Attention-Deficit/Hyperactivity Disorder: Endophenotypes, Structure, and Etiological Pathways

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ABSTRACT

Several lines of research are revising our picture of attention-deficit/hyperactivity disorder (ADHD). I highlight four emerging themes. First, models from temperament and personality research have been fruitful in clarifying the basic pathways to ADHD and their relation to typical development. Second, many kinds of attention are normal in ADHD, but cognitive control and vigilance are not. These last two are among present candidates for clinical markers that may help identify causes of ADHD. Third, any one cognitive marker pertains to only a subset of the ADHD population; the syndrome’s heterogeneity increasingly is a focus of research. Fourth, along with energetic pursuit of genes related to ADHD, resurgent interest in environmental causes of ADHD is notable. New insights into environmental effects are illustrated by recent data concerning lead exposure and ADHD.

Attention-deficit/hyperactivity disorder (ADHD) evokes strong opinions among nonexperts (and experts) regarding both its proper conceptualization and its causes. ADHD’s behavioral hallmarks are impulsivity (darting out into traffic, blurting out in class), overactivity (running around “as if driven by a motor”), and inattention-disorganization (unable to stay on task, losing materials). Although these individual behaviors are common in all children, in youngsters with ADHD they converge with an intensity that disrupts school progress, peer relations, or family well-being. The problems are serious enough to place affected children at elevated risk of accidental injury, school failure, peer rejection, and subsequent substance use, antisocial behavior, underemployment, and driving accidents. The syndrome persists into adolescence and adulthood in many but not all cases, and is among the costliest of medical or behavioral disorders in our society.

Because the surface behavioral syndrome is multifaceted, research has often searched for simpler markers that may lead to causes. These markers are referred to as *endophenotypes*. An endophenotype may be a biological, cognitive, or behavioral measure. It is intended to provide better signal (or signal-to-noise ratio) regarding causal factors such as genes that may be related to the disorder. For example, in the case of reading disorder (dyslexia), a useful endophenotype has been phonological awareness (the ability to recognize distinct sounds that make up words).

In the case of ADHD, one method for identifying possible endophenotypes has been to use personality measures, which are helpful in evaluating whether ADHD reflects multiple underlying behavioral or psychological systems. A second method has been to identify cognitive problems associated with ADHD, which are helpful in isolating psychological mechanisms. If either the personality traits or cognitive problems are closer to the cause than the ADHD symptoms are, then they may help us to detect genes or experiences that cause ADHD. Even if that hope proves false, personality or cognitive markers may still provide a useful way to improve clinical characterization of ADHD. However, this search for markers and for causes is complicated by ADHD's etiological heterogeneity. Heterogeneity can be thought of in two ways. From a person-centered perspective, the causes of ADHD in some children are different from the causes of ADHD in other children (i.e., causal "types"). From a variable-centered perspective, component dimensions of ADHD (inattention vs. hyperactivity) have distinct influences.

TEMPERAMENT AND PERSONALITY CAN CLARIFY COMPONENTS OF HETEROGENEITY

Personality ratings in children and adults can distinguish a factor related to extraversion, approach, or positive affect from one related to effortful control, constraint, or planfulness. Other factors, such as negative emotionality, are also routinely identified in temperament and personality research. On this basis, many theorists now distinguish between (a) reactive incentive-response tendencies and (b) a broadly conceived regulatory ability. This distinction can be mapped at the level of the behavioral tendency (or "trait"—how the person tends to behave in a given context), peripheral physiology, and brain circuits in relation to cognition (Serences, Shomstein, Leber, Egeth, & Yantis, 2005).

This basic two-level analysis (i.e., "reactivity" and "regulation") enables the use of personality and cognitive measures together to attempt to clarify the structure of ADHD from a variable-centered perspective. When it comes to the fundamental problem of controlling one's behavior (an obvious difficulty in ADHD), this perspective suggests that complex and goal-oriented behavior is "controlled" (interrupted, regulated, or changed) under at least two kinds of influence. The first is driven by immediate affective incentives. Goal-directed behavior is interrupted by an “alert” signal to threatening, promising, or novel information that warrants immediate inspection. One can think stereotypically of the child who stops playing when a stranger enters the room (see Kagan & Snidman, 2004) or whose behavior pauses on mention of a coveted reward that may now be attainable—or at risk. We can speculate that this response is “bottom up” in the sense that it is driven initially by activation in subcortical or posterior brain regions.

The second type of behavioral inhibition is driven by evaluation of new information that is goal relevant. One can think of the child who ignores the teasing of a peer in order to earn the praise of parents later in the day, or who resists the impulse to leave her seat when horseplay begins so as to earn a privilege in the next period (i.e., restraint mainly due not to fear but to planful evaluation). We can speculate that this kind of control is “top down” in the sense that it is informed by prefrontal brain activation and corresponding suppression of other activations and behaviors.

Our work suggests that ADHD is a combination of problems in both kinds of control systems (bottom up and top down), with distinct influences leading to their occasional convergence. What psychopathologists call attention problems reflects difficulty in regulation, constraint, and effortful control, whereas impulsivity and perhaps hyperactivity are related to breakdown in incentive response systems (for related ideas, see Nigg, 2006; Sonuga-Barke, 2002).

Several lines of work suggest that this personality perspective has promise for understanding ADHD. We showed in a series of studies that hyperactivity-impulsivity was related to a trait called reactive control (related to spontaneous impulsive response), whereas symptoms of inattention were related to low conscientiousness (a trait related to planful control).

Figure 1 illustrates the creation of a statistical model in which two hypothetical constructs (called latent variables because they are not directly observed) are created. The observed measures reflect parent ratings from a model of personality and a model of temperament. They also include two laboratory response time measures. Four measurements are used to indicate each construct. Controlled responding is hypothesized to reflect both personality traits and laboratory measures of control (discussed more in the next section), which all combine to create the latent control variable. Reactive responding reflects several traits that are each in some way related to incentive response or affective response tendencies. The results of this model confirm the expected relationship among the measures and the constructs, and between the constructs and ADHD. It shows distinct associations of each type of response process with the two ADHD component domains of inattention versus hyperactivity in children age 6 to 13 years. Although there is a significant association between the two underlying constructs, their relations to the two ADHD symptom dimensions are rather specific, as shown in the diagram (Martel, Nigg, & von Eye, in press). These results suggest two kinds of behavioral or psychological process are involved in ADHD, which map somewhat onto the two symptom domains.

COGNITION AND ADHD

Cognitive mechanisms involved in ADHD have mostly been linked to either of two major brain networks: (a) cortical-thalamic-cerebellar or cortical-thalamic-striatal pathways involved in regulation and cognitive control, and (b) ascending arousal circuitry involved in alertness and motivation. In the cognitive control set (a), recent interest has focused on a range of executive functioning operations, such as response suppression (ability to interrupt a response), working memory, set shifting, and temporal information processing. In the state regulation set (b), interest has focused on functions such as reinforcement learning, arousal, alertness, effort, and motivation.

ADHD is associated with weakened cognitive control as compared with typically developing individuals, even when associated disruptive behavior and learning problems are statistically controlled. This seems to hold in children (Willcutt, Sonuga-Barke, Nigg, & Sergeant, 2008), adolescents (Martel, Nikolas, & Nigg, 2007), and adults (Nigg, Stavro, et al. 2005; Murphy, Barkley, & Bush, 2001). The aggregate effect size (*d*) for measures such as response inhibition and working memory in these comparisons is between .50 and 1.0 (Willcutt et al., 2008)—that is, between one half and one standard deviation. That effect is modest in clinical terms, yet meaningful. As explained by Cohen (1988, pp. 26–27), an effect of $d = .8$ is comparable to the difference in IQ between college students and those with a Ph.D. or the difference in height between 13- and 18-year-old girls. Yet this also indicates considerable overlap in the distribution of scores between youth with ADHD and typical youth. Thus, the cognitive measures are not diagnostic.

Indeed, other disorders also appear to be associated with some aspects of executive dysfunction, and not all children with ADHD can be characterized as having an executive functioning problem. Instead, ADHD is heterogeneous, with some youth showing an executive function problem and others not. Thus, it is not yet agreed whether executive functioning is the most important or central cognitive problem in ADHD, or for that matter whether it is part of a causal pathway or merely another symptom of the disorder. The answer may depend on which kind of cognitive control is at issue, as well as on which symptom domain one considers.

Yet it is worth noting that some candidate cognitive problems are being ruled out as central players in the ADHD story. One interesting discovery has been that most kinds of attention are intact in ADHD. Normal attention in ADHD was suspected by experimental researchers more than two decades ago but has recently been confirmed with newer measures that are better integrated with contemporary cognitive neuroscience. Two examples will suffice. Huang-Pollock and Nigg (2003) averaged together all studies that looked at attentional orienting to fast cue/target displays, which activate a posterior (automatic) brain system for spatial orienting of attention. They found that automatic spatial orienting of attention is not an important marker of ADHD. Using a new paradigm that takes into account the influence of perceptual load on attention, Huang-Pollock, Nigg, and Carr (2005) also found no evidence of abnormality in attentional selection for the most common group of children with ADHD (those with both inattentive and hyperactive-impulsive behavior problems).

Thus, if attention is thought of as having three fundamental aspects—orienting, selecting, and vigilance (watching effectively for something important)—only the last aspect appears to be related to ADHD. The contenders for cognitive endophenotypes for ADHD are in the realm of executive functioning, state regulation, alertness, or learning and motivational style.

RELATIVES OF CHILDREN WITH ADHD: ENDOPHENOTYPES AND HETEROGENEITY

We have pursued executive functioning in ADHD. One classic test for an endophenotype is to look at performance in relatives. If a marker for causal risk has been discovered, relatives are expected to show some effect on the endophenotype, even if they do not have the illness. The logic is that the marker will emerge before the disorder does, after a subset of causes have occurred. The disorder is theorized to lie on a spectrum of control problems, and subtle problems in control appear on relatives who share the risk spectrum with the ill person. On the other hand, if the cognitive measures are merely extra symptoms of the disorder, then relatives should show normal performance on them. We and others have looked at relatives of ADHD children, using several cognitive measures. For simplicity, this discussion focuses on data for one popular measure, called response inhibition (using a task known as the stop task). This task is intended to measure the efficiency of the process that interrupts a prepared or “about to go” response when new information appears (like the check swing in baseball). This ability likely involves a neural circuit including the inferior frontal gyrus, supplementary motor cortex, and possibly portions of the thalamus and striatum (Aron & Poldrock, 2006). Over 25 studies have looked at this ability in ADHD, with a clear aggregate effect (Willcutt et al., 2008). Although not unique to ADHD, the effect is apparently larger for ADHD than it is for other disorders. The association with ADHD is not able to be explained by overlap with other disorders (Willcutt et al., 2008).

Historically, studies attempting to validate the endophenotype idea for ADHD have had mixed results. However, support for the endophenotype idea was found by Bidwell, Willcutt, Defries, and Pennington (2007), who found that unaffected twins of individuals with ADHD had weaker response inhibition on the stop task than did twins of non-ADHD youth, even when IQ, subthreshold ADHD symptoms, and other covariates were considered. In another positive development, Nigg, Blaskey, Stawicki, and Sachek (2004) examined heterogeneity. Children were classified as “normal” and “impaired” on response inhibition scores (at the arbitrary level of the 90th percentile in the control group). Strikingly, the relatives (parents and siblings) of children with ADHD who had “intact” response inhibition performed exactly as did the relatives of the control children. But the relatives of the “affected” ADHD youth had slower response inhibition than did relatives of the other groups, including relatives of the other ADHD youth. This finding provides support for the idea that response inhibition is an endophenotype, but only for a subset of children with ADHD.

ETIOLOGY AND MECHANISM: RETURN OF THE ENVIRONMENT

How do these diverse problems arise? In the first decades of the twentieth century, ADHD was seen as a form of diffuse brain injury (the ill-fated and ultimately overinclusive “minimal brain dysfunction” idea). By the end of the 20th century, twin studies had shown a strong genetic influence on ADHD. About 70% of variation among children in hyperactivity or inattention appears to be related to genetic variation (this varies a bit if one focuses on parent versus teacher ratings). As a result, molecular genetic studies of ADHD are being aggressively pursued, albeit with results that are, so far, both tantalizing and inconclusive. However, it seems plausible that genes convey susceptibility to ADHD whereas experiential activators may bring the disorder to fruition. Thus, interest in environmental influences on ADHD is returning.

Low-level lead exposure is among the most interesting of several candidates for experiential activators, for several reasons. First, it has population-wide “background” occurrence, rendering it a likely near-universal exposure—despite the lower levels of exposure in the population now that regulation has somewhat reduced lead in the environment. This is important because it means lead can function as a widely shared environmental trigger, with substantial explanatory power in terms of ADHD incidence. While still needing to be confirmed, gene-by-environment interplay may appear as a genetic main effect in twin studies of heritability. Second, lead has numerous effects in the developing brain, but these include effects on gene expression in the striatum and prefrontal cortex—circuitry of consensus importance in ADHD. Third, animal studies have shown that lead exposure early in life causes problems in reinforcement response and response inhibition.

If we knew that lead contributed to ADHD even at very low exposure levels, and if we knew how it did so, then we might describe a specific pathway to ADHD that was preventable—

and that might provide sufficient clues to allow identification of additional paths. Therefore, clarifying one causal route to ADHD from a common environmental risk would be a major advance. Of course, one has to bear in mind that effects like lead exposure probably interact with genotype, stress, and other factors. Overall, lead is one possible environmental trigger worth pursuing in relation to understanding ADHD.

Lead in blood is measured in micrograms (a thousandth of a gram) per deciliter (1/10th of a liter) of blood (µg/dL). The U.S. federal level of unacceptable blood lead is 10 µg/dL as defined by the Centers for Disease Control. It has been known for some time that lead exposure much higher than that level is associated with several cognitive, behavioral, and medical problems including inattention and hyperactivity (hence its regulation in automobile fuel and paint over a generation ago). Although lead has been reduced in children's environments, it has not been eliminated. Nearly all children still have measurable levels of lead in their bodies.

Blood lead appears to be associated with reduced IQ and more ADHD symptoms, even at much lower levels than previously believed. Three years ago, a population survey in the United States showed that background exposure level—blood lead amount typical in the U.S. population—was related to parent reports that their children had been diagnosed with ADHD (Braun, Kahn, Froehlich, Auinger, & Lanphear, 2006). Lacking until last year was confirmation of this in a sample that was formally diagnosed with ADHD, but such confirmation was provided by Nigg et al. (2008) and confirmed in a larger sample by Nigg, Nikolas, Knotterus, Cavanagh, and Friderici (in press). The population average blood lead level among children in the United States at the turn of the 21st century was about 1 µg/dL. In our first study (Nigg et al., 2008) a sample of children selected to have ADHD and typically developing controls had exactly the population average of exposure, yet the youth with ADHD had slightly more blood lead than the non-ADHD youth (Nigg et al., 2008), confirming the finding of Braun et al. The effect was confined to ADHD combined subtype and to the symptom domain of hyperactivity-impulsivity, but not to the symptom domain of inattention. In the second study (Nigg et al., in press) this effect was reproduced. In addition, blood lead was related to parent and teacher ratings of ADHD problems. Both hyperactivity and inattention showed effects, though results depended somewhat on method of assessment (normative rating scale, symptom checklist, interview). Effects were also masked if treatment status was not considered; once children's medication status was taken into account, teacher ratings of ADHD symptoms were robustly related to blood lead. In both studies, the association of blood lead with ADHD was not accounted for by IQ, family income, child sex, child age, or race of the ADHD individual; in the second study, it also was not accounted for by child blood hemoglobin (an index of iron, one important component of nutritional health related to lead) or by maternal smoking in pregnancy.

The conceptual logic of how this effect of lead might work is illustrated in panel A of Figure 2. Since lead occupies sites in striatum and frontal cortex (among having many other effects in the developing brain), it may alter their development and, by that route, influence ADHD. It shows the hypothesis that an experiential influence like lead may alter neural development and consequently alter the effectiveness of the psychological processes supported by those networks. In turn, diminished behavioral control and altered behavioral tendencies develop toward ADHD via two symptom components. The effect is doubtless moderated by genetic liability, which also has main effects on neural development.

Based on this logic, we hypothesized that the association with hyperactivity might be mediated by weakened cognitive control. The cognitive measures serve as measures of the functional effectiveness of the psychological systems in the control network. Panel B in Figure 2 shows the implementation of a portion of the model by Nigg et al. (2008), showing that this mediation effect was observed. That is, blood lead was related to both cognitive control and to hyperactivity. The association of blood lead with hyperactivity was fully explained (in statistical sense) by the effect on cognitive control. This is consistent with the idea that lead disrupts striatal-frontal circuitry, which alters development of cognitive control, which in turn contributes to hyperactivity. If this suggestive finding can be confirmed, it brings us a step closer to specifying a causal model with this risk factor. The effect also shows how the cognitive endophenotype can help clarify causal mechanisms for ADHD.

CONCLUSIONS AND FUTURE DIRECTIONS

Research in the past decade has attempted to translate cognitive methods into markers of risk for ADHD. It is now apparent that whereas some forms of attention are normal in ADHD, cognitive control and vigilance are impaired. The relative importance of these findings in relation to etiology now needs to be determined. Doing so will require considering the heterogeneity of ADHD: It is probable that multiple neural routes to the disorder and multiple etiologies exist. One promising environmental risk factor is low-level lead exposure. Findings relating such exposure to ADHD illustrate the effort to identify etiological influences that alter cognitive mechanisms believed to be involved in the disorder. The next steps in this work will entail continuing to map etiological triggers (environmental exposures and genes) onto a range of related phenotypes at different levels of analysis: symptoms, cognitions, and physiological and brain recordings. The next stages will also see more focused study of moderators—that is, gene-by-environment interplay—in relation to lead and other experiential stressors. The result in this century should be a fascinating and differentiated picture of how ADHD develops.

Recommended Reading

Nigg, J.T. (2005). Neuropsychological theory and findings in ADHD: The state of the field and salient challenges for the coming decade. *Biological Psychiatry*, 57, 1424–1435. Summarizes major neuropsychological approaches to ADHD

Nigg, J.T., Hinshaw, S.P., & Huang-Pollack, C. (2006). Disorders of attention and impulse regulation. In D. Cicchetti & D. Cohen (Eds.), *Developmental psychopathology* (2nd ed., pp. 358–403). New York: Wiley. Provides a comprehensive overview of ADHD and embeds it in a developmental context.

Nigg, J.T., Knottnerus, G.M., Martel, M.M., Nikolas, M., Cavanagh, K., Karmaus, W., & Rappley, M.D. (2008). (See References). A report on the relation of blood lead with ADHD even at population-average levels.

References

Aron, A.R., & Poldrack, R.A. (2006). Cortical and subcortical contributions to Stop signal response inhibition: Role of the subthalamic nucleus. *Journal of Neuroscience, 26,* 2424–2433.

Bidwell, L.C., Willcutt, E.G., Defries, J.C., Pennington, B.F.(2007). Testing for neuropsychological endophenotypes in siblings discordant for attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *62*, 991–998.

Braun, J., Kahn, R.S., Froehlich, T., Auinger, P., & Lanphear, B.P. (2006). Exposures to environmental toxicants and attention deficit hyperactivity disorder in U.S. children. *Environmental Health Perspectives*, 114, 1904–1909.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.

Huang-Pollock, C.L., & Nigg, J.T. (2003). Searching for the attention deficit in attention deficit hyperactivity disorder: The case of visuospatial orienting. *Clinical Psychology Review*, *23*, 801–830.

Huang-Pollock, C.L., Nigg, J.T., & Carr, T.H. (2005). Deficient attention is hard to find: Applying the perceptual load model of selective attention to attention deficit hyperactivity disorder subtypes. *Journal of Child Psychology and Psychiatry*, *46*, 1211–1218.

Kagan, J., & Snidman, N. (2004). *The long shadow of temperament.* Cambridge, MA: Harvard University Press.

Martel, M.M., Nigg, J.T., & von Eye, A. (in press). How do trait dimensions map onto ADHD symptom domains? *Journal of Abnormal Child Psychology*.

Martel, M.M., Nikolas, M., & Nigg, J.T. (2007). Executive functions in adolescents with ADHD. *Journal of the American Academy of Child and Adolescent Psychiatry*, *46*, 1434–1444.

Murphy, K., Barkley, R.A., & Bush, T. (2001). Executive functions in young adults with attention deficit hyperactivity disorder. *Neuropsychology*, *15*, 211–220.

Nigg, J.T. (2006). *What Causes ADHD? Toward a Multi-Path Model for Understanding What Goes Wrong and Why*. New York: Guilford Press.

Nigg, J.T., Blaskey, L., Stawicki, J., & Sachek, J. (2004). Evaluating the endophenotype model of ADHD neuropsychological deficit: Results for parents and siblings of children with DSM-IV ADHD Combined and Inattentive Subtypes. *Journal of Abnormal Psychology*, *113*, 614–625.

Nigg, J.T., Knottnerus, G.M., Martel, M.M., Nikolas, M., Cavanagh, K., Karmaus, W., & Rappley, M.D. (2008). Low blood lead levels associated with clinically diagnosed attention deficit hyperactivity disorder (ADHD) and mediated by weak cognitive control. *Biological Psychiatry*, *63*, 325–331.

Nigg, J.T., Nikolas, M., Knottnerus, G.M., Cavanagh, K., & Friderici, K. (in press). Confirmation and extension of association of blood lead with attention deficit hyperactivity disorder (ADHD) and ADHD symptom dimensions at population typical exposure levels. *Journal of Psychology and Psychiatry.*

Nigg, J.T., Stavro, G., Ettenhofer, M., Hambrick, D., Miller, T., & Henderson, J.M. (2005). Executive functions and ADHD in adults: Evidence for selective effects on ADHD symptom domains. *Journal of Abnormal Psychology*, *114*, 706–717.

Serences, J., Shomstein, S., Leber, A., Egeth, H., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. *Psychological Science*, *16*, 114–122.

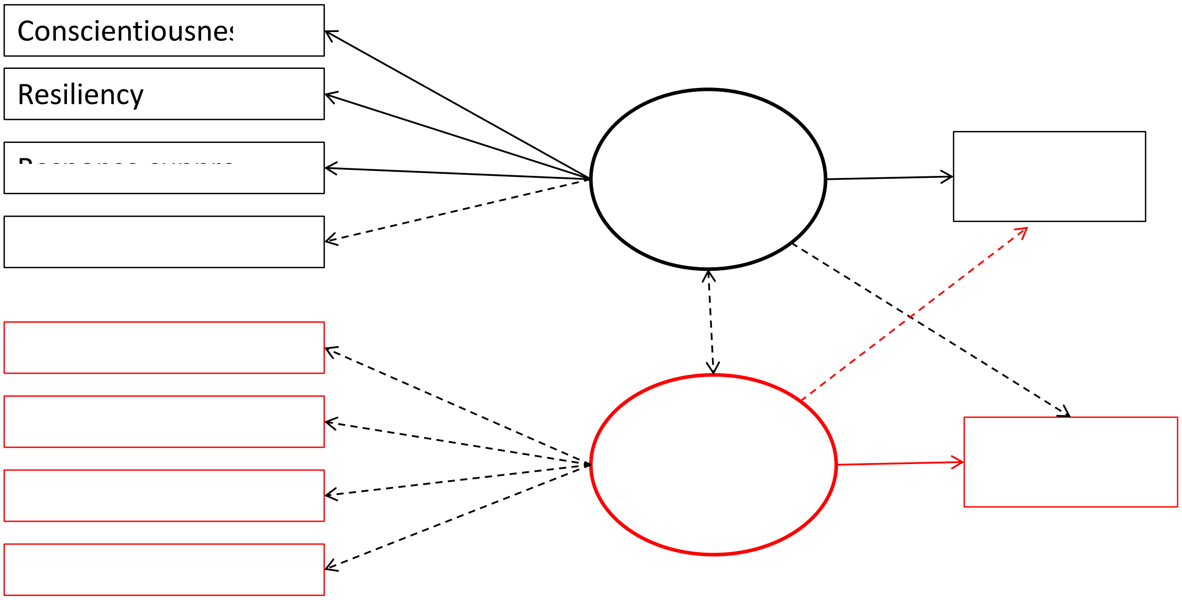
Sonuga-Barke, E.J. (2002). Psychological heterogeneity in AD/HD: A dual pathways model of motivation and cognition. *Behavioral Brain Research*, *130*, 29–36.

Willcutt, E., Sonuga-Barke, E.J., Nigg, J.T., & Sergeant, J.A. (2008). Neuropsychology of childhood disorders. In T. Banaswhewski & L.A. Rohde (Eds.), *Biological Child Psychiatry: Recent Trends and Developments (Advances in Biological Psychiatry)* (pp. 195-226). Basel: Karger.

Fig. 1. Psychological processes hypothesized to influence ADHD. Four indicators (left) are used to estimate the value for each of two hypothesized processes: controlled responding (“top down”) and reactive responding (“bottom up”). “Top down” control is hypothesized to rely on intact cognitive control. It is indicated here by one personality trait (conscientiousness) and one temperament trait (resiliency) that are both rated by the mother, and by laboratory cognitive

control measures of response inhibition and set shifting. The construct of top-down control is uniquely related to teacher rated inattention. The second construct, reactive responding, is related to three personality dimensions (negatively with agreeableness), and one temperament measure (negative emotionality) rated by the mother. It is uniquely related to hyperactivity. This model fits the data quite well. Solid lines are statistically significant paths; dashed lines are nonsignificant, and can be omitted without worsening model fit. See Martel, Nigg, & von Eye (2009).

Fig. 2. Hypothesized effect of causative elements on two behavior domains via alterations in neural development (A) and illustrative data attempting to test a portion of this type of model (B). Experiential activators should have some main effect, but moderated by genetic liability. Distinct influences may exist on inattention and hyperactivity-impulsivity, which are hypothesized to relate to partially distinct cognitive and neural operations. The tested portions of the model—using one experiential activator, blood lead (from Nigg et al., 2008)—are illustrated by red lines. Cognitive control is a proxy (or endophenotype) that is hypothesized to be sensitive to functional effectiveness of neural circuits affected in ADHD. It is represented by response inhibition on the stop task and response variability on the go task; here, for simplicity, only the stop signal reaction time data are shown. The standardized path weights convey the strength of the association, and can range from 0 (no association) to 1 (perfect association), similar to a correlation coefficient. The indirect path via cognitive control is significant ($p < .01$) whereas the remaining path from blood lead to hyperactivity (parent reported symptoms, structured interview) is nonsignificant and trivial in size; this shows that the association of blood lead with hyperactivity was statistically accounted for by the association of blood lead and hyperactivity with response inhibition.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