggests that TC network alterations in pediatric OCD and anxiety could be targeted to enhance cognitive control and thereby help young patients to overcome symptoms. Given that TC networks are still developing during childhood and adolescence (20, 27, 31, 32), an early intervention such as cognitive control training (CCT) that is targeted to more plastic TC networks may facilitate the maturation of these systems. Indeed, younger age in pediatric OCD patients associates with better response to CBT (114) --- a therapy linked to TC network function (106, 108). In studies testing CCT effects in healthy children, younger age predicts greater transfer to distal cognitive domains (i.e., improved performance on non-trained cognitive tasks; 115).We posit that CCT could serve to increase both CON-mediated error signaling and FPN-based inhibitory control function in youth with OCD and anxiety disorders, thereby helping resolve symptoms.

Brain indices of cognitive control have not been specifically targeted for the treatment of pediatric OCD or anxiety disorders; however, prior work suggests that CCT can enhance activation of the TC networks in response to increasing cognitive demands (116–119) *and* resolve neurocognitive insufficiencies observed in other patient groups (118, 120, 121). For example, four weeks of a computer-delivered cognitive training “game” has been shown to improve behavioral capacity for cognitive control, increase TC network activity and ameliorate cognitive decline in older adults (118). Further, an adaptation of the same intervention, styled as a fun and engaging video game, improves performance on non-trained cognitive tests and reduces attention deficit hyperactivity symptoms in children, suggesting transfer to functionally meaningful behaviors in the “real world” (120–122). Interestingly, in a clinical trial of adolescents with anxiety disorders, CCT had similar benefits as CBT in reducing anxiety severity (123).

Extending from this work, we hypothesize that CCT-induced increases in brain-behavioral capacity for cognitive control may help young patients resolve interference between distressing, repetitive thoughts (i.e., obsessions, fears and worries) and dismiss prepotent, but contextually inappropriate avoidance responses in favor of more adaptive behaviors. CCT could serve to augment CBT effect by “priming” the TC-based cognitive control capacity that the reviewed literature suggests is necessary for patients to successfully engage in, and thus benefit from currently available treatments (e.g., CBT). Alternatively, it is possible that CCT could serve as a stand-alone treatment for pediatric OCD and anxiety disorders if, as we suggest, cognitive control is needed by patients to break the vicious cycle of illness (i.e., resist avoidance behaviors to engage with fears).

3.2. Limitations

Discrepancies across the existing literature are likely due, in part, to methodological differences, thus we encourage efforts to employ consistent techniques across future studies. For example, task-based, resting-state and structural MRI studies often use regions of interest or parcellations to examine specific areas of the brain. No clear cut “best” parcellation of the brain exists, and different atlases include, for example, the CON with

the salience and ventral attention network as one network (e.g., the 7-network solution from 124) while others separate these three networks into distinct entities (e.g., 15, 125). Some atlases describe putative functional brain areas (126) while others describe larger scale functional networks based on connectivity patterns (15, 124). Future studies might apply several of these parcellation atlases (124, 125), reporting results from one as primary while also including results for others as supplemental material to facilitate comparison with other studies. Other important technical considerations are choice of fMRI tasks used, MRI pulse sequences, and data processing methods; development of standard methodology is likely to improve replicability of findings. Critically, poor test-retest reliability in both fMRI and ERP research limits reproducibility across studies (127, 131), presenting a challenge that must be overcome if neuroimaging metrics are to guide treatment development or inform clinical management (e.g., treatment selection).

In addition, discrepancies between studies may relate to sample variation in age, task performance, medication status, comorbidities, and symptom severity --- factors shown to impact TC circuit function (26, 78, 128, 129). This is exacerbated by small sample sizes, which bias fMRI estimates (130), and is common among pediatric samples which have more motion artifact and data loss.. Future work could benefit from increased sample size and more data collected from each participant, potentially with novel tasks designed to capture both within- and between-subject effects (131). Large, diverse samples will be especially important for testing the premise that mechanisms of psychopathology can be revealed by understanding how brain-behavioral indices of constructs like cognitive control associate with the normal-to-abnormal range of psychopathology (132). Future work will also need to consider that different psychological constructs (e.g., cognitive control, threat sensitivity), each with unique underlying neurobiology, may combine in different ways in relation to patient-specific presentations (133). Finally, we must consider the implications inherent in using cross-sectional data to inform developmental changes in control processes (42, 128). Because the extant literature in of pediatric OCD and anxiety disorders is limited to cross-sectional studies, developmental changes in TC network functions should be tested in future longitudinal studies assessing error-monitoring, inhibitory control in relation to other relevant processes (e.g., threat responding) in the same patients over time, as OCD and non-OCD anxiety symptoms emerge and progress.

4. Conclusion

In sum, altered cognitive control and/or TC network function has been demonstrated in youth with OCD and anxiety disorders, suggesting TC-based cognitive control alterations may underlie expression of symptoms. However, extant cross-sectional correlational data are insufficient to establish casual roles of TC networks in disease pathophysiology. Yet, data suggesting that TC networks predict and change with treatment (107, 108, 111) implicates these circuits in the expression of OCD and anxiety disorder symptoms. To translate these lines of research into the treatment and prevention of illness, research must now establish interventions that modulate TC network function in the service of reducing symptoms, particularly at young ages when these circuits are more plastic (29, 134) and likely receptive to modulations that could alter symptom expression. Studies of CCT in pediatric OCD and anxiety disorders may be especially promising to assess whether changes in TC function

drive symptom reduction, potentially resolving the imbalance between TC networks and those responsible for introspective and emotion processing (DMN and amygdala). Moving forward, we envision an iterative process in which neuroscience-guided interventions, such as CCT, will be used to refine understanding of mechanisms underlying pediatric OCD and anxiety disorders, and then be adapted to treat and/or prevent the development of these disorders in young children.

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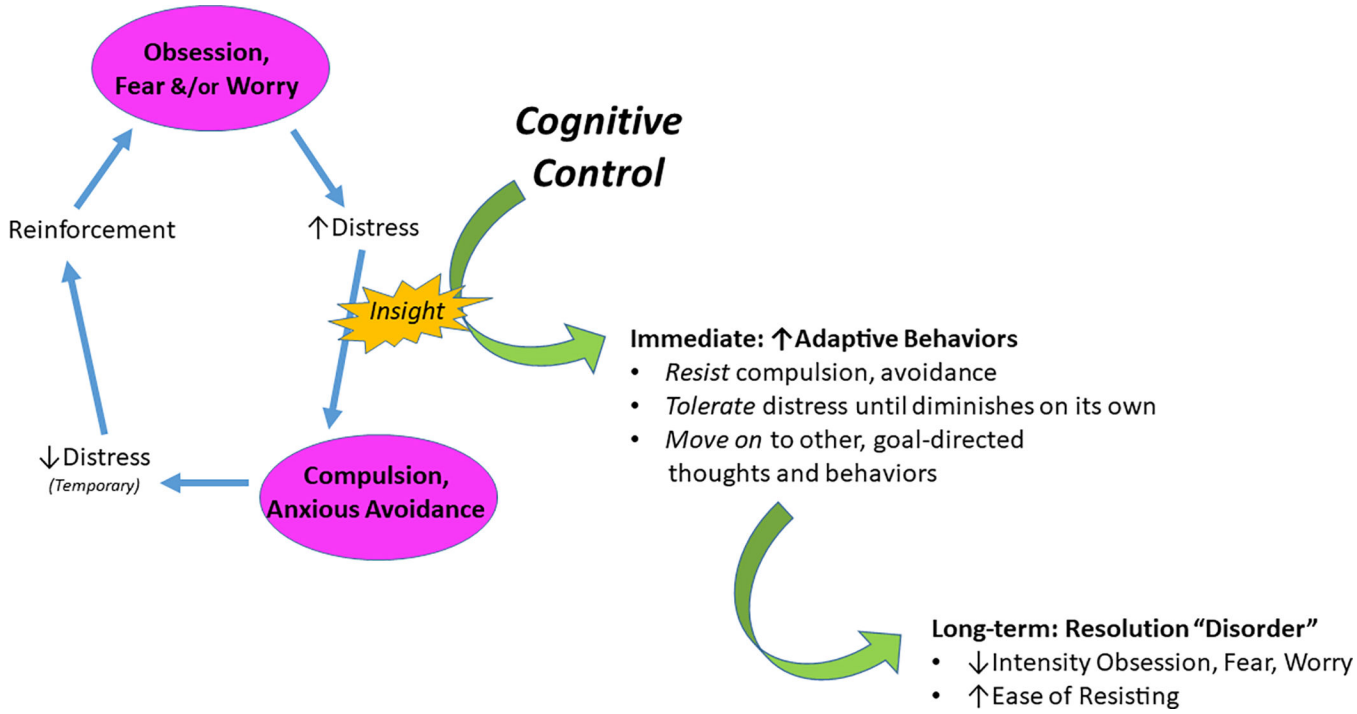

Figure 1.

We posit that *cognitive control* is a key mechanism by which patients with obsessive-compulsive (OCD) and non-OCD anxiety disorders resist the urge to act on fear that they recognize as excessive and unreasonable. By effectively recruiting cognitive control, patients are able to resist the avoidance behaviors (e.g., compulsions in OCD; escape or over-preparation in phobias or generalized anxiety) that reinforce obsessions, worry and fear. Thus, cognitive control is the core process that enables patients to build from insight that obsessions, fears and worries "do not make sense" to resist the pathological urge to avoid, and thereby break the vicious cycle of illness.

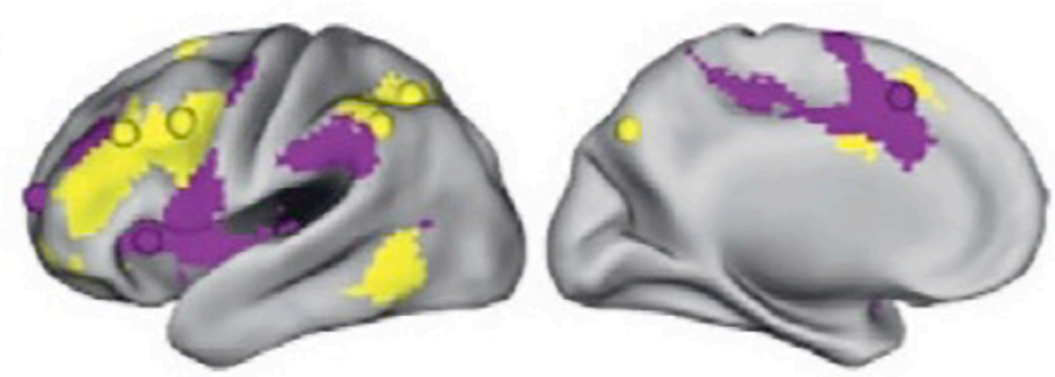

Figure 2.

Task control circuits: Cingulo-opercular and frontoparietal networks, adapted from 20. The colors in the figure identify the CON (purple) and FPN (yellow).

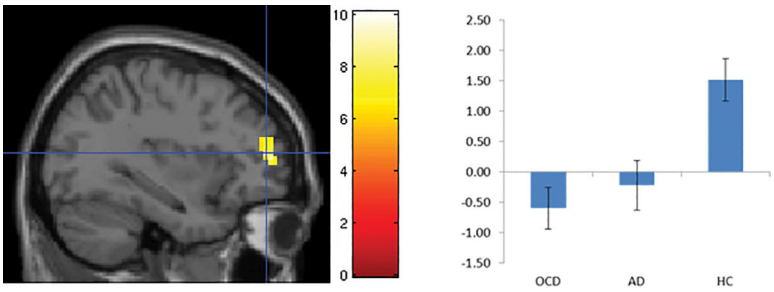

Figure 3.

Error-related hypoactivation of left dorsolateral prefrontal cortex in pediatric patients with obsessive compulsive (OCD) and anxiety disorders (AD) compared to healthy controls (HC), originally published in 81.