The Prefrontal Cortex Is Out of Tune in Attention-Deficit/Hyperactivity Disorder

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Issue: *The different symptoms of attention-deficit/hyperactivity disorder are hypothetically linked to inefficient information processing in various areas of the prefrontal cortex.*

Pyramidal neurons, shaped like a triangular pyramid, are key regulators of neuronal networks in the prefrontal cortex.[1–3] These cortical networks send messages that can be either accepted as signals or ignored as noise.[1–4] When the prefrontal cortex is functioning properly, pyramidal neurons within these networks can tell the difference between signals and noise. However, in attention-deficit/hyperactivity disorder (ADHD), pyramidal neurons seem to have problems distinguishing signals from noise.[1,2] Another way to state this is that pyramidal neurons and their prefrontal cortex networks are "out of tune" (see Figures 1 and 2).

Theoretically, such problems with information processing in prefrontal cortex may be caused in part by imbalances in various neurotransmitters.[1–7] Norepinephrine, for example, may be particularly important in enhancing signals, whereas dopamine may be particularly important in reducing noise.[1,2,4–7] (These concepts were discussed in the last Brainstorms.[7]) In this issue, we discuss the potential link of dopamine and norepinephrine imbalances at key neurotransmitter receptors that result in problems differentiating signals from noise in prefrontal cortex in ADHD. We also discuss where in the prefrontal cortex specific symptoms of ADHD may be hypothetically mapped (see Figure 3).

Take-Home Points

- In ADHD, pyramidal neurons in the prefrontal cortex are hypothetically "out of tune," causing either deficient signals, excessive noise, or both.
- Specific malfunctioning brain areas within the prefrontal cortex theoretically mediate the various symptoms of ADHD.
- Inefficient information processing in related areas of prefrontal cortex may also cause the specific symptoms of the common comorbidities of ADHD, such as bipolar disorder, anxiety disorders, conduct disorder, and oppositional defiant disorder.

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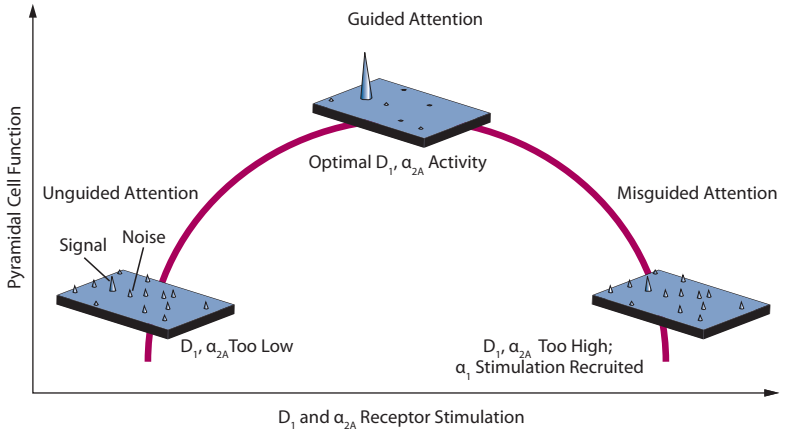
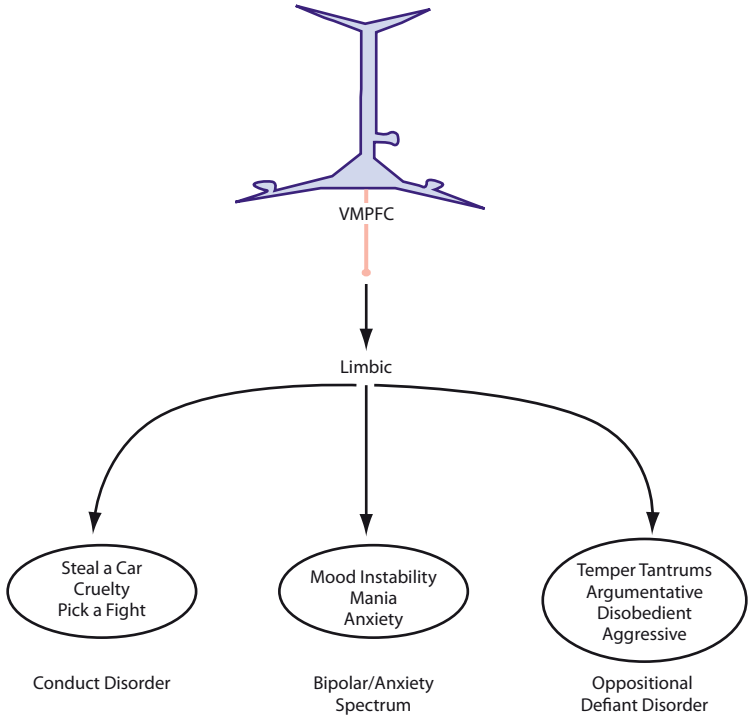
Figure 1. Maladaptive Signal-to-Noise Ratios (Deficient Signals or Excessive Noise) in ADHD May Cause "Out of Tune" Cognitive Function



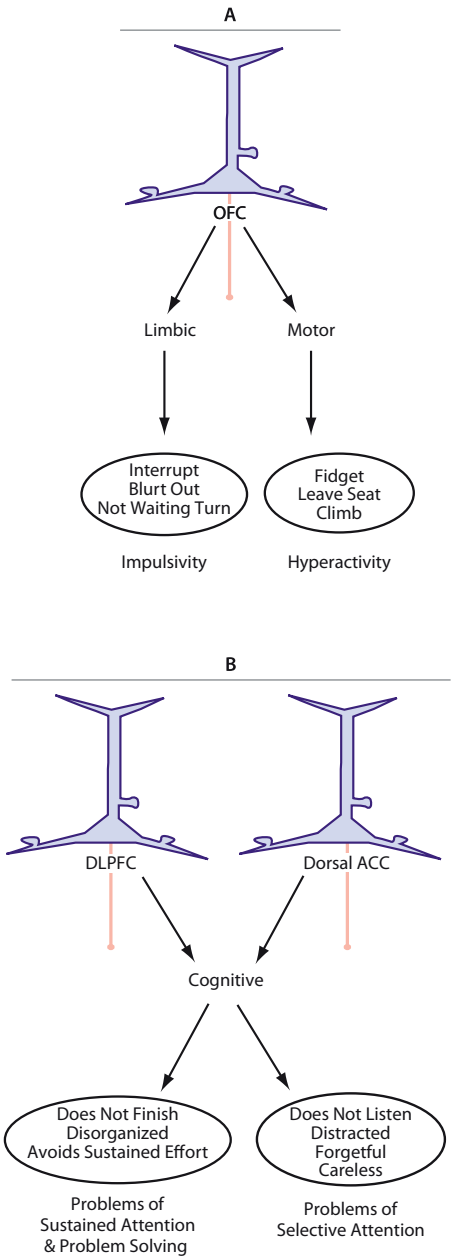
In attention-deficit/hyperactivity disorder (ADHD), adequate stimulation of dopamine D_1 and noradrenergic α_{2A} receptors in the prefrontal cortex is important.[1,2,4–7] As seen by the inverted U-shaped curve, too little stimulation of these receptors (not enough to cause a reaction, which yields unguided attention) or too much stimulation (so much reaching the system that it is overloaded and shuts down, thus attention is misguided) leads to maladaptive signal-to-noise ratios and therefore inadequate attention.[1,2,4] Pyramidal neuron function will be optimal (at the top of the curve) when stimulation of both receptor types is moderate, resulting in guided attention and reinforcement of the signal.[1,2]

Figure 3. Imbalances in Cortical and Limbic Networks of Prefrontal Cortex Can Result in a Wide Array of Comorbid Symptoms in ADHD or Other Disorders



ADHD can often be comorbid with other behavioral problems, especially in children.[1,2] Abnormalities in the ventromedial prefrontal cortical-limbic networks (VMPFC) are hypothetically involved in the aggressive and destructive symptoms of conduct disorder, the mood instability of bipolar disorders, the irrational fears of anxiety disorders, and the disobedient and oppositional symptoms of oppositional defiant disorder.[1,2]

Figure 2. Regional Problems of Prefrontal Cortex "Tuning" Result in Various Core Symptoms of ADHD



Different brain areas are hypothetically important in mediating the various symptoms of ADHD.[1,2] Alterations within the orbital frontal cortex (OFC) can theoretically lead to problems with impulsivity or hyperactivity (A). On the other hand, inadequate tuning of the dorsolateral prefrontal cortex (DLPFC) or the dorsal anterior cingulate cortex (dorsal ACC) can respectively lead to problems with sustained attention or selective attention (B).