REVIEW

Neurobiological Circuits Regulating Attention, Cognitive Control, Motivation, and Emotion: Disruptions in Neurodevelopmental Psychiatric Disorders

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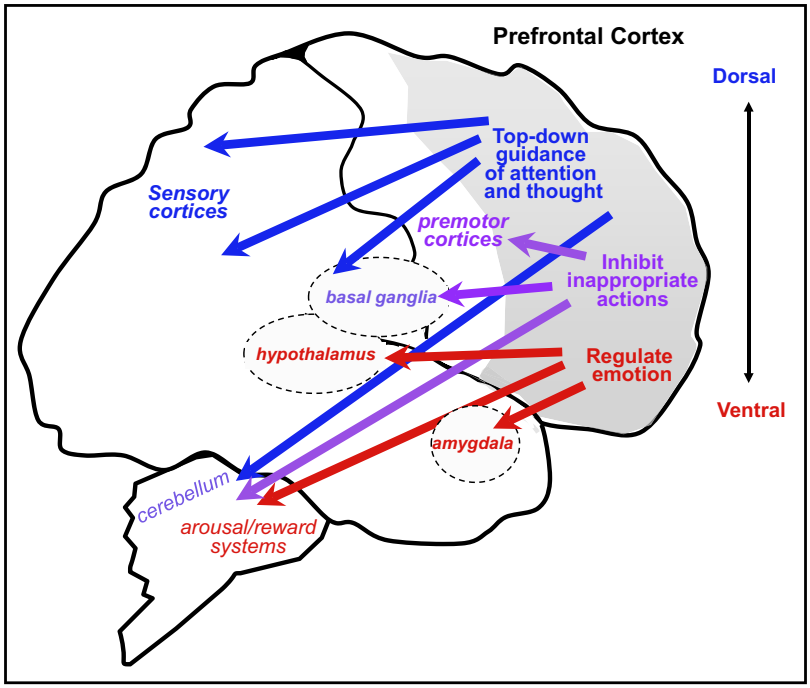
Objective: This article aims to review basic and clinical studies outlining the roles of prefrontal cortical (PFC) networks in the behavior and cognitive functions that are compromised in childhood neurodevelopmental disorders and how these map into the neuroimaging evidence of circuit abnormalities in these disorders. **Method:** Studies of animals, normally developing children, and patients with neurodevelopmental disorders were reviewed, with focus on neuroimaging studies. **Results:** The PFC provides "top–down" regulation of attention, inhibition/cognitive control, motivation, and emotion through connections with posterior cortical and subcortical structures. Dorsolateral and inferior PFC regulate attention and cognitive/inhibitory control, whereas orbital and ventromedial structures regulate motivation and affect. PFC circuitries are very sensitive to their neurochemical environment, and small changes in the underlying neurotransmitter systems, e.g. by medications, can produce large effects on mediated function. Neuroimaging studies of children with neurodevelopmental disorders show altered brain structure and function in distinctive circuits respecting this organization. Children with attention-deficit/hyperactivity disorder show prominent abnormalities in the inferior PFC and its connections to striatal, cerebellar, and parietal regions, whereas children with conduct disorder show alterations in the paralimbic system, comprising ventromedial, lateral orbitofrontal, and superior temporal cortices together with specific underlying limbic regions, regulating motivation and emotion control. Children with major depressive disorder show alterations in ventral orbital and limbic activity, particularly in the left hemisphere, mediating emotions. Finally, children with obsessive-compulsive disorder appear to have a dysregulation in orbito-fronto-striatal inhibitory control pathways, but also deficits in dorsolateral fronto-parietal systems of attention. **Conclusions:** Altogether, there is a good correspondence between anatomical circuitry mediating compromised functions and patterns of brain structure and function changes in children with neuropsychiatric disorders. Medications may optimize the neurochemical environment in PFC and associated circuitries, and improve structure and function. J. Am. Acad. Child Adolesc. Psychiatry, 2012;51(4):356–367. **Key Words:** prefrontal cortex ADHD, OCD, MDD, arousal

There is a remarkable convergence between basic neuroscience studies in animals and imaging studies in humans regarding the brain circuits regulating attention, cognitive control, motivation, and emotion. They show a dissociation of several fronto-striato-cerebellar circuitries that mediate these functions, differing in the precise localization of these functions within the prefrontal cortex and the basal ganglia, and their specific connections to limbic and parieto-temporal association cortices and the cerebellum. Furthermore, there is evidence for relatively late and progressive development of these fronto-cortical and fronto-subcortical "top–down" control systems between childhood and adulthood. Children with neurodevelopmental disorders show deficits in precisely these late developing fronto-cortical and fronto-subcortical circuitries. This article reviews the animal and human imaging literature that delineates these dissociated fronto-striatal circuitries and the functions they mediate, and provides examples of how these

FIGURE 1 The prefrontal cortex (PFC) regulates attention, behavior, and emotion through extensive network connections with other brain regions. Note: Dorsal regions (blue) subserve higher cognitive functions and regulate "top–down" attention through extensive projections to posterior cortical regions. In contrast, ventromedial PFC (vmPFC) regulates emotion through extensive projections to subcortical areas such as the amygdala, nucleus accumbens, and brainstem. In humans, the right inferior frontal cortex (IFC) is specialized for the inhibition of inappropropiate motor responses through projections to the basal ganglia. The PFC also has extensive connections with the cerebellar cortex via the pontine nuclei, which parallel projections through the basal ganglia. Thus, the PFC is positioned to orchestrate all aspects of behavior.



circuitries are compromised in specific neurodevelopmental disorders. We thus review a few very specific "model disorders" that are illustrative for abnormalities in these fronto-cortical and fronto-subcortical circuitries that mediate attention, cognitive control, motivation, and emotion. Thus we review the neuroimaging literature of attention-deficit/hyperactivity disorder (ADHD) as an example of a disruption of inferior fronto-striatal networks of cognitive control and attention; pediatric major depression (MDD) as a model for fronto-limbic disruption mediating emotion control; pediatric obsessive-compulsive disorder (OCD) as a model for disruption of both orbito-frontal inhibitory and fronto-limbic anxiety mediating networks; and conduct disorder (CD) as a model disorder for deficits in fronto-limbic circuits of motivation. A delineation of the dissociated neurofunctional circuitries and their mediating functions based on the basic neuroscience literature, together with the description of abnormalities of these circuitries in these very specific model neurodevelopmental disorders, will hopefully help with a better understanding of the abnormalities and the development of more targeted treatments for these disorders.

METHOD

The ISI Web of Science and Pubmed were searched using the following search criteria from 1966 onward: "prefrontal cortex", "basal ganglia circuits", "cerebellar circuits", "catecholamines", "serotonin", "neurotransmitters", "ADHD/CD/OCD/MDD and MRI/fMRI", "Methylphenidate/Atomoxetine and MRI/FMRI", "SSRI and MRI/FMRI".

Brain Circuits Regulating Attention, Cognitive Control, Motivation, and Emotion

The prefrontal cortex (PFC) is a highly evolved cortical area that is essential for regulating attention, cognitive control, motivation, and emotion. As shown in Figure 1, distinct regions of PFC regulate this spectrum of functions, with the dorsolateral PFC (DLPFC) regu-

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