Stahl's Illustrated | Chapter 1

Neurobiology, Circuits, and Genetics

Section 1: Symptoms and Circuits

In this chapter, the hypothetical pathophysiology underlying attention deficit hyperactivity disorder (ADHD) is discussed. Besides providing an overview of the main hypothesis underlying the symptoms of ADHD, such as problems with executive functioning, this chapter will also peruse old and new views on the environment-neurobiology interaction of this disorder. By giving a holistic view of the disorder, it will hopefully become clear that many different treatment options are available for every symptom of ADHD. Section 1 of Chapter 1 will focus on the symptoms of ADHD, and the circuits underlying these symptoms.

Deconstructing the Syndrome into DSM-IV Diagnostic Symptoms

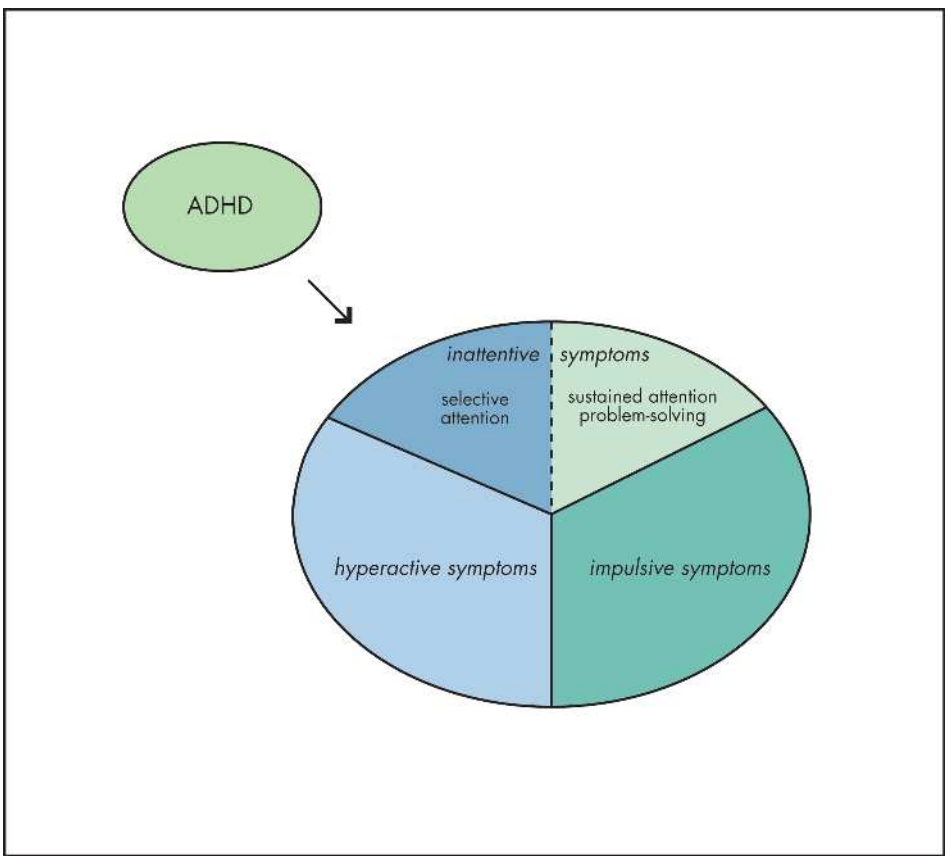
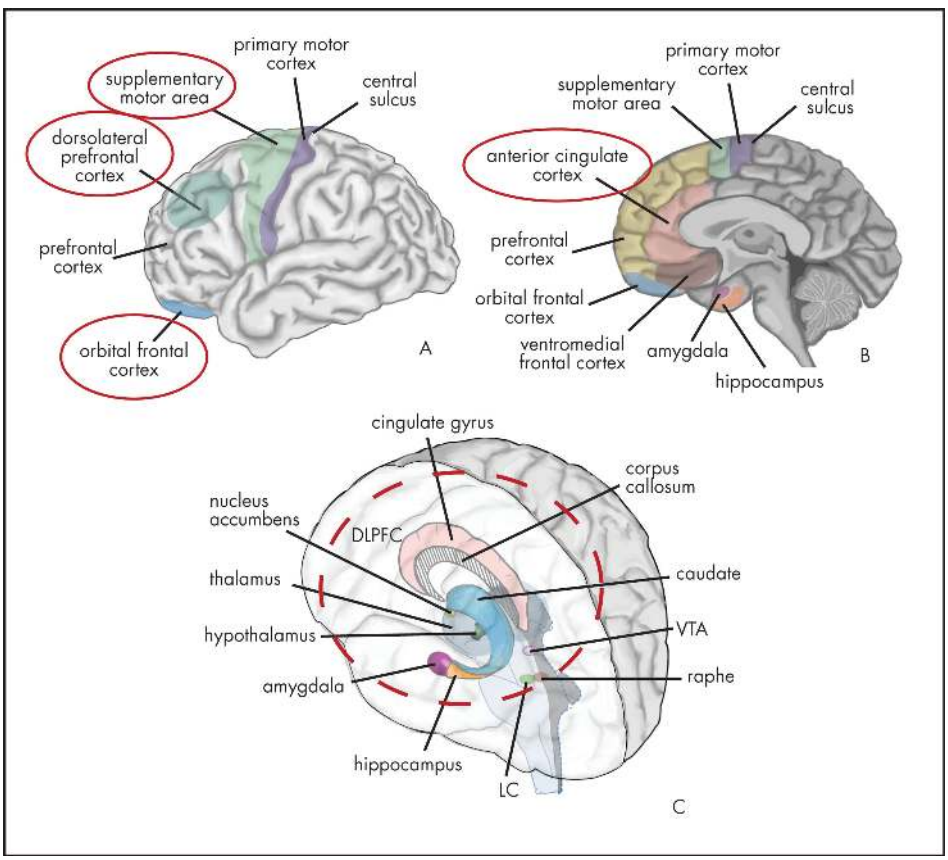


FIGURE 1.1. Attention deficit hyperactivity disorder (ADHD) is divided into three clusters of symptoms: hyperactive, impulsive, and inattentive. As each patient presents with a specific degree of impairment in these three categories, a patient can, according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV), be cast into the following subtypes: the predominantly inattentive type, the predominantly hyperactive-impulsive type, and lastly the combined type, which is also the most frequent one.

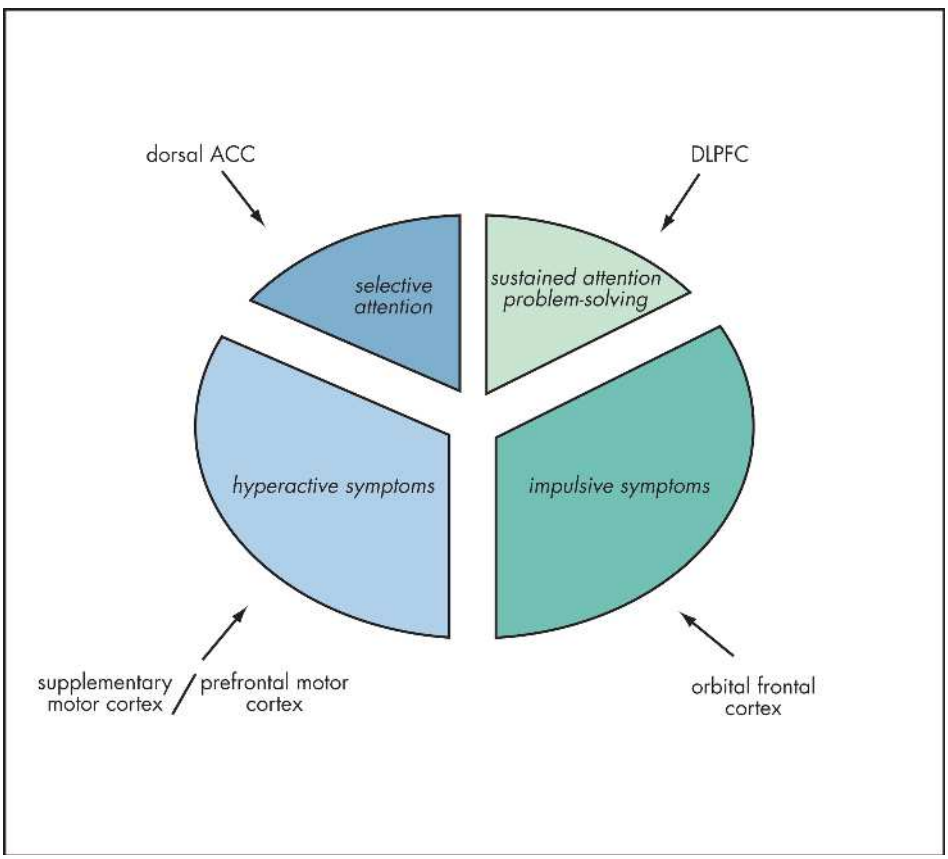
Important Brain Areas in Executive Function and Motor Control



LC: locus coeruleus; VTA: ventral tegmental area

FIGURE 1.2. To understand better the underlying pathophysiology of ADHD, it is important to know which brain circuits are affected and how they can impact other processes. At least four different brain regions (red circles in A and B) are affected in ADHD, and may lead to altered functioning of their respective cortical-striatal-thalamic-cortical (CSTC) loops (dotted red circle in C, and Figures 1.4), impacting executive functioning and motor control.

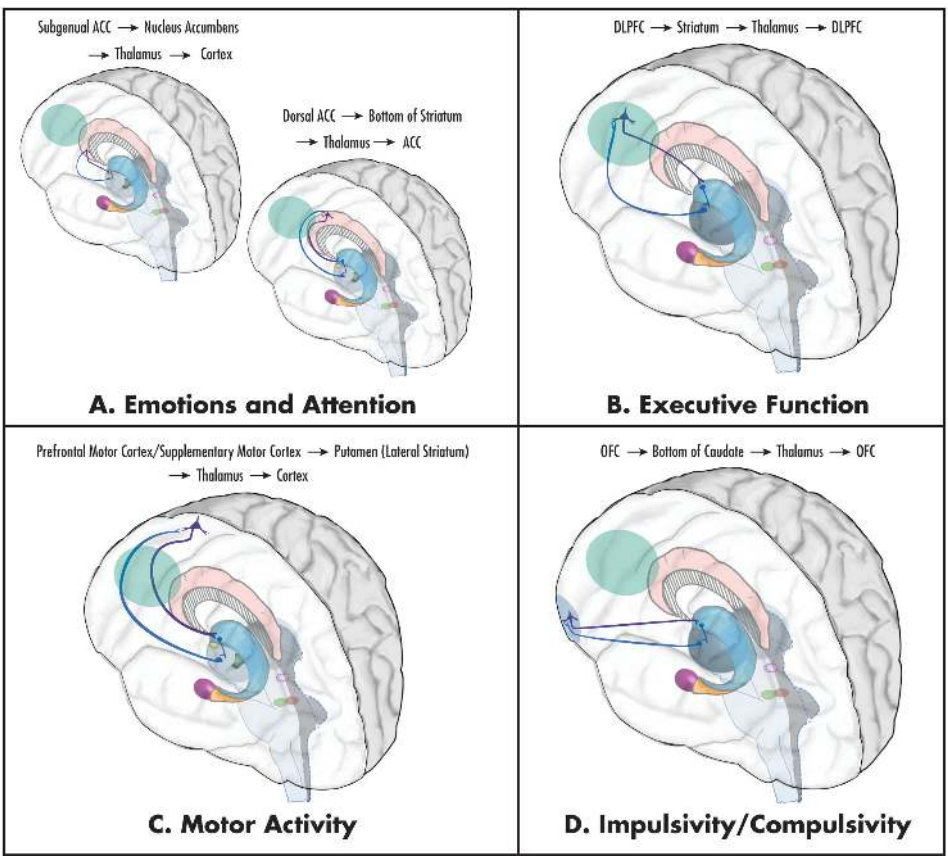
How Are Core Symptoms of ADHD Linked to a Malfunctioning Prefrontal Cortex?



ACC: anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex

FIGURE 1.3. Inefficient information processing in the brain areas shown in Figure 1.2 can hypothetically lead to the different symptoms of ADHD and other psychiatric disorders: malfunctioning of the dorsal ACC can result in problems with selective attention; malfunctioning of the DLPFC can result in problems with sustained attention; impairments in the supplementary motor cortex/prefrontal motor cortex can theoretically lead to symptoms of hyperactivity; impairments in the orbital frontal cortex can lead to impulsive symptoms. These various brain areas are part of a circuitry referred to as the cortical-striatal-thalamic-cortical loops, which are further explained in Figure 1.4.

Hypothetical Malfunctioning CSTC Loops in ADHD



ACC: anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex; NAcc: nucleus accumbens; OFC: orbital frontal cortex

FIGURE 1.4. (A) Emotions and attention are hypothetically regulated by the subgenual ACC–NAcc–thalamus loop and the dorsal ACC–bottom of striatum–thalamus loop, respectively. (B) Executive function is hypothetically regulated by the DLPFC–striatum–thalamus loop, and the prefrontal motor cortex–lateral striatum–thalamus loop hypothetically regulates motor activity (C). (D) Impulsivity and compulsivity are hypothetically regulated by the OFC–bottom of striatum–thalamus loop.

The N-Back Test

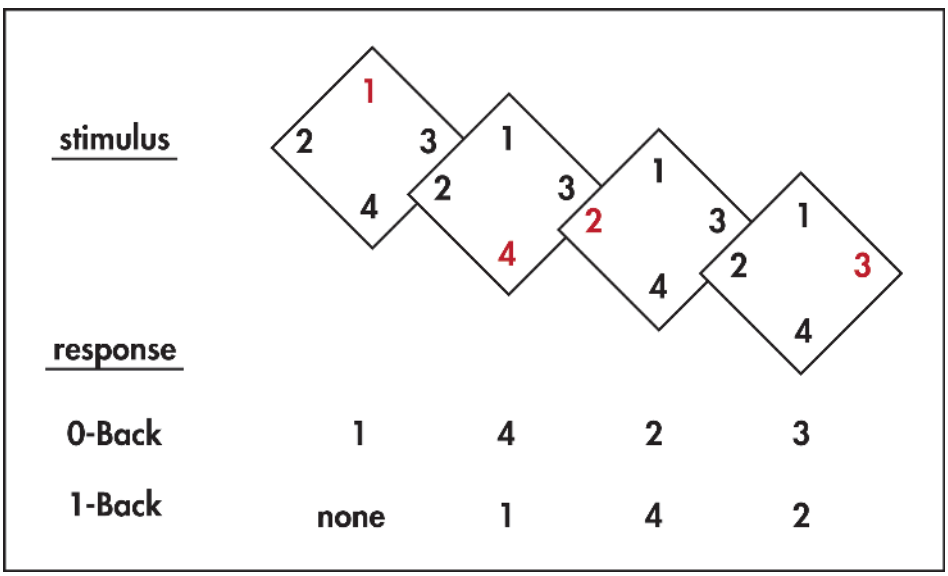


FIGURE 1.5. The N-Back test is used to assess executive function, especially sustained attention. In the 0-back variant, a participant looks at a number on the screen, and presses a button to indicate which number it is. In the 1-back variant, a participant only looks at the first number; when the second number appears the participant is supposed to press a button corresponding to the first number. Higher "N" numbers are correlated with increased difficulty in the test.

Assessing Sustained Attention and Problem-Solving With the N-Back Test

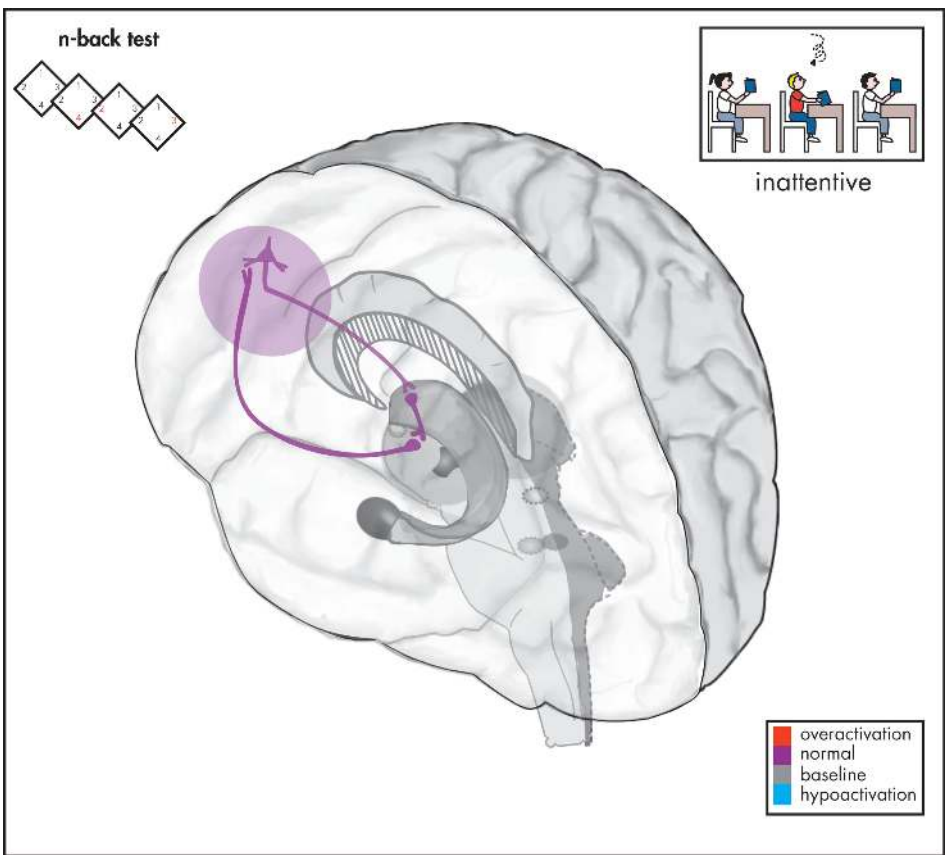


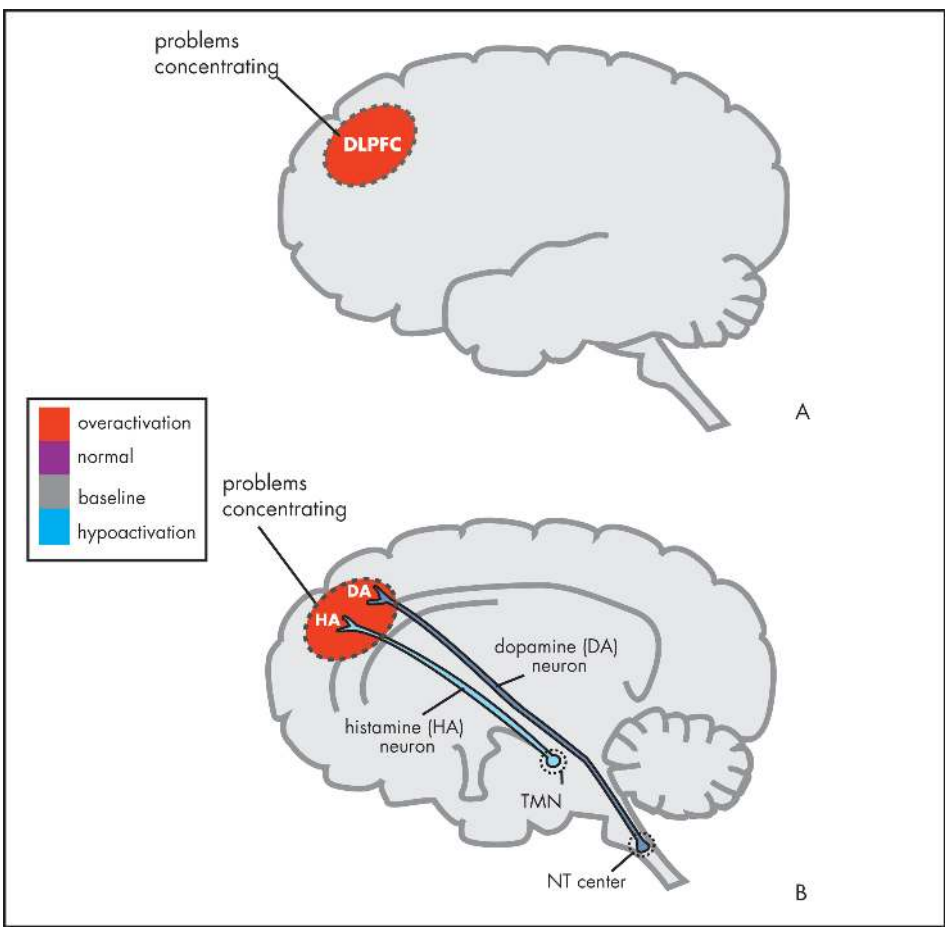
FIGURE 1.6. The level of activation of the dorsolateral prefrontal cortex (purple circle) can be assessed using the N-back test. As shown in Figure 1.4B, executive function, especially sustained attention, is hypothetically associated with the following CSTC loop: DLPFC–striatum–thalamus. Inefficient information processing within this loop would theoretically cause a person to lack sustained attention on a task and have problems with organization, follow-through, and problem-solving.

Symptom Overlap Among Many Psychiatric Syndromes

symptom	*psychiatric syndromes with the same overlapping symptoms*		
 problems concentrating	major depression	ADHD	narcolepsy

FIGURE 1.7. Concentration problems are symptoms of many disorders besides ADHD. The dimensional approach suggests to deconstruct psychiatric disorders into symptoms, and treat the symptoms rather than the disorder (see also Table 1.1).

From Circuits to Neurotransmitters



DA: dopamine; DLPFC: dorsolateral prefrontal cortex; HA: histamine; TMN: tuberomammillary nucleus; NT: neurotransmitter

FIGURE 1.8. Once a malfunctioning circuit has been exposed, the appropriate treatment can be selected based on the neurotransmitter system involved in that circuitry (A). For example, problems concentrating are hypothetically linked to the DLPFC, which is regulated by dopamine (DA) and histamine (HA), thus treatments affecting DA or HA neurotransmission could potentially improve concentration (B).

The Stroop Task

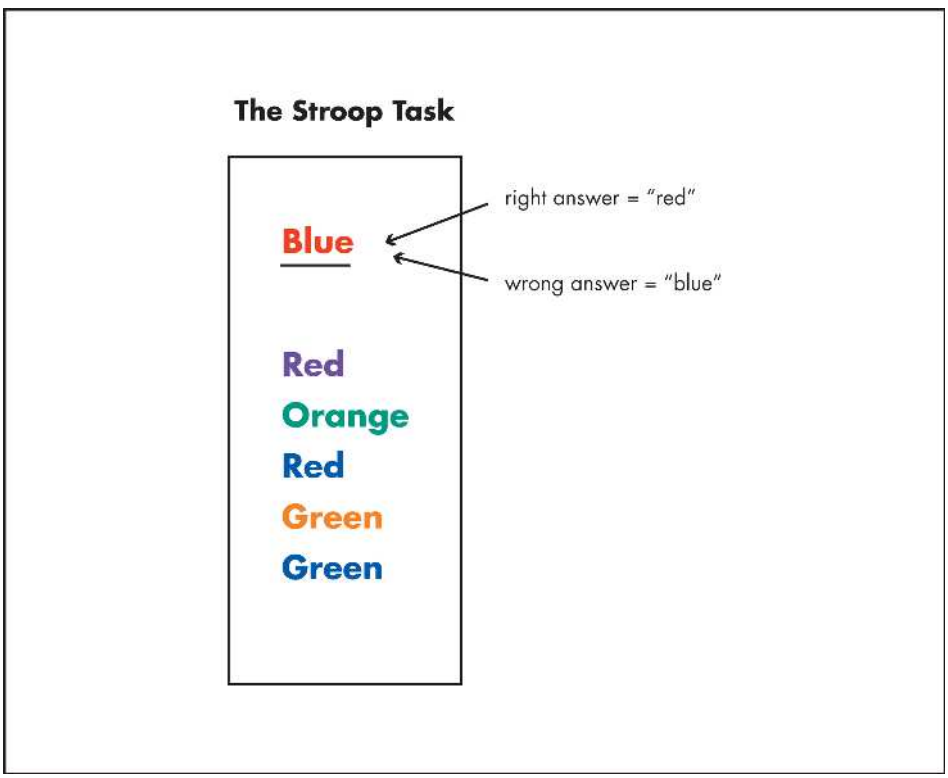


FIGURE 1.9. The Stroop task is used to assess selective attention, and requires the participants to name the color with which a word is written, instead of saying the word itself. In the present case, for example, the word "blue" is written in red. The correct answer is therefore "red," while "blue" is the incorrect choice.