be done in this area. Progress seems likely to depend in turn on a better theoretical understanding of the causes of the disorder and its possible heterogeneity.

Summary and Conclusions

Developmental coordination disorder (DCD) is a common form of learning difficulty that occurs in quite a severe form in around 5% of children. DCD also commonly co-occurs with a range of other disorders such as ADHD, dyslexia, language impairment, and autism. The problems of children with DCD seem to reflect basic problems in the development of brain mechanisms that control movement. It appears that risk factors operating to cause DCD include genetic susceptibility as well as environmental insults that may compromise brain development (being born prematurely is a powerful risk factor). At a cognitive level, we have argued that a likely cause of this disorder is a visuospatial perceptual deficit that in turn compromises the development of a sensorimotor map that relates "seen" positions to "felt" positions in space. In addition, it is likely that problems with systems responsible for balance may play an additional role in causing motor difficulties in some children with DCD. Studies of the treatment of DCD are in their infancy, but recent functional skill approaches suggest that these children can be helped to master key motor skills by appropriate training.

7

Attention Deficit Hyperactivity Disorder

Attention deficit hyperactivity disorder (ADHD) is a chronic, debilitating condition that, as its name implies, affects an individual's ability to control attention and behavior in an optimal and adaptive manner. The disorder often occurs together with the tendency to be overactive and impulsive and is frequently associated with educational underachievement, antisocial behavior, underperformance at work, and poor psychosocial adjustment.

ADHD has often been portrayed negatively by the media and there are many misconceptions surrounding its nature and etiology; while some have asserted that ADHD is "on the increase," others doubt its very existence. So unhelpful has this confusion been that a consortium of scientists signed an International Consensus Statement in 2001. According to this statement, "ADHD involves a serious deficiency in a set of psychological abilities and ... these deficiencies pose serious harm to most individuals possessing the disorder" (Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001, p. 89). Indeed, as children with ADHD grow up, they are more likely than their peers to experience teenage pregnancy, have multiple car accidents, and to suffer depression and personality disorders. Moreover, although psychological and pharmacological interventions are known to help the condition, less than half of those affected receive any form of treatment.

We begin this chapter with a discussion of the nature and prevalence of ADHD and how it is usually assessed. We then outline what is known about how children learn to regulate their behavior and, within this framework, we consider theories of the possible causes of ADHD in which self-regulation appears to be lacking. In contrast to the other disorders considered in this book, progress in understanding ADHD has been heavily influenced by pharmacological studies, which have demonstrated the effectiveness of certain drugs for its treatment. This evidence in turn relates to ideas about the neurobiology of ADHD and, in particular, the roles of the frontal and prefrontal cortex and frontobasal circuits in the regulation of behavior.

ADHD: Definition and Prevalence

DSM-IV defines ADHD on the basis of elevated symptoms on two dimensions: inattention and hyperactivity/impulsivity. According to DSM-IV, children meet criteria for the disorder by having six or more symptoms of inattention, hyperactivity/impulsivity, or both. Thus, there are three main subtypes of ADHD: the primarily "hyperactive–impulsive" (HI) type, the primarily "inattentive" (IA) type, and the combined type (see Box 7.1). The most thoroughly researched is the combined subtype, and less is known about the primarily hyperactive–impulsive and primarily inattentive subtypes. It is important to note that each of these subtypes may show subclinical symptoms relating to the other impairment (inattention or hyperactivity/impulsivity). Gomez, Harvey, Quick, Scharer, and Harris (1999) studied the relationships between the different symptoms used to diagnose ADHD using the DSM-IV criteria in a large (1275) representative sample of children ranging in age from 5 to 11 years. They found that a two-factor model that separated hyperactivity/impulsivity from inattention was much better than a one-factor model that combined all items. However the two factors correlated quite strongly (around .7). This study found quite low rates for the different subtypes: IA (1.6%), HI (0.2%), and combined (0.6%), giving an overall rate of 2.4% when the subtypes were combined.

Other terms that may be seen in the literature referring to ADHD include ADD (now an outdated term) and "hyperactive" and hyperkinetic disorder (ICD-10; World Health Organization, 1992). The ICD-10 category of hyperkinetic disorder requires both hyperactivity and inattention (i.e., symptoms of the combined type of ADHD) and it also requires that such symptoms are displayed at a rate that is sufficiently high to reach a diagnosis in more than one setting (i.e., typically at both home and school). Thus the diagnostic criteria for hyperkinetic disorder (ICD-10) are more stringent than those for ADHD using the DSM-IV criteria.

Formally the diagnostic criteria for ADHD in DSM-IV require that symptoms of inattention or hyperactivity should be displayed (to some degree) in at least two settings (e.g., home and school), and have persisted for at least 6 months to a degree that is maladaptive and out of line with age expectation. Signs of inattention include difficulty in focusing or maintaining attention, failing to listen carefully or to follow instructions, distractibility, organizational difficulty, and forgetfulness. Signs of hyperactivity or impulsivity relate more to overt behavioral tendencies such as fidgeting, being "on the go" all the time, talking excessively, blurting-out answers, and interrupting other people when speaking to them. Normally, some of the signs should have been recognized before the age of 7 years and there must be clear evidence of significant impairment in social, academic, or occupational functioning. The definition of hyperkinetic disorder requires the presence, simultaneously, of attention deficit, hyperactivity, and impulsivity in more than one situation and therefore this diagnosis is closest to that of the combined type of ADHD.

Box 7.1 ADHD: Diagnosis and Symptomatology (adapted from *http://www.nimh.nih.gov/health/publications/adhd/symptoms.shtml*)

There are three subtypes of ADHD: the predominantly hyperactive–impulsive type; the predominantly inattentive type; and the combined type (both inattentive and hyperactive–impulsive symptoms).

Hyperactivity–impulsivity

Hyperactive children always seem to be "on the go" or constantly in motion. They dash around touching or playing with whatever is in sight, or talk incessantly. Sitting still at dinner or during a school lesson or story can be a difficult task. They may squirm and fidget in their seats or roam around the room. Or they may wiggle their feet, touch everything, or noisily tap their pencil. Hyperactive teenagers or adults may feel internally restless. They often report needing to stay busy and may try to do several things at once.

Impulsive children seem unable to curb their immediate reactions or think before they act. They will often blurt out inappropriate comments, display their emotions without restraint, and act without regard for the later consequences of their actions. Their impulsivity may make it hard for them to wait for things they want or to take their turn in games. They may grab a toy from another child or hit out when they are upset. Even as teenagers or adults, they may impulsively choose to do things that have an immediate but small payoff rather than engage in activities that may take more effort yet provide much greater but delayed rewards.

Some signs of hyperactivity–impulsivity are:

- feeling restless, often fidgeting with hands or feet, or squirming while seated;
- running, climbing, or leaving a seat in situations where sitting or quiet behavior is expected;
- blurting out answers before hearing the whole question;
- having difficulty waiting in line or taking turns.

Inattention

Children who are inattentive have a hard time keeping their minds on any one thing and may get bored with a task after only a few minutes. If they are doing something they really enjoy, they have no trouble paying attention. But focusing deliberate, conscious attention to organizing and completing a task or learning something new is difficult.

Box 7.1 *(cont'd)*

Homework is particularly hard for these children. They will forget to write down an assignment, or leave it at school. They will forget to bring a book home, or bring the wrong one. The homework, if finally finished, is often full of errors and erasures. Homework is often accompanied by frustration for both parent and child.

The DSM-IV gives these signs of inattention:

- often becoming easily distracted by irrelevant sights and sounds;
- often failing to pay attention to details and making careless mistakes;
- rarely following instructions carefully and completely losing or forgetting things like toys, pencils, books, or tools needed for a task;
- often skipping from one uncompleted activity to another.

Children diagnosed with the predominantly inattentive type of ADHD are seldom impulsive or hyperactive, yet they have significant problems paying attention. They may appear to be daydreaming, "spaced-out," easily confused, slow-moving, and lethargic. They may have difficulty processing information as quickly and accurately as other children. When the teacher gives oral or even written instructions, these children may have a hard time understanding what they are supposed to do and make frequent mistakes. Yet these children may sit quietly, unobtrusively, and even appear to be working but not fully attending to or understanding the task and the instructions.

These children do not show significant problems with impulsivity and overactivity in the classroom, in the playground, or at home. They may get along better with other children than the more impulsive and hyperactive types of ADHD, and they may not have the same sorts of social problems so common with the combined type of ADHD. Often their problems with inattention may be overlooked, but they need help just as much as children with other types of ADHD who cause more obvious problems in the classroom.

According to DSM-IV the prevalence rate for ADHD is around 3–5% of children of primary school age. A recent study involving a representative sample of more than 10,000 children in the UK (Meltzer & Gatward, 2000) indentified children at risk of hyperkinetic disorder based on rating scales and structured interviews, and arrived at a population estimate of 1.4%. As noted earlier, the criteria for hyperkinetic disorder are more stringent than the DSM-IV criteria for ADHD, and as such hyperkinetic disorder can be considered a more severe, and so less common, form of ADHD.

It is generally accepted that ADHD is more common in boys. Boys outnumber girls by approximately 3:1 in community samples, and in clinically referred samples the ratio may be as high as 9:1. Consistent with the referral of fewer girls than boys,

many research studies have used exclusively male samples and therefore less is known about ADHD in girls. Although it used to be thought that ADHD resolved with age, with its effects diminishing from adolescence onwards, this is no longer considered to be the case. An important issue is the extent to which the same symptoms are valid markers of the disorder at different ages, and for boys versus girls. Some adults who refer themselves because of ADHD symptomatology do not have a childhood diagnosis and this is particularly likely to be the case when women (who are at low risk of disruptive disorders) are affected (Willoughby, 2005). It should be noted that many studies of the prevalence of ADHD exclude children with the purely inattentive (IA) form of the disorder (which by definition is hard to detect) and it is estimated that this occurs in around another 1% of the school-age population (Gomez et al., 1999; Taylor & Sonuga-Barke, 2008).

Comorbidities between ADHD and Other Developmental Disorders

ADHD tends to co-occur with other developmental and psychiatric disorders at high rates. Most of the negative outcomes for ADHD are exacerbated by the presence of comorbid conditions, especially aggression and conduct problems. Estimates for comorbidities in childhood are approximately 60% for oppositional defiant disorder, 20% for conduct disorder, 25% for mood disorders, 25% for anxiety disorders, 30% for learning disorders such as dyslexia, and somewhat higher for developmental coordination disorder (Taylor, 2006). In adulthood, documented comorbidities also include mood and anxiety disorders, and alcohol or drug abuse (Biederman, 2005; Tannock, 1998). These are possibly secondary consequences of the primary disorder. Much of the research on ADHD has not controlled carefully enough for comorbid conditions and must therefore be interpreted cautiously. An important challenge for research is to unravel the causes and consequences of the core problems of ADHD, and to understand the nature of its association with different comorbid conditions (Oosterlaan, Logan, & Sergeant, 1998).

The Assessment of ADHD

The clinical assessment of ADHD in childhood normally comprises a multidisciplinary assessment that includes school observations, semistructured interviews with parents, clinical observations, and parent and teacher ratings of a child's behavior. Evidence from teacher and parent ratings, even though these may be discrepant, are weighted heavily when deciding whether a diagnosis of ADHD is appropriate. This might at first appear somewhat subjective. However, one of the trademarks of ADHD is the marked fluctuation in performance observed across time, settings, and tasks. So the key to diagnosis is not whether a child can pass a given test in a structured situation but how well they can regulate their behavior during everyday activities over extended periods of time. Viewed in this way parent and teacher observations are essential as they are based on large samples of a child's behavior.

Generally, two basic techniques are used to assess a child's behavioral status. The first involves a semistructured interview, either with the child or with the child's parents (e.g., The Parental Account of Children's Symptoms (PACS); Taylor, Schachar, Thorley & Wieselberg, 1986). The second and most frequently used method is a behavior rating scale. Such scales take the form of questionnaires, which ideally are completed by both a parent and a teacher in order to reduce bias and allow an assessment of any cross–situational variability in behavior. Scales that are used widely include the Conners' Rating Scales (Conners, 1996), the Child Behavior Checklist (CBCL: Achenbach & Edelbrook, 1983), and the Strength and Difficulties Questionnaire (SDQ: Goodman, 1997). Items on the latter ask parents or teachers to indicate whether each of a number of statements applies to a child's behavior recently, for example whether the child can sit still and to what extent they think before they act. For more information, see *http://www.sdqinfo.com/*.

In addition, the use of standardized tests of attention can be very useful in helping to make a diagnosis and a vigilance task will often be administered. In one such task, the Continuous Performance Test (Conners, 1996), the participant has to monitor a display of signals for an extended amount of time, pressing a button whenever a nontarget stimulus appears. When a target appears, the participant has to withhold responding. In the classic version of this test monitoring is required for 14 min, during which time participants view a sequence of letters on a computer screen. The task is to press a button whenever a given letter occurs (say X) but *only if* it is followed by an O – not when it is followed by another letter of the alphabet. Performance on vigilance tasks is typically measured by the frequency of errors of omission (missing a target letter) and commission (responding to an *X* when it is not followed by an O.

In addition there are a number of standardized attention tests for the assessment of adults (Test of Everyday Attention (TEA): Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994; Behavioral Assessment of Dysexecutive Syndrome (BADS): Wilson, Alderman, Burgess, Emslie, & Evans, 1996) and children (Behavioural Assessment of Dysexecutive Syndrome in Children (BADS-C): Emslie, Wilson, Burden, Nimmo-Smith, & Wilson, 2003; Test of Everyday Attention for Children (TEA-Ch): Manly, Robertson, Anderson, & Nimmo-Smith, 1998; NEPSY II: Korkman, Kirk, & Kemp, 2007). Some of these tests are widely used in the diagnosis of ADHD as well as in assessments of children with dyslexia to assess attention control (e.g., Snowling, Muter, & Carroll, 2007).

To increase the reliability of the diagnostic information from parent and teacher rating scales, direct behavioral observations are sometimes used. However, because they are time consuming, they have rarely been included in research studies. A limitation inherent in using direct observations is that observers are most likely to detect externalizing behaviors – so the child whose behavior is characterized by hyperactivity or disruptiveness is more likely to be identified than the child whose inattention goes unnoticed, perhaps because of a quieter temperament. The corollary of this is that children with attention disorders who internalize their difficulties (and may experience emotional problems) may not give cause for concern. For this reason it can be argued that there is pressing need to identify objective markers of ADHD that are not subject to observer bias.

There are three core symptoms of ADHD (of the combined type): inattention, hyperactivity, and impulsiveness. Arguably, given the fractionation of ADHD into the inattentive (ADHD-IA) and hyperactive–impulsive (ADHD-HI) subtypes, these three symptoms need to be considered as somewhat independent. In particular, hyperactivity (being restless, fidgety, and "on the go") and impulsiveness (acting out of turn, interrupting people, being reckless) seem to separate from pure inattention (failing to persist with activities, failing to focus on details of a task, being "in a dream"). In practice, virtually all of the research on ADHD has focused on children who show the more noticeable symptoms of hyperactivity and impulsiveness (since it is these symptoms that get the children noticed and diagnosed as having ADHD).

In relation to explaining the problems of hyperactivity and impulsiveness seen in children with ADHD, there has been a strong consensus that this reflects a problem of behavioral inhibition/executive control. However, there is a degree of circularity in this view since ADHD is diagnosed when there are signs that an individual has difficulty with self-regulation in a variety of settings and so behaves in an uninhibited way. Therefore, in order to understand the causes of ADHD it is important to operationalize the term "behavioral inhibition" and to consider the development of executive control in the typically developing child.

Before we go further, it should be stated that ADHD as a disorder is clearly quite different to those we have considered so far in this book. The disorders considered so far (dyslexia, reading comprehension impairment, specific language impairment, developmental coordination disorder, mathematics disorder) might all be seen as "modular" disorders, in which a fairly specific brain system (or small set of modules) fails to develop adequately. In contrast, in ADHD it is much less clear that we would want to consider common explanations for the disorder, such as "behavioral inhibition" or "executive function," as modules. Instead, such systems appear to reflect higher-level "supervisory" systems (Pennington & Ozonoff, 1996; Shallice, 1988) that could be characterized as "horizontal" faculties (Fodor, 1983) that are involved in the planning, execution, and monitoring of diverse forms of behavior. In this respect, ADHD is clearly going to be a difficult disorder to characterize at a cognitive level (due to the broad range of factors affected) and we have sympathy for Morton's (2004) concerns about the usefulness of broad concepts such as executive dysfunction as explanations for the disorder. Nevertheless, a dominant theory of ADHD has been that it reflects a deficit in one or more aspects of executive function (Barkley, 1997; Pennington & Ozonoff, 1996). Before considering this and other theories we will first consider ideas about the nature of executive functions and their typical development.

The Nature of Executive Control/Behavioral Inhibition and their Typical Development

Executive function (or functions) is a term that is widely used in psychology but it is a broad term that different theorists use in somewhat different ways. At a broad level, executive functions are considered to be processes that operate in a "top-down"

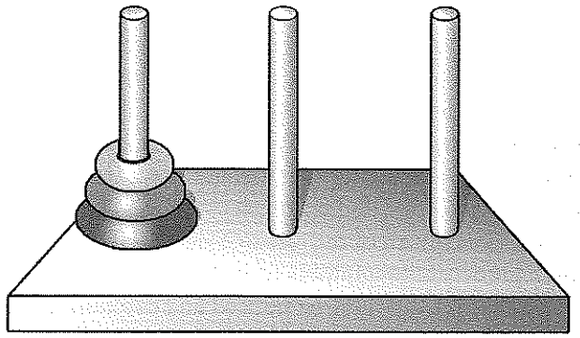


Figure 7.1 The Tower of Hanoi. In this neuropsychological test, the aim is to move the three rings on the left peg to the far right peg in as few moves as possible. A ring can only be placed either on an empty peg or on top of a larger one. To try out the test for yourself go to *http://www.mazeworks.com/hanoi/*.

fashion to control and organize cognitive processes during the performance of complex cognitive tasks. It is important to point out that much of the original impetus for studies of executive functioning came from studies of neuropsychological patients who had suffered damage to the frontal lobes of the brain. A very famous example was Phineas Gage, who showed great changes in his behavior and personality following massive damage to the frontal lobes of his brain. Although some patients with damage to the frontal lobes may show quite well-preserved performance on a variety of well-defined cognitive tasks, many of them show severe difficulties on complex tasks that appear to involve (among other things) the ability to plan and monitor one's performance (Shallice, 1988). One example of such a task is the classic Tower of Hanoi (Figure 7.1), which involves moving rings in the correct order from one peg to another. Another frequently used task is the Wisconsin Card Sorting Task (described below).

The difficulty surrounding the use of the term "executive function" is real because it is used to explain aspects of behavior that can be difficult to characterize rigorously or define clearly. To improve our understanding of what constitutes executive functions, research has used broad sets of possible measures and subjected the results to factor analysis (a statistical technique that assesses the extent to which different measures tend to correlate together to define separable constructs). Based on such studies (see Miyake et al., 2000) it appears that executive functions depend upon at least four separable (but correlated) factors: (1) response inhibition and execution; (2) working memory and updating; (3) set shifting and task switching; (4) interference control. In addition it seems that planning or organization might be seen as an additional (and perhaps higher-level) executive function. As will be clear from this brief discussion, executive functions appear to be diverse, and nonmodular in the sense that they cut across different tasks; indeed it is a defining characteristic of executive functions that they may be involved in managing and coordinating the performance of different tasks.

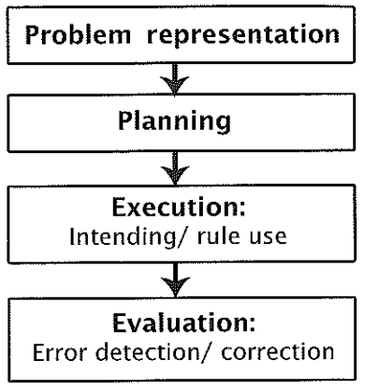


Figure 7.2 A problem-solving framework for understanding executive functions. (Zelazo, P. D., Carter, A., Reznick, J. S., and Frye, D., Early development of the executive function: A problem-solving framework, *Review of General Psychology*, 1(2), p. 200, 1997, published by the American Psychological Association and adapted with permission.)

Zelazo, Carter, Reznick, and Frye (1997) considered how best to conceptualize the development of executive functions and developmental difficulties in self-regulation. Focusing on preschool development, they outlined a framework for the study of executive functions that lays out a sequence of steps required for problem-solving. This framework consists of four stages: problem representation, planning, execution, and evaluation (see Figure 7.2). Children's plans are literally rules formulated in silent self-directed speech. An increase in the complexity of children's rules and levels of embedding in these systems allows increased control over thought.

Considerable research involving typically developing preschool children has focused on the processes of planning, execution, and evaluation. Planning has been tested using tasks such as mazes and the Tower of Hanoi as well as social planning tasks, for example trying to deceive another person. Importantly, none of these tasks can be considered pure in the sense of tapping planning alone; they inevitably draw upon other skills as well, including verbal and spatial abilities.

Converging evidence (reviewed by Zelazo et al., 1997) suggests that there are marked changes between 3 and 5 years of age in children's inclination to plan, although planning skills continue to develop into the school years. Plan execution has been explored in tasks tapping rule-use, for example the use of conditionals to guide behavior as in the children's game "Simon says," where children are instructed to perform different acts but only when the instruction is preceded by the signal "Simon says." Here there are changes between 40 months when children do whatever is instructed regardless of what "Simon says" to around 49 months when they can accomplish the task. Success on more difficult tasks, such as one in which two rules have to be obeyed simultaneously (squeeze the ball when you see the red light and refrain from squeezing when you see the green light), does not occur until around 5 years. Finally, problem evaluation (which comprises knowing when a goal has been reached, and error detection and correction) can be considered fundamental to

development, learning, and metacognition. Whereas children can detect another person's errors very early in development (between 2.5 and 3 years), they take much longer to correct errors, perhaps because such a process requires flexibility of thought and the ability to take an objective stance.

Overall, there are dramatic changes in all four aspects of executive function during the preschool period as children gradually become able to control their problem-solving behavior. Zelazo et al. (1997) argue that developmental changes in executive control are limited by the growth of working memory capacity and the ability to reflect.

Cognitive Theories of ADHD

Children with ADHD have marked problems in regulating their behavior and inhibiting their responses (hyperactivity and impulsivity are two core features of the ADHD profile). In this respect the disorder clearly relates to ideas about the executive control of behavior. The idea that ADHD reflects a core deficit in "behavioral inhibition" was first proposed by Barkley (1997). This cognitive theory is closely related to earlier views that the problems of behavioral regulation observed in children with ADHD are similar to those seen in patients with damage to the frontal lobes of the brain (which is sometimes referred to as the frontal metaphor of ADHD; Pennington & Ozonoff, 1996).

Barkley's model of behavioral inhibition

Building on earlier work by Douglas (1972) and Quay (1988), Barkley (1997) proposed a conceptual model of ADHD in which the proximal cause of the disorder was a deficit of behavioral inhibition. In so doing, Barkley drew heavily on two complementary theories – one of the evolution of language (Bronowski, 1977) and one of the role of frontal and prefrontal cortex in primates and man (Fuster, 1989). Both theoretical accounts ascribed to the frontal lobes the capacity for hindsight, forethought, and linking events over time, and for the self-regulation of emotion. In addition, the internalization of language was considered to provide a means of reflection and exploration, analysis, and synthesis (reconstitution), while functioning of the premotor cortex was essential for the execution of novel sequences of behavior. From this perspective, Barkley argued that the development of adaptive and flexible behavior depends on the child's capacity to delay responding to external stimuli in order to bring responses under self-directed control. In turn, this depends on the development of neural networks in the prefrontal lobes, the socialization of the child, the success of these actions in the past for maximizing the net consequences of behavior, and the ongoing reinforcement of self-regulatory behaviors.

In Barkley's model, behavioral inhibition was the core deficit in ADHD, and a degree of behavioral inhibition was necessary for the development of other aspects of executive function. Barkley distinguished four components of executive function that depended on behavioral inhibition for their development and operation: working memory (holding information in mind), self-regulation of affect, motivation, and arousal (emotional self-control), internalization of speech (describing and reflecting on one's behavior), and reconstitution (abstracting rules to govern behavior and generating contextually appropriate behaviors). All of these executive abilities are involved separately and together in the control and organization of motor responses.

Barkley's theory emphasized the possible importance of executive functions in accounting for the symptoms seen in ADHD. In practice, however, many of the studies in this area have not been guided strongly by theories of executive function. Often diverse executive tasks have been selected based on the "the frontal metaphor" view of ADHD (e.g., Pennington & Ozonoff, 1996), which notes that such tasks are often impaired in adults with damage to the frontal lobes who sometimes appear to show similar behavioral deficits to children with ADHD. We will begin by describing some of the tasks typically used for assessing executive skills before turning to consider evidence for deficits on a range of executive tasks in children with ADHD.

Executive function tasks

A wide range of tasks has been used to assess executive function in children and adults. Amongst the most common of these are planning tasks, such as the Tower of Hanoi (shown above in Figure 7.1), and tasks tapping working memory and memory updating as described in Chapter 3 (see Boxes 3.3 and 3.4). Other tasks tap the ability to attend selectively to a given set of cues, whilst ignoring or suppressing extraneous information. The most widely used task tapping such interference control is the Stroop task (Stroop, 1935). Here participants have to name the color of the ink of a set of color-words (e.g., the word *red* printed in "blue") and, to do so, have to suppress the automatic tendency to respond with the name of the printed word. The speed with which a participant can do this is compared with the speed at which they can name neutral stimuli in the same colors (e.g., color-patches or strings of symbols devoid of meaning – XXXX). A measure of interference control is derived by subtracting the naming speed in the neutral condition from the naming speed in the Stroop condition and the size of this effect depends on the relative speed of the reading and the color-naming responses, as well as on the individual's ability to resist interference. Finally, a classic task that requires the participant to inhibit habitual responses and to shift set in order to solve a problem is the Wisconsin Card Sorting Task (see Box 7.2).

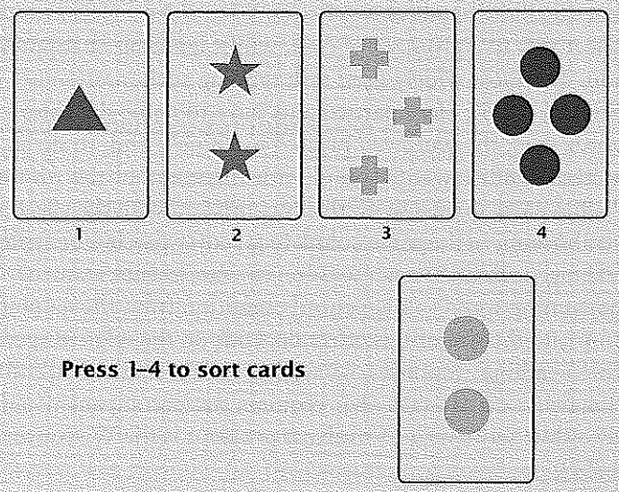
Response inhibition

According to Barkley's model (1997), ADHD can be traced to a fundamental disorder of behavioral inhibition: an inability to inhibit a prepotent response (the default) to stop responding and to control interference. The task that has been used most widely to test this idea is the Stop-Signal Task (Schachter & Logan, 1990). In this task, the child performs a primary "go task," whilst monitoring for a "stop signal" that indicates the response to the primary task should be inhibited. For a child, such ability may be required when they are engaged in a game of chase and the school bell rings, indicating that the child needs to stand still. In the stop-signal paradigm, the

Box 7.2 The Wisconsin Card Sorting Task

The Wisconsin Card Sorting Task (WCST) is a classic test of set-shifting. The figure below shows four stimulus cards, each bearing symbols differing in number, color, and shape. The participant is given a set of response cards each showing symbols comprising a different combination of number, color, and shape (as in the card in the second row). At the start of the test, the examiner places the four stimulus cards on the table, and tells the person to sort the response cards onto each pile. Feedback is provided to allow the examinee to abstract the sorting rule (which for the card shown could be either its color or the number of symbols on it). The examinee is also warned that the sorting rule will change as the test progresses (e.g., reinforcement might first be for color and then shift to number).

There are a number of ways of scoring the test, including the number of shifts accomplished and the number of perseverative responses following a shift in the rule, but basically the difficulty here is for the participant to realize the rule has changed and search for a new rule.



primary task is usually a visual choice reaction time task (e.g., pressing the "x" button on a keyboard when an X is presented and the "o" button when an O is presented). On a randomly occurring proportion of trials (usually about 25%), the primary task stimulus is followed by a stop signal (e.g., a tone/beep). This stop signal is the cue to inhibit the planned response to the primary task or "go signal". In one version of the stop-signal paradigm, the interval between the stop signal and the individual's own mean reaction time (RT) is varied across trials. This involves first calculating the participant's expected RT on the "go task" from their performance

across a block of trials, and then in the next block presenting the stop signal at different time intervals before this RT – say 100, 250, 350, and 500 ms (in the extreme, for children with a low hit rate, the stop signal may be presented simultaneously with the onset of the go stimulus; see Box 7.3). Importantly, children are instructed to respond as quickly as possible on the task and not to slow their responding to wait for the stop signal.

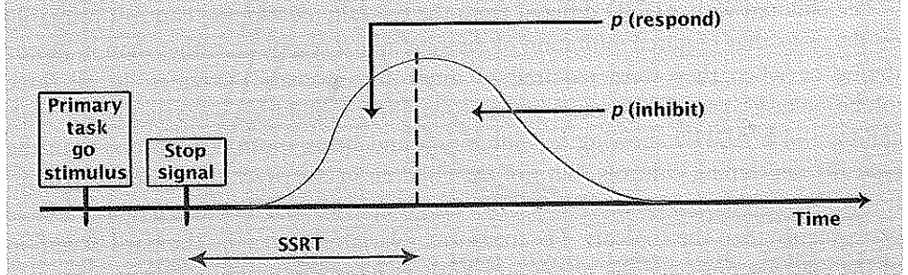
It should be clear that the probability of inhibiting the go response will be related to the delay between the go and stop signals: the Stop-Signal Delay (SSD). It will also depend on an individual's ability to inhibit their motor response. More formally, the probability of response inhibition depends on the outcome of a "race" between the go process and the stop process (Logan, Cowan, & Davis, 1984). If the go process is faster than the stop process, then the individual executes the response; if the stop process is faster than the go process, then the response is inhibited. The speed of the stopping process is referred to as the Stop-Signal Reaction Time (SSRT) and this is calculated

Box 7.3 The Stop-Signal Task (adapted from Solanto, Arnsten, & Castellanos, 2001)

The Stop-Signal Task (SST) provides an index of the ability to inhibit a prepared motor response.

The primary task is a speeded visual choice reaction time task. The child presses a key as quickly as possible to indicate which of two possible letters has been presented on the screen. Performance on the primary task provides an estimate of an individual child's overall speed (mean RT).

The stop signal is a tone presented randomly on a proportion of trials after the go signal; the stop signal indicates that the child is to inhibit the response to the go signal (not press the key). The interval between the stop signal and the individual's mean RT is varied over trials.



The measure derived from this task is the Stop-Signal Reaction Time (SSRT). This measure can be interpreted as a measure of the speed of a stopping process. SSRT is not measured directly but rather is inferred on the basis of the distribution of RTs when there is no stop signal and on the probability of inhibition to signals presented at different times.

from the proportion of successful stop trials across blocks of trials where the delay between the go and stop signals is varied. Children with ADHD typically show longer SSRTs than typically developing children. However, they also differ from controls on other measures derived from the task. In particular, the slope of the inhibition function relating the probability of inhibition to the stop interval is flatter in children with ADHD, the mean RT for the go trials has sometimes been found to be longer, the standard deviation of the RTs is greater, and often children with ADHD make a lower proportion of successfully inhibited responses (e.g., Solanto et al., 2001).

Rubia et al. (2001) compared a clinical sample of 56 children with ADHD aged 7–15 years with both a psychiatric control group of 16 children and a group of 23 typically developing children on a range of tasks designed to assess impulsivity in the broadest sense (monitoring of responses and inhibition). The three groups were matched for age and IQ. The test battery consisted of the Stop-Signal Task, a simpler Go/No-Go Task and a Reversal Task. In the Go/No-Go Task, a motor response had to be executed or inhibited depending on whether an image of an aeroplane appeared on the screen (which it did on 70% of trials); the response had to be inhibited if a bomb was presented (on 30% trials). In the SST, a plane appeared for 1000 ms followed 30% of the time by a bomb, either after 150 ms (10%) or 250 ms (20%). The task was to press a button with the right finger if the plane appeared alone. The Reversal Task was a test of cognitive flexibility; in this task, the previously learned stimulus–response association had to be inhibited in order to learn a new association. Thus, in the Go/No-Go Task, the instruction switched from "respond to planes not bombs" to "respond to bombs not planes."

Three additional tasks were included to assess response output and timing processes in more detail. The first required finger tapping in synchrony with a sensory input at the rate designated by the stimulus onset. The second required the child to finger-tap continuously when a plane appeared on the screen, to periodically interrupt the tapping when a stop signal appeared, and to resume tapping when the plane reappeared (after 2500 ms). The third task required tapping to be synchronized with the appearance of a plane that appeared every 5 s for 200 s (the Delay Task).

The children with ADHD differed from the typically developing controls primarily on the tasks that required inhibition of discrete motor responses rather than in motor timing or when they were required to interrupt automatic activities. In all three inhibition tasks, group differences in the probability of inhibition were significant, with children with ADHD showing less inhibition and being more error prone than the typically developing controls (but not the children in the psychiatric control group). It was also notable that on all of these tasks the group with ADHD showed more variable performance than the controls. The measure of variability was the standard deviation of the reaction times for the primary task; there were substantial effect sizes for this group difference, ranging from 0.52 for the Reversal Task to 2.45 for the SST. Moreover, although group differences in SSRT were not statistically significant, the ADHD group was three times more variable in terms of this measure than the controls.

Variability in the performance of children with ADHD is underlined by the findings of a comprehensive study by Kuntsi, Oosterlaan, and Stevenson (2001). This study failed to find robust differences between children with ADHD and controls in

inhibition in the SST. However, there were group differences in both the mean RT for the primary task and the standard deviation (variability) of the RTs. Indeed the effect size was highest for the standard deviation of RTs (0.83) and this was the strongest predictor differentiating children with ADHD from controls in a discriminant function analysis. Together these findings are in keeping with those of a meta-review by Oosterlaan, Logan, and Sergeant (1998), which concluded that children with ADHD are not less likely to inhibit their responses than typically developing children but, rather, they show both slow RTs on the primary task and variable inhibitory responses. Such variability is not captured well by statistics that assume the underlying distribution of RTs is normal when in fact, particularly for children with ADHD, it shows a significant positive skew with many long reaction times (Leth Steenson, King-Elbaz, & Douglas, 2000; see Figure 7.3 for an example).

In summary, while there is some evidence for a deficit in response inhibition in children with ADHD, the pattern from these studies is not overwhelmingly clear. The SST is a complex one involving a primary task (a choice reaction time task) coupled with the requirement to inhibit responding on some trials in response to an auditory stop signal. On the primary reaction time task children with ADHD tend to be slower and more variable in their response times and to commit more errors. It has been suggested that the overall pattern of data from the SST is compatible with a generally slow, and variable, speed of information processing in children with ADHD (Kuntsi et al., 2001; Sergeant, Oosterlaan, & van der Meere, 1999). This, however, does not amount to a specific deficit in "response inhibition" and as such provides only weak support for Barkley's claim that this is a primary cognitive deficit in children with ADHD.

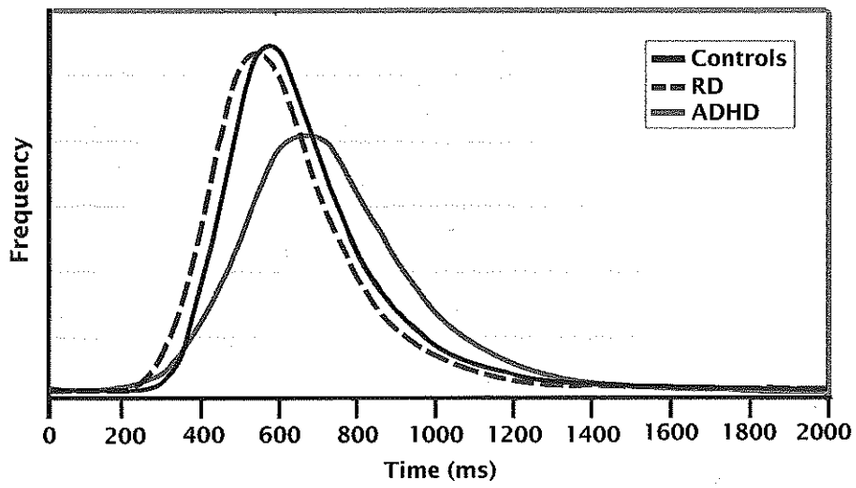


Figure 7.3 Distribution of reaction times in ADHD. The distribution of reaction times for children with ADHD (positively skewed) and for controls and children with dyslexia (who both have less skewed distributions). The greater positive skew (higher rates of very slow reaction times) in the distribution for children with ADHD is highly diagnostic. (Data from an unpublished study conducted by Gooch: Gooch, Hulme, & Snowling, 2008.)

Working memory and temporal processing

As well as controlling impulses and inhibiting prepotent responses, the frontal lobes are involved in planning, shifting, and maintaining strategy sets and organizing and implementing strategies. Arguably, many of these processes depend upon working memory and a number of studies have investigated working memory skills in children with ADHD. In addition to tasks such as sentence span and counting span, many studies have used spatial span tasks such as Corsi blocks (see Figure 5.6), or the CANTAB test in which the participant searches spatial locations to find tokens while remembering not to return to any locations where tokens were previously found.

Martinussen, Hayden, Hogg-Johnson, and Tannock, (2005) report a meta-analysis of studies of working memory deficits in children with ADHD. They report that children with ADHD show deficits on spatial memory storage tasks (average $d = 0.85$) and spatial central executive tasks (average $d = 1.06$) that are greater than the deficits found on comparable verbal storage tasks (average $d = 0.47$) or verbal central executive tasks (average $d = 0.43$). These deficits in working memory could not be accounted for by differences in measures of language skill or general IQ between the children with ADHD and controls. These results suggest that deficits on working memory tasks (particularly spatial working memory) are an area of difficulty for children with ADHD. Approaching this association from the opposite angle, Gathercole et al. (in press) have reported that problems of inattention are widespread among children who are screened and selected as having low working memory.

In recent years, there has been growing interest in the possibility that some of the behavioral symptoms of ADHD are due to temporal processing deficits. An ability to judge and keep track of the passage of time is fundamental to planning, organization, and time management, all areas of behavioral deficit in ADHD that in turn are associated with working memory problems.

A number of different experimental methods have been used to investigate temporal processing. The most widely used method involves the comparison of two brief intervals of similar duration (e.g., 500–600 ms). However, tasks requiring durations to be reproduced are also common; these typically use visual stimuli with durations of up to 1 min. Since these kinds of temporal processing task are attention demanding and require the control of interference as well as the temporary storage and updating of visual or auditory stimuli, it is perhaps not surprising that some studies have reported a positive association between temporal processing and working memory measures. According to a meta-review of six studies conducted by Toplak, Dockstader, and Tannock (2006), children with ADHD show deficits on duration discrimination tasks in both the visual and auditory modalities. They also tend to be more variable in their performance and they are prone to underestimate temporal durations in time reproduction tasks. Questions remain as to the causes of these difficulties and further research is needed to elucidate these.

Summary: Deficits in executive functions as a cause of ADHD

As we made clear earlier, an executive impairment seems worryingly broad as a potential explanation for the deficits observed in children with ADHD (cf. Morton,

2004). However, the studies we have reviewed here have made some progress in making the idea of an executive deficit in children with ADHD more specific.

There are now a number of meta-analyses examining the usefulness of executive function tasks for differentiating ADHD from other disorders (Pennington & Ozonoff, 1996; Willcutt, Doyle, Nigg, Faraone, & Pennington 2005). Willcutt, Doyle et al. (2005) considered 13 executive function tasks tapping four domains of functioning: response inhibition and execution, working memory and updating, set shifting and task switching, and interference control. From this analysis it would appear that differences have been reported between children with ADHD and controls on all of the 13 executive tasks considered, with a mean effect size of $d = 0.54$. The largest effect sizes were associated with studies of response inhibition, vigilance, planning, and working memory. Children with ADHD have also been consistently reported to be slower on measures of perceptual speed, such as Coding and Digit Symbol tasks from the Wechsler scales (Pennington & Ozonoff, 1996). In contrast, small effects and inconsistent results have been reported for set shifting, Stroop interference, and visuospatial orienting.

However, as Willcutt, Doyle et al. (2005) noted in their meta-analysis, the magnitude of group differences in executive function measures (d=0.4–0.6) is much smaller than the group differences in ADHD symptoms (d=2.5–4.0). One might object to this comparison: Given that children with ADHD are selected on the basis of parental and teacher reports of symptoms, it would be difficult to find equally large differences between ADHD and control children on more purely cognitive measures such as executive function tasks. Nevertheless, the effect sizes for the deficits on executive function tasks do seem smaller than would be expected if these executive tasks tap a major cause of the disorder. In addition it has been reported that fewer than half of the children studied with ADHD typically show reliable deficits on executive function tasks (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005) and the correlations between measures of executive function and the severity of ADHD symptoms are typically quite small (r=0.15–0.35). These observations therefore raise problems for the idea that deficits in executive function are either a sufficient or necessary cause of ADHD.

It remains possible that executive function deficits are one contributory cause of ADHD, but this is at best a tentative claim and one that will require large-scale longitudinal studies with diverse measures to test it.

ADHD as a problem of fluctuating performance

The ideas we have considered so far try to explain ADHD in terms of a deficit in certain cognitive processes. So, for example, ADHD might reflect a difficulty in inhibiting responses or a deficit in working memory. In each case, however, the explanation is in terms of a consistent deficit in a given cognitive process (in this respect such explanations are like many we have dealt with earlier in this book in relation to other disorders).

There is, however, a very different way of thinking about the cognitive problems in children with ADHD, which is in terms of variability of performance. In this view children with ADHD can perform cognitive functions normally; it is just that their

performance is highly variable. Some of the evidence we have already considered is consistent with this view, for example, Kuntsi et al. (2001) found that the variability of RTs in children with ADHD was larger (with more very slow responses) than for control children.

One paper has recently suggested that ADHD might be conceived of as reflecting variable performance (Castellanos et al., 2005). Such a view requires a different approach to data analysis; specifically, it requires analyses that look at variations in performance within an individual across time (time series analyses). Castellanos et al. (2005) present analyses of RT data from ADHD and control children. Both groups of children showed variations in RT across time with the same periodicity; such a pattern is consistent with some basic oscillatory process that affects the efficiency of the nervous system in all children (Castellanos et al. review data from a number of animal studies that reveal similar oscillations in several physiological processes, including heart rate). Most interestingly, however, the analyses presented showed much greater increases in RT as a function of these oscillations in the children with ADHD, that is, both groups showed slowed RTs at similar time intervals but these slowings were much larger in the children with ADHD.

It is too early to judge the likely generality or importance of intrachild variations in performance as a potential explanation for the cognitive deficits seen in children with ADHD, but this appears to be a potentially important avenue for future studies.

Motivational Theories of ADHD

In contrast to cognitive accounts of ADHD, other theories have emphasized possible abnormalities in systems responsible for motivation or arousal as explanations for ADHD. According to such theories, an altered state of arousal or motivation leads to a different response pattern in children with ADHD.

ADHD as a problem of signaling delayed rewards

According to the most prominent theory of this type, children with ADHD may show an aversion to the delay of rewards (Sonuga-Barke, Taylor & Heptinsall, 1992; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). Such "delay aversion" can be thought of as a motivational style; the child could wait if necessary but strongly prefers not to. One possible consequence of delay aversion is that children may show different preferences for rewards that vary in their timing. This idea is embodied in theories that make use of terminology taken from animal learning theory that stress the role of reinforcers (rewards) in regulating behavior. Rewards tend to be more effective in strengthening a response if they occur soon after the response. A hypothetical gradient showing this "delay of reinforcement" is shown in Figure 7.4 for children with ADHD and controls.

The delay gradient is assumed to be steeper and shorter in children with ADHD (Aase & Sagvolden, 2006). Thus, children with ADHD experience a faster decline in the effectiveness of reinforcement as the delay between behavior and reward increases.

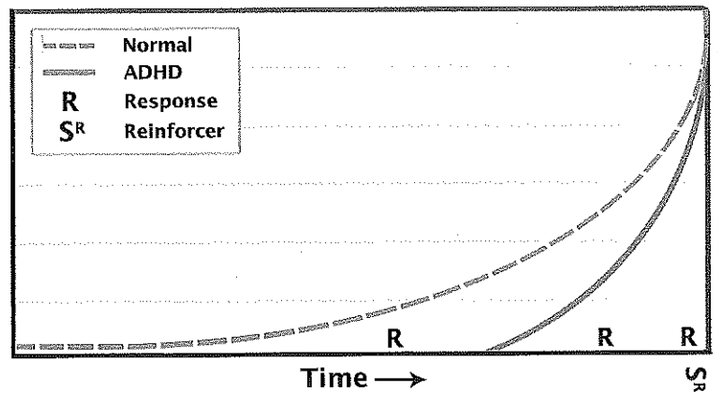


Figure 7.4 Theoretical delay-of-reinforcement gradients for ADHD (solid line) and controls (dotted line). (Redrawn from Aase & Sagvolden, 2006, with permission.)
Infrequent, but not frequent, reinforcers produce more variable responding in young children with attention deficit/hyperactivity disorder (ADHD). *Journal of Child Psychology and Psychiatry, 47*, 457–447.

It follows that they do not like to wait and they cannot defer gratification; hence they present as impulsive in cognitive style and cannot work effectively over extended periods when sustained attention is required. Sonuga-Barke and colleagues (Sonuga-Barke, Taylor, & Heptinsall, 1992; Sonuga-Barke, Taylor, Sembi, & Smith, 1992) have argued that ADHD is the outcome of a neurobiological impairment in the power and efficiency with which the contingency between present action and future rewards is signaled. As a consequence, children with ADHD become delay-averse and, unlike typically developing children, do not learn to control their impulses; instead they avoid delays by choosing immediate rewards or they fill delays with hyperactive and distracting behaviors.

In the laboratory, delay aversion has been demonstrated using a task in which the child has to make a choice between a small reward associated with a shorter delay and a large reward associated with a longer delay. The rewards are usually given as tokens as the task proceeds and the tokens are exchanged at the end of the session for money or for small gifts. Using this technique, Sonuga-Barke, Taylor, Sembi, and Smith (1992) found that children with ADHD preferred to choose a one-point reward associated with a delay of 2 s rather than a two-point reward following a delay of 30 s. In contrast, there were no group differences when delays were not followed by a reward, or when the session length was fixed, such that the optimal strategy for everyone was to choose small rewards.

Kuntsi et al. (2001) tested delay aversion using a computer-presented Space game. In the game the child had to make a choice between an immediate reward (one point, involving a 2 s prereward delay) and a larger delayed reward (two points, involving a 30 s prereward delay). The experimenter also rated the child's apparent delay aversion during the task on a scale of 1–3. Consistent with earlier findings, the children with ADHD chose the larger reward significantly less often than controls and this

difference remained significant after IQ was controlled. The groups also differed on ratings of aversion to delay. However, when symptoms of comorbid conduct disorder were controlled, the main effect of group was no longer significant for either measure. Since few studies examining delay aversion have controlled for comorbid conduct problems, it is difficult to say how specific the delay aversion impairment is to ADHD. Moreover, it is important to be explicit that different causes of impulsivity are not mutually exclusive and delay aversion and inhibition may tap different aspects of the ADHD phenotype.

With this in mind, a collaborative study between the proponents of different theories of ADHD assessed the validity of the SST and the choice delay task as measures of impulsivity in ADHD (Solanto et al., 2001). This study drew children from a database of rigorously diagnosed children with ADHD; 45 children took part in both the choice delay and SST and their performance was compared with that of 29 age-matched controls. In addition, parents and teachers completed the Conners' scale as well as a checklist for symptoms of ADHD and oppositional defiant disorder (ODD). A novel aspect of this study was the inclusion of structured observations of the classroom behaviors of the children (such as annoying others, clowning, interference to teacher, gross-motor movements, and acts of physical aggression). These observations were completed using a modified time-sampling technique yielding 16 min of data. Each observer recorded the behaviors of one child with ADHD and one "control" from the same classroom, blind to diagnostic status.

As expected, there were robust differences between groups in mean SSRT (d = 0.68) and in the probability of inhibition (d = 0.89). In the delay aversion task (choice delay), the children with ADHD chose the larger reward 34% of the time compared with 58% for the control group (d = 0.90). Performance on the choice delay task was moderately correlated with teacher ratings of impulsivity, hyperactivity, and conduct problems, and with classroom observations of interference, gross-motor movements, and physical aggression, while SSRT correlated with classroom observations of interference and physical aggression.

A limitation of this study was that the data from the SST for 14 children had to be excluded either because of a high number of omission errors on "go" trials or a low probability of inhibition. It is also unfortunate that no data on IQ for the control group were available. Notwithstanding this, the measures that best discriminated the ADHD from the control group were the probability of inhibition in the SST and the percentage of large reward (long delay) choices in the delay aversion task. When considered separately in a discriminant function analysis the probability of inhibition classified 68% of children correctly and the percentage of long delay choices classified 71% of children correctly; when entered simultaneously these two measures gave an overall correct classification rate of 87.5%, suggesting that the two measures may indeed tap partially independent aspects of the ADHD condition.

The cognitive energetic model of ADHD

One of the issues that we have alluded to is that performance in children with ADHD is variable; coupled with this, they display slow speeds of processing. This kind of

behavioral profile – sometimes described as "sluggish" – could potentially be explained either in terms of cognitive deficiencies in executive control, or by recourse to suboptimal levels of arousal and a lack of consistent effort. Sergeant and his colleagues (Oosterlann, Logan & Sergeant, 1998; Sergeant, 2005; Sergeant & van der Meere, 1988) have proposed that the overall efficiency of information processing is determined by the interaction of computational resources (e.g., processing and storage capacity), state factors such as motivation and arousal, and executive functions. From this perspective, "single-deficit" models of ADHD are not sufficient because they fail to take into account the role of task parameters in the determination of performance (Sergeant, 2005). For example, the rate of stimulus presentation alters the energetic state of an individual and thereby affects performance (through a change in speed–accuracy trade-off). In this way, fast rates of stimulus presentation can lead to overarousal, with fast inaccurate responding as a consequence. On the other hand, slow rates of stimulus presentation may lead to underarousal and slow, inaccurate responding. Children with ADHD appear to have difficulty in modulating their energetic state such that they generally perform more poorly at slow rates of presentation but more normally with a fast rate of stimulus presentation. Generally, they may have difficulty in maintaining an optimal arousal state with consequent difficulties for the organization of motor responses.

Sergeant uses what he describes as the "cognitive energetic" model to explain the variable profile of arousal and responding in ADHD. The model has three interacting levels. At the highest level is the executive or management system, which ultimately controls four general stages of processing at the lowest level: encoding, search, decision, and motor organization. The executive control in this system is mediated by three distinct energetic pools: effort, arousal, and activation. Effort refers to the energy necessary to meet task demands and encompasses motivation and response to contingencies. Arousal refers to phasic responding that is time-locked to stimulus presentation and typically influenced by novelty and signal intensity. Activation refers to physiological readiness to respond and is affected by preparation, alertness, time of day, and time on task. The cognitive energetic model is appealing in that it provides an account of both cognitive and motivational differences in ADHD; however it is, as yet, not well specified and, as acknowledged by its proponents, the model is complicated and testing it will depend upon finding satisfactory measures of arousal, activation, and effort.

ADHD Subtypes: Different Etiologies for Inattention and Hyperactivity?

As we said earlier, DSM-IV distinguishes between two dimensions of impairment that occur in children with ADHD: inattention and hyperactivity/impulsivity. This gives rise to the three subtypes of ADHD: the primarily "hyperactive–impulsive" (HI) type, the primarily "inattentive" (IA) type, and the combined type. Inattention and hyperactivity/impulsivity seem like quite different symptoms (though they correlate quite well, around .7) and we need to consider carefully the extent to which

these symptoms may depend upon different underlying impairments at the biological (genetic and brain mechanisms) and cognitive levels of explanation.

An early study by Barkley, Dupaul, and McMurray (1990) suggested that subtypes of ADHD may differ in etiology. This study involved 90 clinically referred 6–12-year-old children with attention disorders: 42 classified as showing ADD with hyperactivity (ADD+H) and 48 with ADD but without hyperactivity (ADD–H) (as defined by DSM-III; American Psychiatric Association, 1980). They were compared to a group of 16 children with learning disabilities and 34 control children.

There were no differences between the groups in prenatal, perinatal, or early development but both ADHD groups were reported to have poorer motor control than the learning disabled or the control groups. Similarly, there were no significant group differences in family background factors, such as marital satisfaction, life stress, or depression, but all clinical groups reported more psychological distress than controls. Comparisons between the two subtypes revealed some important differences. Those with hyperactivity were noisier and more disruptive, had problems with peer relationships, and were more likely to be in classes for children with emotional and behavioral disorders. Moreover, they had more relatives with ADHD, aggressiveness, and substance abuse. Those without hyperactivity tended to appear more confused, to daydream, and to present as lethargic; they showed fewer off-task behaviors but more problems on vigilance tasks. Although they did not differ in attainments from the hyperactive subgroup, they were more likely to be in special education classes for learning disabled children and were less likely to have pervasive conduct problems but were more likely to be depressed (though rates of depression were generally low). In addition, more of their relatives had learning difficulties and suffered anxiety disorders. This study provides a description of the different clinical manifestations of the ADHD-HI and ADHD-IA subtypes, but does not clarify the extent to which these subtypes may reflect different underlying causal mechanisms.

Chhabildas, Pennington, and Willcutt (2001) compared the neuropsychological profiles of children with ADHD diagnosed according to DSM-IV criteria as predominantly HI (n=14), predominantly IA (n=67), or of the combined subtype (n=33) who were recruited from the Colorado twin study. In addition to completing tests of reading, spelling, and IQ, each child was assessed on two tests of inhibition (the continuous performance task and the SST), two tests of processing speed (the Trail-Making Test and WISC coding), and a measure of sustained attention (vigilance).

The HI subgroup did not differ from a control group of nonaffected twins in IQ but the other two subgroups gained lower IQ scores (IA and combined); in addition, these latter two subtypes also had poorer reading skills. It is important to bear these differences in mind when assessing the performance of the different ADHD subgroups. The profiles of impairment differed somewhat across tasks. However, a reasonable summary is that the IA and combined subtypes performed similarly to one another and less well than controls whereas the HI subgroup (of whom there were only 14) had less difficulty overall on the cognitive tasks. In dimensional analyses in which symptoms of IA or symptoms of HI were used to predict variations in the cognitive tasks (measures of inhibition, processing speed, and vigilance), every

cognitive measure was best predicted by measures of inattention whereas hyperactivity was not a predictor of these impairments.

Thus, children who showed symptoms of inattention (whether in isolation or in combination with hyperactivity) showed a range of cognitive impairments that are typical of children with ADHD, while children from the predominantly HI subgroup generally performed normally on these cognitive processing tasks. This study suggests that a number of the cognitive symptoms (impairments of inhibition, processing speed, and vigilance) that are said to characterize children with ADHD are actually associated with inattention but not with symptoms of hyperactivity. This seems to be a finding of great importance, and it suggests that future studies should measure symptoms of inattention and hyperactivity separately, and look for separable causes for these different symptoms. However, as the authors note, the sample of children in the predominantly HI group was small and the samples studied here were relatively old (10–12 years old on average), which means that the pattern reported really needs to be replicated.

The Role of Comorbidities in Accounting for some Symptoms of ADHD

ADHD shows high rates of comorbidity with a range of other disorders, particularly general learning difficulties, anxiety, conduct disorder, and oppositional defiant disorder. An important issue, therefore, is the extent to which some characteristics found in samples of children with ADHD may reflect such comorbid conditions. It could be that some of these characteristics are a product of comorbid impairments that are not central to understanding the nature and causes of ADHD.

This question has been pursued most with respect to the relationship between ADHD and reading disorders (Adams & Snowling, 2001; August & Garfinkel, 1989, 1990). An important design feature of such studies is exemplified by an early study by Pennington, Grossier, and Welsh (1993), which revealed some striking findings. This study involved three groups of children: a group of children with ADHD, a group of children with reading disorders (RD) who did not have attentional problems, and a comorbid group of children who had ADHD and RD. The children were given two sets of tasks to complete, one set to tap executive function (the putative core deficit in ADHD) and the other to tap phonological skills (the core deficit in dyslexia; see Chapter 2). As expected, the pure ADHD group showed executive deficits while their phonological processing was normal. In contrast, the pure RD group performed poorly on tests of phonological processing but they had no difficulty with the executive function tasks. Of particular interest was how the comorbid group would perform. In fact, the comorbid group in this study resembled the RD group in showing phonological deficits. They were not impaired on the executive tasks, suggesting that their attentional problems may be a secondary consequence of their learning difficulties rather than the primary outcome of an underlying attentional deficit. Pennington and colleagues referred to this interpretation as the "phenocopy" hypothesis, by which they meant that the comorbid group displayed behaviors

mimicking those of ADHD but without sharing the same underlying cognitive profile. Interestingly, children in this group also appeared to be subject to more social and family adversity than children in the pure RD group, suggesting that environmental factors may be important in determining their behavioral symptoms.

Despite the intuitive appeal of the phenocopy hypothesis, subsequent studies, including some by the same group, have not supported its predictions (Willcutt et al., 2001; Willcutt, Pennington, Chhabildas, Olson, & Huslander, 2005). Willcutt et al. (2001) used the same factorial design to investigate two cognitive phenotypes (executive function and phonological awareness) in children with ADHD, RD, or both disorders. The children who took part were all twins aged between 8 and 16 years and were diagnosed on the basis of parent ratings of behavior; all had IQ above 70; 93 of them had RD alone, 28 had ADHD alone, and 48 had comorbid RD + AD, and their performance was compared with that of 102 typically developing children. The test battery was comprehensive and included several measures of phonological awareness and executive function. A phonological awareness composite measure was derived from performance on three tasks: Pig Latin, in which the task is to strip away the first phoneme from a word and place it at the end of the word followed by "ay" (e.g., mat – "atmay"), phoneme deletion (say "plift" without the /p/), and the Lindamood auditory conceptualization test in which blocks represent phonemes and the task is to add, remove, or transpose blocks to reflect changes in nonwords spoken by the examiner. The executive function measures tapped the ability to maintain and shift set, behavioral inhibition, and working memory. Once again composite scores were derived. The working memory composite comprised performance in sentence span, counting span, and the Trail-Making Test, the inhibition composite comprised performance on the Stop-Signal Task (SSRT) and errors of commission on the continuous performance task, and the set-shifting composite comprised perseveration on the Wisconsin Card Sorting Task and errors on a continuous naming task.

Before reporting the results of Willcutt et al.'s (2001) study it is important to point out that the "pure" RD and ADHD subgroups were not completely free of symptoms of the other disorder. Thus, the RD group had significantly more symptoms of ADHD than did the controls, and the ADHD group scored more poorly than the controls on the reading tests. Both of these findings remained significant when IQ was controlled, highlighting the fact that children with categorical diagnoses may still show subclinical versions of other disorders. Notwithstanding this, there was a significant effect of RD for all the reading and executive function measures, whereas the main effect of ADHD was only significant for inhibition and phonological awareness. When IQ was controlled the group effects on the inhibition composite remained significant and the RD effect remained significant for phonological awareness and working memory, whereas none of the group differences were significant for set-shifting. Importantly, the profile shown by the comorbid RD+ADHD group was not like that of the RD group, as predicted by the phenocopy hypothesis. Rather, the children in this group were more impaired than the other groups on the working memory and inhibition composites, suggesting that they may have a more severe form of disorder involving deficits associated both with ADHD and with dyslexia.

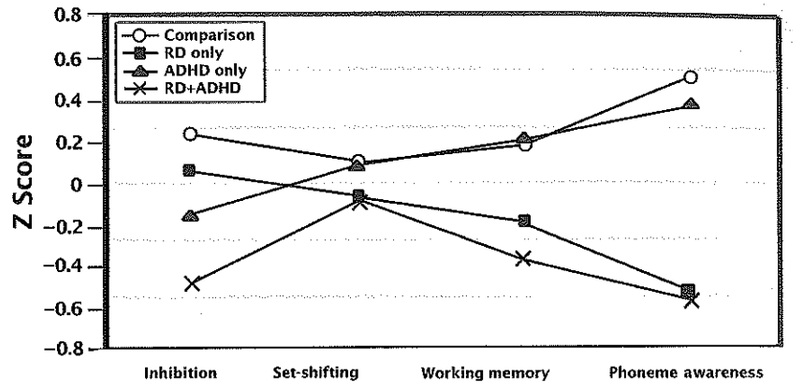


Figure 7.5 Profiles of groups with RD (dyslexia), ADHD, and comorbid RD+ADHD on tests of inhibition, set-shifting, working memory, and phoneme awareness. (Willcutt, E. G., Pennington, B. F., Tunick, R. A., Boada, R. J., Chhabildas, N. A., et al., A comparison of the cognitive deficits in reading disability and attention-deficit/hyperactivity disorder, *Journal of Abnormal Psychology*, 110, p. 166, 2001, published by the American Psychological Association and adapted with permission.)

In line with previous research, the findings of Willcutt et al.'s (2001) study support a double dissociation between executive function and phonological awareness phenotypes. This is shown clearly in Figure 7.5, which depicts the performance of the three clinical groups alongside that of controls on tests of inhibition and phonological awareness. However, there is reason to believe that this double dissociation may not be complete – a subsequent study by the same group, using a very similar sample of children, found that RD groups were impaired on several measures of executive function, including inhibition, with deficits most pronounced on tests of processing speed and working memory (Willcutt, Pennington, et al., 2005). The reason for the discrepancy between these sets of findings is not clear; they highlight that there is a pressing need to examine more carefully the relationships between reading and attention disorders and to explore the possibility that they may have a shared etiology.

Etiology of ADHD

Research on the biological bases of ADHD has arguably been more influential in helping to understand the disorder than for the other disorders considered so far in this book. Research in this area has involved psychopharmacology (drug treatments and their mode of action on psychological and brain processes), genetics, and studies of brain structure and function. We will begin with studies of psychopharmacology because these studies have, in turn, been highly influential in guiding studies of genetic risk factors for ADHD.

Psychopharmacology of ADHD

Research on ADHD has attracted the interest of psychopharmacologists far more than any of the other disorders we have considered. This interest follows from the idea that ADHD reflects impairments in the regulation of the brain's neurotransmitter systems and evidence that certain drug treatments can help to reduce the symptoms of ADHD. Before we go on to discuss what is known about the etiology of ADHD, it is therefore important to outline the mechanisms of neural transmission.

Nerve cells transmit information by electrical signals called action potentials. However, the transmission of information from one nerve cell to another depends upon chemicals called neurotransmitters. Nerve cells communicate with each other at structures called synapses. In simple terms, neurotransmitters can be found in nerve cells, packaged into "vesicles," and they are released into the synaptic cleft (the gap between nerve cells) when an action potential arrives and causes depolarization of the presynaptic neuron. The effect of a neurotransmitter depends on the receptors to which it binds, leading either to excitation or inhibition of the postsynaptic cell. In other words, the neurotransmitter can encourage the next neuron to fire or inhibit its action. Many of the neurotransmitters that are released into the synapse are removed by a process called reuptake, which is regulated by neurotransmitter transporters.

Among the neurotransmitters, catecholamines play a critical role in the functioning of the brain's prefrontal cortex (PFC). The PFC appears to play a critical role in guiding attention and inhibiting distracting stimuli. Two important catecholamines are dopamine, generally considered to be involved in voluntary movement and motivation, and norepinephrine, which is involved in the mechanisms regulating arousal. In fact, it has been demonstrated that depletion of both dopamine (DA) and norepinephrine (NE) can be as detrimental to performance on tasks tapping PFC as removing the cortex itself (Arnsten & Li, 2005). Either too little or too much stimulation of the DA receptors impairs working memory function in rats and monkeys, with performance following a U-shaped curve in response to dosage of dopamine agonists (drugs that block the operation of dopamine as a neurotransmitter). In a similar vein, low to moderate levels of NE have beneficial effects on the functioning of prefrontal cortex, whereas high concentrations (such as those released during stress) impair performance.

The role of the basal ganglia in relation to neurotransmitters also deserves mention. The basal ganglia are subcortical structures (two in each hemisphere) that are involved in the biosynthesis of neurotransmitters. The basal ganglia comprise the caudate nucleus, putamen, and globus pallidus (see Figure 7.6); they have interconnections with the cortex and thalamus, and receive inputs from frontal and motor areas via the striatum. Arguably, knowledge of the mechanisms of action of neurotransmitters both in animals and in man has set the stage for investigations of the etiology of ADHD, which is characterized by difficulties in the voluntary control of movement and arousal.

Interest in the possible role of the catecholamines in ADHD was stimulated by observations that treatment with drugs that affect catecholamine transmission

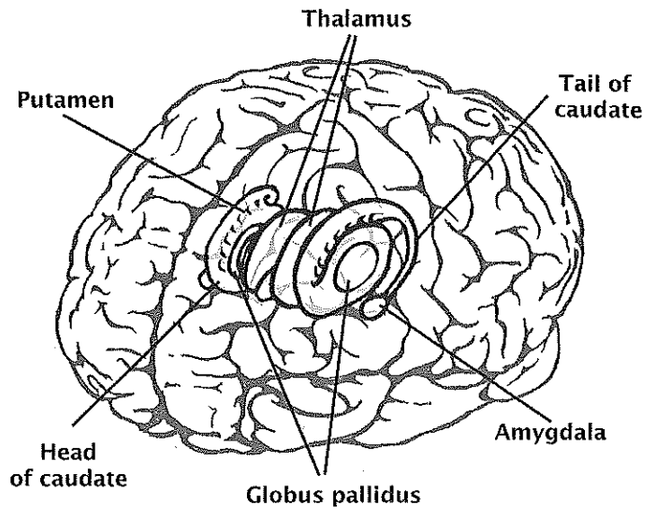


Figure 7.6 Schematic diagram showing basal ganglia.

improved the symptoms of children with ADHD, for example, methylphenidate (Ritalin), which blocks both dopamine and norepinephrine transporters and improves the symptoms of ADHD (Arnsten & Li, 2005). The blocking of these transporters (that reabsorb dopamine and norepinephrine and so reduce their action as neurotransmitters) equates to increasing the effective availability of both these neurotransmitters in the brain. (Other drugs such as amphetamines have similar effects on these neurotransmitters, but are used only occasionally now in the treatment of ADHD because of their potentially harmful side effects.) More direct evidence for abnormalities in dopamine transport (reabsorption) in ADHD comes from brain imaging studies that have measured levels of dopamine transporter in different brain regions using drugs containing radioactive isotopes that bind selectively to the dopamine transporter. These studies show increased activity of the dopamine transporter in various brain regions of interest (particularly the striatum) in adults and children with ADHD (for a review, see Spencer et al., 2005). Furthermore three studies using the same methods have shown reduced levels of dopamine transporter activity after treatment with methylphenidate (Ritalin). Finally treatment with methylphenidate has been shown to improve measures of neuropsychological functioning in people with ADHD, including measures of inhibition (Boonstra, Kooij, Oosterlaan, Sergeant, & Buitelaar, 2005; Turner, Blackwell, Dowson, McLean, & Sahakian, 2005) sustained attention (Boonstra et al., 2005), and working memory (Turner et al., 2005).

In summary, the evidence for a disorder of dopamine transmission (and to a lesser degree norepinephrine) in ADHD seems strong. The best interpretation of this finding, and whether abnormalities of dopamine reuptake are a fundamental biological cause of ADHD or a downstream consequence of other more fundamental disturbances in brain function, remains open to debate.

Genetic influences on ADHD

Quantitative genetics

ADHD is considered to be one of the most highly heritable of psychiatric disorders. Family studies report a high incidence of ADHD among both first and second degree relatives of probands (children diagnosed as having ADHD), and the rates of ADHD are also greater among biological relations than among adoptive relatives of children with ADHD. In line with the view that these family resemblances in ADHD reflect genetic effects, the concordance rates differ for MZ and DZ twins. A large number of twin studies of ADHD have reported concordance rates that are significantly higher for MZ (58–82%) than DZ pairs (31–38%), providing evidence that ADHD is heritable (Levy, McLaughlin, Wood, Hay, & Waldman, 1996; Levy, McStephen, & Hay, 2001; Sherman, McGue, & Iacono, 1997; Willcutt, Pennington, & DeFries, 2000). In addition, the fact that the MZ concordance was less than 100% in all studies suggests that environmental influences also play a role in the etiology of ADHD. However it appears that estimates of heritability differ depending on who is the informant regarding behavioral symptoms and what instruments are used. For example, Levy et al. (1996) used data from a questionnaire based on DSM-III and completed by mothers of an Australian sample of probands with ADHD and found concordance rates of .82 for MZ and .38 for DZ twins. In contrast, Goodman and Stevenson (1989) reported wide ranging concordance rates from .48 to .79 for MZ and .08 to .44 for DZ twins in a UK sample, depending on the informant and instrument used. Notwithstanding the issue of bias raised by these figures, a recent meta-review reports a mean heritability estimate of .75 for individual differences in attention, which is very substantial and there is evidence of considerable stability by age (Reitveld, Hudziak, Bartels, van Beijsterveldt & Boomsma, 2004).

Molecular genetic approaches

Most molecular genetic studies of ADHD have focused on genes that operate to influence the functioning of dopamine systems in the brain. These genes are of specific interest because drugs such as methylphenidate (Ritalin) that reduce the reuptake of dopamine are known to be effective treatments for ADHD. So far, two gene variants of the dopamine receptor (DRD4) and the dopamine transporter (DAT) have been found to be associated with ADHD. In addition a further five gene variants that aid neurotransmitter release have also been identified. However, the effects of each of these genes are small, with odds ratios ranging from 1.18 to 1.46 (Faraone et al., 2005). This means that the effects of such genes are not going to explain the occurrence of the disorder in most individuals (and suggests they may only contribute to the risk of ADHD in combination with other genes). Moreover, because of comorbidities, ADHD is likely to be genetically heterogeneous. In fact, there appears to be some overlap on chromosome 6 between linkage regions reported for ADHD and for reading disorder (RD), which might be explained by pleitropy, a term used to refer to the process whereby the same set of genes is linked to a number of different phenotypes (Willcutt et al., 2002).

To investigate genetic overlap between ADHD and RD, Gayan et al. (2005) assessed 505 individuals from 119 nuclear families on tests of reading and language and recorded ADHD symptoms via an interview. Each individual also contributed DNA, which was analysed to identify genetic markers across 22 chromosomes. The rationale behind the method was to ask whether higher levels of genetic resemblance between siblings at a certain locus correlated with greater similarity for a behavioral trait (e.g., a component of reading or of ADHD). As expected, there were large correlations between reading and language variables in this sample, with the correlation between reading and inattention being moderate (and low with hyperactivity). The criterion for affectation status (for RD and ADHD) was set at 1.5 or more SD below/above the population mean in either phenotype. On this basis, 36% of the RD individuals also met the criteria for ADHD. The investigators proceeded to conduct linkage analysis to identify markers associated with ADHD and bivariate analyses to identify markers associated with both ADHD and RD.

There were two informative behavioral phenotypes: one was a composite ADHD score and the other ADHD symptoms in combination with poor orthographic coding (OC) as measured by a test requiring the participants to say which of two spellings was correct (e.g., salmon/sammon). The main linkage peaks were on chromosomes 14 (for ADHD and for ADHD-OC) and 20 (for ADHD-OC). Thus, there was suggestive evidence of pleitropic loci in the regions of chromosomes 14q32 and 20q11. In addition, the univariate analysis suggested three areas of linkage to ADHD, depending on how the phenotype was defined: for hyperactive symptoms, these were 7q21; for symptoms of inattention, 9p24; and for the composite ADHD score, 16p13. The region on chromosome 7 overlaps with a previously identified region of linkage and contains one of the genes implicated in the dopaminergic pathway. More research is required to clarify the genes and gene pathways that carry the risk of ADHD; this poses a serious challenge, given the heterogeneity of the disorder and its overlap with other disorders.

Endophenotypes

Arguably, symptom-based classifications (i.e., categorical diagnoses) have been slow to bear fruit in unraveling the mappings between susceptibility genes and behavioral outcomes in ADHD. As a consequence, there is increasing interest in an alternative approach, namely the identification of "endophenotypes" (Skuse, 2001). Endophenotypes can be defined as heritable traits that index an individual's liability to develop or manifest a given disease (Castellanos & Tannock, 2002). It is hoped that endophenotypes will relate more directly to the biological etiology of a disorder than many of the symptoms that currently are studied – though it is important to note that endophenotypes are just as likely to be modified by environmental influences as any other brain process or behavior trait.

Doyle et al. (2005) suggested that in order for a process to be a useful endophenotype it should be possible to measure it reliably, it should show evidence of heritability, and it should appear in unaffected relatives, although it need not be universal in the condition. Possible endophenotypes of ADHD include working memory (especially

visuospatial memory), inhibition, temporal processing, state regulation, and a shortened delay gradient, all of which show some genetic influence and partial familial overlap, especially inhibition and processing speed (Doyle et al., 2005). The investigation of endophenotypes is likely to grow rapidly in the coming years, and holds the potential for identifying both risk and protective factors in the etiology of ADHD.

Social and environmental risk factors

The majority of research suggests that the effects of individual gene products on ADHD are small and that genes involved in the transmission of ADHD are probably also involved in the transmission of other disorders (e.g., autism). This means it is important to also consider the contribution of environmental risk factors to ADHD. Environmental factors that have been associated with ADHD include prenatal factors such as maternal smoking and exposure to maternal alcohol drinking during pregnancy, lead exposure both in utero and in childhood, birth complications and low birthweight, severe early deprivation such as major disruptions of attachment, ongoing family and psychosocial adversity, and, in some cases, dietary effects (Biederman, 2005; Taylor, 2006).

One particularly clear form of evidence concerning diet comes from a double-blind trial of the effects of artificial food color and additives (McCann et al., 2007). In this well-controlled study it was found that artificial colors and a preservative added to fruit drink led to increased hyperactivity in 3- and 8/9-year-old children in the general population. The effect sizes here were around 0.2, suggesting that this is a small effect, but this study shows very clearly that these food additives are one potential cause of hyperactivity in children.

Of course some other associations between environmental risks and ADHD may be the consequence of ADHD in parents rather than direct causes of the disorder. Indeed, both the active and passive correlation of genetic and environmental factors can influence behavioral outcomes in ADHD. Parents of children with ADHD will often themselves exhibit continuing patterns of hyperactivity and impulsivity that provide poor models for the development of organization and self-management skills. Children's own ADHD behaviors may also evoke negative or critical responses from parents and these may in turn increase oppositional behaviors or compound feelings of low self-esteem leading to a downward spiraling of behavior. More specifically, a delay-averse motivational style may elicit punitive reactions from parents and perpetuate the failure to engage with delay-rich environments. These within-family processes may serve to reinforce patterns of persistent pathology. For this reason, parent training programs may provide an important component of the management of ADHD.

Neurobiology of ADHD

The majority of the early studies of the brain bases of ADHD focused on the structure of the prefrontal lobes and its reciprocal connections with the ventromedial region of the striatum. More recent investigations have included the basal ganglia.

Research samples have ranged widely in age, which may mean that some results are artefactual, although in an important study Castellanos et al. (2002) showed that developmental changes in brain structure were parallel in ADHD and control samples, suggesting that brain differences appear to be consistent across age.

A number of studies of brain structure now indicate that total cerebral volume is smaller in ADHD, and localized abnormalities of several brain regions, notably the prefrontal cortex, basal ganglia, and corpus callosum, have been reported (Castellanos, et al., 1996; Tannock, 1998). In contrast, no differences have been found in the region of the putamen (shown on Figure 7.6). In light of this, it is interesting to note that Casey et al. (1997) found that behavioral measures of response inhibition in ADHD correlated with anatomical measures of frontal-striatal circuitry but not the putamen.

Neuroimaging studies have built on structural studies to test hypotheses regarding the neurobiological bases of ADHD. Following a review of 12 studies using a variety of experimental paradigms, including those tapping inhibition, working memory, and vigilance, Bush, Valera, and Seidman (2005) reported that individuals with ADHD show a consistent pattern of frontal dysfunction with altered patterns of activity in anterior cingulate, dorsolateral prefrontal, and ventrolateral prefrontal cortices, as well as associated parietal, striatal, and cerebellar regions. Taking a narrower focus, Aron and Poldrack (2005) examined studies investigating inhibition and found deficits in right inferior prefrontal cortex, basal ganglia, and related neurotransmitter systems.

Building on these reviews, Dickenstein, Bannon, Castellanos, and Milham (2006) used a meta-analytic technique to provide an overview of the findings from all of the studies of ADHD to that time. The technique used is called activation likelihood estimation, a quantitative analysis that examines, voxel by voxel, the likelihood of activation across neuroimaging studies. This voxel-wise approach gives good spatial resolution, which is important in the case of ADHD considering that spatial distinctions are substantial in the frontal lobes.

Dickenstein et al. (2006) identified 16 studies yielding 134 foci of activation in ADHD and 180 in controls. Separate analyses were conducted for each group and the two activation maps were then compared to investigate differences in patterns of activation. Moreover, because various different paradigms were used in these studies, the authors also report a subanalysis restricted to studies of inhibition (e.g., Go/No-Go and Stop-Signal tasks). Taken together, the findings of the meta-analysis confirmed previous studies in highlighting widely distributed regions of underactivity in individuals with ADHD affecting anterior cingulate, dorsolateral prefrontal, inferior prefrontal, and orbitofrontal cortices, as well as regions in the basal ganglia and parietal cortices. These differences may reflect decreases in the spatial extent of activations, more spatial dispersion, or decreased functional connectivity. The authors also caution that they may be the result of statistical noise (e.g., more movement in ADHD group).

Finally, a small number of studies employing electrophysiological measurements have found significant differences in EEG measured at several sites between children with ADHD and controls. However, it is unclear whether to interpret these as indices

of under- and overarousal, or of delayed brain maturation. In a similar vein, ERP studies have investigated the P300, which is generated when participants attend and discriminate events. Together these studies suggest that in ADHD the P300 is smaller in amplitude in response to targets, and its latency is longer. Perhaps most interestingly, Lazzaro et al. (1997) reported greater variability in P300 responses in children with ADHD and also found that such variability was reduced by stimulant medication. This variability is consistent with evidence of greater variability in reaction time (RT) measures found in ADHD described earlier. Such findings are also broadly consistent with the predictions of the cognitive–energetic model that views difficulty in the maintenance and control of arousal and activation to be a significant factor in ADHD.

In sum, although there are still relatively few studies of the neural correlates of ADHD, findings converge well with those of behavioral studies. A limitation of these studies has been the focus on brain regions of interest and therefore other areas of abnormality may have been missed. More generally, the effects of age and stage of development on patterns of activation have not been investigated. Hence it is difficult to ascertain what the primary impairments are and whether other impairments may be secondary consequences of these. Indeed, there is still a long way to go before it will be possible to trace causal pathways from biology through cognition to the social and behavioral outcomes of this complex disorder.

Interventions for ADHD

The complexities of ADHD are such that intervention demands a multiprofessional approach and ideally there should be a management plan that addresses behavioral, educational, and social issues (Taylor, 2006). From a theoretical perspective it is important to distinguish between treatments that address core problems (and may therefore help to demonstrate causes) and those that aim to ameliorate symptoms.

The main treatment for ADHD, unlike the other disorders in this book, is pharmacological. Drug treatments are used to improve neural transmission, with the aim of reducing hyperactivity, impulsivity, and inattentiveness. Most effective treatments for ADHD target catecholamine transmission, for example methylphenidate (Ritalin), which blocks dopamine and norepeniphrine transporters (Arnsten & Li, 2005). However, behavior therapy programs are also useful, particularly if parents are involved (Tannock, 1998). Cognitive behavior therapy (CBT) may help older children and young adults with ADHD to manage their difficulties, but it is generally a less effective therapy for individuals with ADHD.

In 1992, a major multicentre study evaluating different interventions for ADHD was funded by the US National Institute of Mental Health and Department of Education. "The Multimodal Treatment Study of Children with ADHD" (MTA) was a randomized trial (Box 7.4) that compared the efficacy of three forms of treatment: medication, behavioral management, or a combination of the two, relative to regular community care (which acted as a control condition). The participants in the trial were 579 children aged 7 years to 9 years 9 months, all of whom met DSM-IV

criteria for ADHD (combined type). On entering the trial, the children were randomly assigned to one of three treatment arms or to community care for 14 months, during which time the researchers monitored behavioral symptoms, social skills and relationships, and educational achievements.

The behavioral treatment program incorporated parent training, child-focused treatment, and a school-based intervention integrated in the school year. By most standards, the treatment was extremely comprehensive; the parent program involved 27 group sessions and 8 individual sessions per family. The same therapist also conducted teacher consultations biweekly. The child-focused therapy involved attendance at an 8-week summer camp (for 5 days per week and 9 hours per day) where assistants worked with the children in recreational settings using a points reward system, time out, social reinforcement, and other well-established techniques for shaping desirable behavior. In addition to the teacher consultations regarding the management of behavioral difficulties, the school-based work also involved a teaching assistant working alongside the child for 60 school days. Throughout the school year, a daily report card was used to communicate between school and home.

The medication treatment was also carefully supervised. It started with a 28-day double-blind trial of different doses of methylphenidate. During this phase, the child's response was monitored by taking parent ratings of attention and behavior. These data were then used in reaching agreement on the correct dose (or to the administration of an alternative drug treatment if the best dose was placebo). Following this phase, children were seen monthly by pharmacotherapists to monitor side effects and for

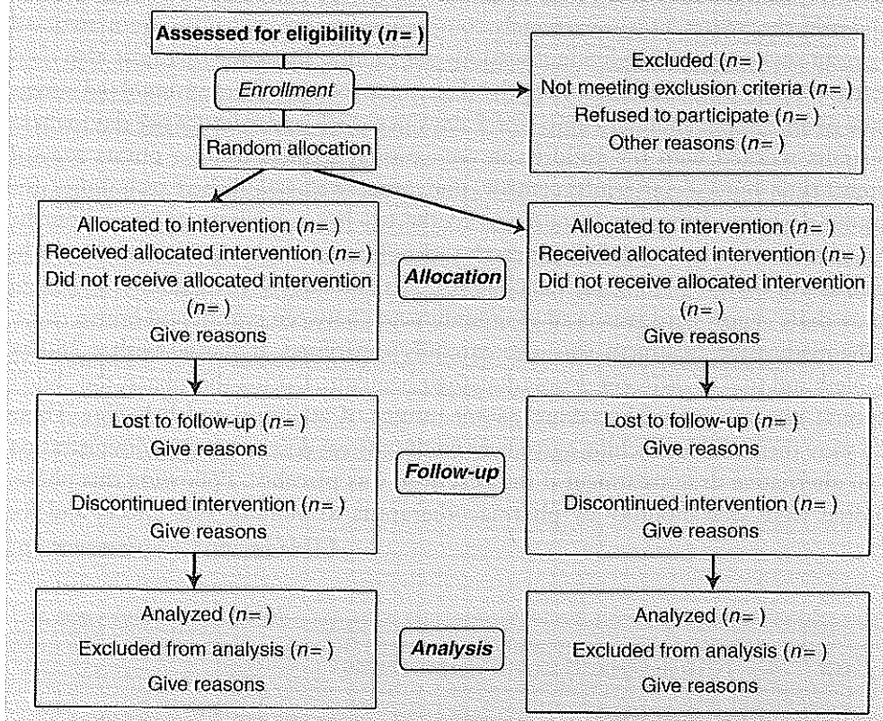
Box 7.4 Randomized controlled trials

A randomized controlled trial (RCT) is now considered the "gold standard" method for evaluating the efficacy of a medical or health treatment, and increasingly RCTs are being used to evaluate educational interventions. An RCT involves the random allocation of participants to different forms of treatment. Such random allocation should minimize any differences between treatment groups (such as severity of symptoms at the beginning of the study) that might bias the outcome of the study.

To provide validation of a treatment's efficacy, it is crucial that an RCT is reported in a standard and transparent way that allows critical appraisal. To safeguard this process, a group known as the Consolidated Standards of Reporting Trials (CONSORT) has devised a minimum set of recommendations for reporting RCTs, known as the CONSORT Statement (Altman et al., 2001). The CONSORT Statement gives a checklist detailing how a trial should be reported in a journal article under conventional headings such as Title, Abstract, Introduction, Methods, Results, and Discussion. It encourages the reporting of participant flow through the trial as a flow diagram (see below).

Box 7.4 *(cont'd)*

When trials are reported in this way, they are easy to interpret and their findings can be used to make clinical recommendations with confidence.



Consort diagram. (After Altman et al., 2001). Reprinted with permission from Elsevier (*The Lancet*, 2001, *357*, 1193.)

support and encouragement. The combined treatment integrated the two management strategies and involved regular liaison between teacher-consultant and pharmacotherapist. A management plan (based on a manual) provided guidelines as to when adjustments should be made to the behavioral or the pharmacological treatment.

The treatment ran for 14 months. At the end of the treatment period, all four groups showed a significant reduction in ADHD symptoms but the combined treatment and medication treatments were more effective than the behavioral intervention and community care programs. The combined and medication treatments showed effect sizes (greater reductions in rated hyperactivity and rated inattention compared to the control group) in the region of $d = 0.5$–0.7, which indicates that being on the medication has quite a substantial effect on the symptoms of ADHD.

The combined treatment was not significantly better than medication alone in reducing the core symptoms of ADHD (in fact the reductions were slightly greater in the medication only group) but it is noteworthy that combined treatment outcomes were achieved with lower levels of medication. There were few treatment arm differences in outcomes as measured by aggressive/oppositional symptoms, social skills, anxiety and depression, parent–child relations, and academic achievement, though the combined treatment proved better than the behavioral treatment for internalizing problems, aggressive/oppositional signs, and for reading achievement.

The findings of the MTA study suggest that the physiological changes brought about by methylphenidate operate to reduce the core symptoms of ADHD. This supports the idea that deficits in dopaminergic systems are one of the proximal causes of the condition. Importantly, however, treatment outcomes for the different arms depended on whether or not the children experienced a comorbid anxiety disorder. In children with anxiety, the behavioral treatment was as good as medical management and combined treatment, whereas in those without anxiety the behavioral treatment was not as effective as the other two active treatments. These findings suggest that some of the behavioral symptoms of children with ADHD who are also anxious may be related to their anxiety. It seems possible that the behavioral treatment was effective in reducing anxiety and as a consequence reduced the symptoms of ADHD. Conversely these results suggest that for children with a "purer" form of ADHD who are not anxious the behavioral treatment given was not particularly helpful in treating the core symptoms of ADHD.

One conclusion from the MTA study is that methylphenidate is an effective treatment for children with ADHD. However, the drug does not cure the condition and needs to be taken continuously in order to reduce the symptoms of inattention and hyperactivity. There is also evidence that long-term use of the drug tends to slow children's rates of growth. Furthermore the follow-up of children from the MTA study suggests that differences in the relative effectiveness of the interventions diminish over time. Swanson et al. (MTA Cooperative Group, 2004) reported that 10 months after the end of the trial the differences in ADHD symptoms between the two groups of children on methylphenidate and the two nonmedicated groups had roughly halved. These changes in the effectiveness of the intervention were accounted for by changes in which children were continuing to take the medication (many of the children who took the drug while in the trial stopped after the trial ended, while other children not given the drug during the trial then started taking it). Interestingly, parallel effects were also noted for differences in children's growth (children who continued taking the drug showed reduced growth compared to children who stopped taking the drug or never took it).

At this same point in time (10 months after the end of the trial) it was reported that phenylphenidate appeared to improve objective measures of inhibition and reaction time in those children taking it. Epstein et al. (2006) studied 316 children from the MTA sample using a continuous performance task in which they had to press a space bar whenever they saw a letter but not when they saw the letter X, which appeared 10% of the time. Children receiving medication had lower errors of omission and commission on this task and showed faster and less variable RTs.

There was also less positive skew in the RT distribution for those on medication, suggesting that they experienced fewer and less severe lapses in attention. Together these findings are consistent with the idea that medication, while it continues to be taken, improves measures of attention and information processing efficiency.

Finally, at a further follow-up 2 years after the trial ended (Jenkins et al., 2007) there were no remaining differences in treatment effectiveness between the groups (though overall all groups showed reduced levels of ADHD symptoms compared to baseline at this time). It is not yet established whether the absence of treatment effects at this long-term follow-up reflects changes in the medication regime adopted by different children from the different intervention groups; in light of the earlier follow-up study (MTA Cooperative Group, 2004) this seems a likely explanation for the pattern found.

In summary, the MTA study is a very large and methodologically rigorous evaluation of the effectiveness of methylphenidate, with and without behavioral intervention as a treatment for ADHD. In the short to medium term it is clear that methylphenidate is effective in reducing the symptoms of ADHD (at least while children continue to take the drug). However, the long-term follow-up of the children in this trial suggests that many children stop taking the drug, while others not initially prescribed the drug may start to take it. It seems important, we believe, to conduct further studies of the effectiveness of purely behavioral interventions for children with ADHD. It seems likely that such interventions, if started early in a child's development and continued over extended periods of time, may prove effective, particularly for children with less severe problems. It seems important that the evidence for the effectiveness of methylphenidate in the MTA study is not overinterpreted and used to dismiss the possible usefulness of behavioral interventions in the treatment and management of ADHD (Westen, Novotny, & Thompson-Brenner, 2004).

Towards a Neurocognitive Theory of ADHD

ADHD is a complex disorder with diverse symptoms. There has been a great deal of work trying to understand the psychological impairments seen in children with ADHD and their genetic, environmental, and neural bases. In our view, there are quite fundamental problems in how best to conceptualize ADHD. Arguably, these problems reflect both the complexity of the disorder and the research strategies that have dominated this area so far.

It is worth taking stock of the "facts" that any adequate theory of ADHD will have to account for. ADHD is a severe neurodevelopmental disorder that is relatively common (it affects around 3% of children to at least some degree). It is a disorder that is strongly influenced by genetic risk factors. ADHD is very different to the other disorders we have considered so far in terms of the complexity of its behavioral manifestations. There is no simple test or set of tests that can be used to diagnose ADHD (unlike in the case of reading or mathematics disorders); instead its diagnosis relies principally on parent and teacher rating scales, though direct observations of children and clinical interviews also play a role. The reason why

rating scales are so widely used is because they tap into large samples of a child's behavior in a range of settings. The symptoms used to diagnose ADHD consist of two partially independent but correlated dimensions: inattention and hyperactivity/impulsivity.

How then should ADHD be conceptualized? A variety of cognitive or motivational deficits have been proposed as possible explanations of ADHD. The most prominent cognitive theory of ADHD has seen it as a deficit in "executive function." In terms of Fodor's (1983) terminology, executive processes are a "horizontal faculty" with the potential to affect the operation and development of a wide range of different cognitive domains. Hence, the executive deficits observed in ADHD will have wide-ranging effects. There are a number of problems with the executive impairment account of ADHD. One problem is that it is too vague and general an explanation: There is evidence for impairments on some executive tasks in children with ADHD, but not others. However, even on executive tasks where impairments are found, these are typically quite small effects (Willcutt, Doyle, et al., 2005), and such deficits are typically only found in a small proportion of children with ADHD (Nigg et al., 2005). These observations mean that an executive deficit in ADHD is very unlikely to provide a complete explanation for the disorder (executive deficits might be one cause of ADHD but it is unlikely that they are the sole, or most important, cause of the disorder).

Limitations to the executive theory of ADHD have led to other types of explanation being sought. A major alternative class of explanation is to see ADHD as a form of motivational deficit. We would term these motivational theories as "noncognitive" insofar as they postulate differences in arousal or emotional processes. The dominant motivational theory has been framed in terms of "delay aversion" in children with ADHD (Sonuga-Barke, Taylor, & Heptinsall, 1992; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). Delay aversion might be seen as a type of motivational style (preferring immediate gratification to a larger reward after a delay). Alternative motivational theories postulate more wide-ranging deficits in the modulation of arousal and motivational processes in children with ADHD (Sergeant, 2005). In a direct comparison between the executive and delay aversion accounts of ADHD it was found that these two deficits were at least partially independent in that the two deficits together did a better job of discriminating between ADHD and control children than did either deficit alone (Solanto et al., 2001).

A reasonable starting point therefore might be to postulate a dual-deficit theory of ADHD. Perhaps the simplest form such a theory might take is represented in Figure 7.7.

In this view there are two broad, relatively independent, cognitive risk factors (executive deficits and motivational deficits) that cause the development of the behavioral symptoms of ADHD. For the moment we have left the details of this theory deliberately vague (both the executive deficits and motivational deficits would need to be more clearly specified). The important point is that the theory postulates two separate areas of impairment in children with ADHD. The two-headed arrows here represent the correlations between the different factors in the population. Current evidence suggests that the correlation between executive and motivational

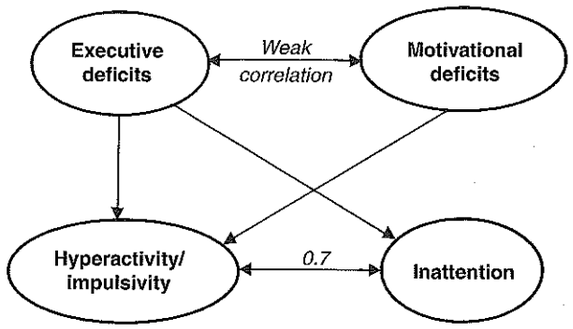


Figure 7.7 Dual-deficit theory of ADHD.

deficits is not strong (Solanto et al., 2001). In contrast there is a substantial correlation between the ratings of hyperactivity/impulsivity and inattention in the population (we have shown this as a correlation of .7, see Gomez et al., 1999). In this model, the executive and motivational deficits both contribute to the observed symptoms of hyperactivity/impulsiveness. In contrast, the symptoms of inattention depend upon the executive deficits alone. The correlation between hyperactivity/impulsivity and inattention reflects the common effect of executive deficits coupled with the unique effect of delay aversion on hyperactivity/impulsivity. This model is essentially a more general and simplified version of the "dual pathway" model proposed by Sonuga-Barke (2002).

According to this model, the development of ADHD is the developmental outcome of two distinct processes. The first deficit is in executive processes, which may be associated with dysfunction in the prefrontal cortex and mesocortical circuits. The second deficit involves differences in motivational mechanisms, which may involve mesolimbic reward circuits. We should emphasize that this is neither a complete nor adequate theory of ADHD. Nevertheless, it seems quite plausible that executive deficits and motivational deficits are two contributory causes to the symptoms seen in many children with ADHD. As discussed earlier, however, the notion of an executive deficit is almost certainly too broad (children with ADHD do not show problems in set switching and susceptibility to interference, though they do show difficulties on speeded tasks, including the Stop-Signal Task, and on a number of working memory tasks), as is the proposal of a general arousal/motivational deficit. One final problem for such a theory is that executive deficits appear to be quite general problems that are also displayed by other groups of children, including those with autism spectrum disorders and broader learning difficulties, so that the extent to which they can be considered a specific cause of ADHD would require careful consideration.

Building on this model, Castellanos, Sonuga-Barke, Millham, and Tannock (2006) draw upon the distinction proposed by Zelazo and Muller (2000) between "cool" executive function, reflecting cognitive aspects associated with the dorsolateral prefrontal cortex, and "hot" executive function, reflecting mechanisms of motivation and

emotion and associated with orbital and medial prefrontal cortex. Within this elaborated model, abnormalities either in maintaining instructional set (cool executive function) or motivational state (hot executive function), or both, may account for the variability seen in responding. However, nonreciprocal connections between these two systems suggest a hierarchy whereby emotion and/or motivation affects cognitive processing, which in turn can regulate motor outputs. Interestingly, there are synergies between this model and the conceptual model of ADHD proposed by Barkley (1997), which distinguished executive skills such as working memory, goal-directed behavior, and creativity from aspects of self-regulation such as motivation, affect, and arousal.

The highly simplified model shown in Figure 7.7 is a purely psychological model of ADHD. However, the evidence we have considered shows that ADHD is a disorder that is under strong genetic influences. Genetic risk factors appear to have clear effects on neurotransmitters in the brain (particularly dopamine and norepinephrine). The details of these genetic mechanisms are not yet understood and it seems likely that many diverse genes of small effect will be causally related to the development of ADHD. There is evidence for genetic effects on dopamine transporter mechanisms that may be related to the development of ADHD, though once again the magnitude of such effects appears to be too small to provide anything close to a complete account of the origins of the disorder (so genetic effects on the dopamine transporter mechanism will not be sufficient to account for ADHD, though such effects may be one contributory cause of the disorder).

It may be, however, that if we take a more biological view of the disorder we should not expect a coherent cognitive or psychological account of the disorder. Figure 7.8 shows a tentative "biological" view of ADHD; the empty ovals at the top of the diagram represent the likely involvement of multiple genes.

According to this model there are numerous genetic influences on dopaminergic and noradrenergic pathways in the brain. It is also assumed that patterns of activity in these two systems interact, so that activity in each system has some effect on the other. These neural systems in turn are postulated to affect the development and operation of diverse psychological processes, including executive functions, motivational processes related to reward, and potentially other unspecified motivational/cognitive systems. These processes in turn ultimately explain the symptoms whose ratings lead to a diagnosis of ADHD. Once again we would stress that this diagram is in no way intended to be a complete model of ADHD and its development. The model is incomplete and underspecified in many ways. However, we believe this model gives a different way of thinking about a disorder such as ADHD. In this model the unifying constructs are biological (abnormalities in dopaminergic and noradrenergic pathways) and such abnormalities in neurotransmitter systems may have diverse psychological functions. However, in this view there may not be any unifying psychological account for the disorder. This is a slightly disturbing prospect (at least for cognitive psychologists like us) and we have deliberately phrased this alternative in a fairly stark way. In reality, the structure of the psychological mechanisms underlying the development of ADHD may yield a clearer picture if given continued scrutiny.

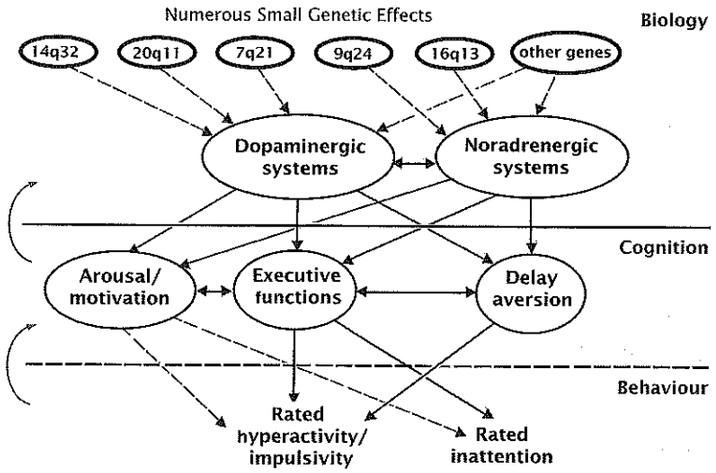


Figure 7.8 Path diagram showing a possible biological model of the origins of ADHD.

We believe, however, that in this field it may be particularly important to relate underlying biological mechanisms (gene effects on neurotransmitter systems) to psychological impairments. This is a case where the study of endophenotypes may be particularly important.

Summary and Conclusions

It is clear that our understanding of ADHD reflects an unusual and uneven state of knowledge. ADHD is a highly heritable disorder that appears related to problems in neurotransmitter function. From a practical point of view, methods for the diagnosis of ADHD have shown major advances and we have good evidence from the MTA randomized controlled trial that stimulant drugs can be an effective treatment. In contrast, our understanding of the psychological mechanisms involved in the development of ADHD remains quite limited. This reflects in part the complexity of the disorder and in part the research strategies that have dominated this area. It may be useful to contrast psychological research on ADHD with research on another disorder where our understanding is more advanced (developmental dyslexia).

In the case of dyslexia the nature of the phenotype we are trying to understand is clearly specified: it is a difficulty in mastering visual word recognition skills in reading. In this sense the deficit in dyslexia is modular (a deficit in the visual word recognition system). There are many longitudinal studies examining the typical development of word recognition skills in reading. There are also well-developed formal models of word recognition processes and their development that allow us to evaluate quite specific hypotheses about the nature of the problems that children with dyslexia

experience in learning to read. Case–control studies and longitudinal studies of children at familial risk of dyslexia have converged on the conclusion that problems in the phonological component of oral language are the proximal cause of problems in learning to read in most cases of dyslexia.

In contrast, in ADHD, the "phenotype" is hard to characterize and the behaviors shown by children with ADHD can vary markedly over time and in relation to the environment they are tested in. In fact one view of the disorder is that variability of performance is one of its defining characteristics (Castellanos et al., 2005). The defining characteristics of the disorder are nonmodular and involve broad constructs such as hyperactivity, impulsivity, inattention, delay aversion, and problems of executive function and arousal (these diverse terms might be brought together under the umbrella term of behavioral regulation). There is a dearth of normative longitudinal studies on how these aspects of behavioral regulation develop, and the theories we have in this area are limited. This is also paralleled by a dearth of longitudinal studies of children with ADHD and theories of limited specificity. In summary, better specified theories of the development of behavioral regulation, coupled with more detailed characterizations of development in this area, may in turn lead to clearer hypotheses about the core deficits in ADHD. It remains likely, however, that the deficits found in children with ADHD may well be heterogeneous and will likely involve diverse aspects of cognitive and motivational functioning.