Executive Functions in Attention-Deficit/Hyperactivity Disorder

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Objective: To examine the association between weaknesses in executive functions and attention-deficit/hyperactivity disorder (ADHD). ***Method:*** Empirical studies examining executive functions in ADHD samples were reviewed, with particular attention to results of recent meta-analyses. ***Results:*** ADHD is associated with impaired performance on measures of response inhibition, working memory, and other aspects of executive functions, yet data also suggest significant neuropsychological variability within and across ADHD samples. ***Conclusion:*** ADHD may be best conceptualized as a neuropsychologically heterogeneous condition. More work is needed to characterize this heterogeneity and its clinical and pathophysiologic implications.

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Although the diagnosis of attention-deficit/hyperactivity disorder (ADHD) is made based on behavioral symptoms of inattention and/or hyperactivity/impulsivity, numerous empirical and theoretical papers over the past 3 decades have highlighted neurocognitive impairments, particularly in the domain of executive functions (EFs), that are associated with the disorder. Despite this large body of literature, the core neuropsychological impairments in ADHD have not been fully resolved. The current article reviews this body of work, emphasizing recent meta-analytic findings as well as evidence suggesting that ADHD is best conceptualized as a neuropsychologically heterogeneous condition.

HISTORICAL PERSPECTIVE

Although early reports of the syndrome now known as ADHD focused on hyperactivity as the defining feature of the disorder,[1] the 1970s saw a major shift in emphasis on attentional deficits as a result of Douglas' studies of vigilance in hyperkinetic children.[2] At the same time came greater insights into the functions of the prefrontal cortex[3] and a growing recognition that certain behaviors in hyperactive youth, including poor planning, difficulty sustaining mental set, and responsiveness to external structure, resembled those of patients and animals with prefrontal lesions.[4] Together, these findings laid the groundwork for the hypothesis that ADHD is associated with impaired prefrontal-striatal neural networks that regulate attention, inhibition, and motor intentional behavior. Over time, this hypothesis has continued to be supported by the success of stimulant medications and animal models of hyperactivity that implicate catecholamine pathways consistent with these neuroanatomical regions[5] as well as structural and functional neuroimaging studies documenting associated abnormalities in the dorsolateral prefrontal cortex, the anterior cingulate cortex, the caudate nucleus, and the globus pallidus in ADHD patients.[6] Recent findings (e.g., Berquin et al.[7]) also highlight involvement of cerebellar regions with a high concentration of dopamine transporters and connectivity to prefrontal regions via midbrain structures.

NEUROPSYCHOLOGICAL FINDINGS

ADHD vs. Control Group Differences

Consistent with the fronto-striatal hypothesis is a large literature revealing that individuals with ADHD exhibit relatively poor performance on clinical neuropsychological tests of attention and EFs presumed to measure prefrontal dysfunction.[8] The term *executive functions* refers to higher-order cognitive processes that underlie self-regulation and goal-directed behavior,[9] including working memory, response inhibition, set shifting, abstraction, planning, organization, fluency, and certain aspects of attention.[10] Although studies of EFs in ADHD have primarily targeted preadolescent boys, impairments on EF

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measures have also been documented in females (e.g., Hinshaw et al.[11]), adolescents (e.g., Seidman et al.[12]), and adults with ADHD (e.g., Lovejoy et al.[13]). Moreover, in many studies, executive deficits are robust to statistical correction for group differences in IQ and comorbid psychiatric or learning disorders (e.g., Willcutt et al.[14]). This large number of studies has prompted several theoretical and meta-analytic papers aimed at more precisely defining the EF deficits in ADHD.

The most well-known theoretical models of ADHD have argued that specific aspects of EFs represent the "core" or "primary" deficit in the disorder. To date, inhibitory control has been the most widely discussed core deficit in ADHD,[15] with numerous studies supporting weaknesses on clinical and experimental measures of inhibition in individuals with ADHD versus non-ADHD controls.[16,17] Nigg[18] has argued for specification of the construct of inhibition as a way of clarifying the core deficits in ADHD, concluding that there is stronger evidence for an inhibitory deficit when the deficit refers to suppression of a prepotent motor response (e.g., on the stop signal test or basic go/no-go tasks), but more variable evidence when inhibition refers to suppression of a conflicting response (e.g., interference control on Stroop or flanker tests). Nigg's argument has been supported by meta-analyses that found moderate to large effect sizes for the stop signal reaction time (SSRT; 0.54–0.85)[16,17,19–21] and small to moderate effect sizes for the Stroop Interference score (0.13–0.35).[20–22]

Working memory represents another aspect of EF that is of significant interest to ADHD researchers[23] due to neuroimaging studies showing that working memory tasks activate fronto-striatal and cerebellar regions (e.g., Lewis et al.,[24] Chen and Desmond[25]) and because of the face validity that trouble holding and manipulating information "on line" contributes to ADHD symptoms. Although results of individual studies are varied, meta-analyses support working memory impairments in ADHD.[19,20,26] The most recent analysis by Martinussen and colleagues[26] suggests larger effect sizes for different measures of spatial working memory (0.85–1.06) versus verbal working memory (0.47–0.56). As these authors point out, such findings are consistent with the neuroimaging literature that finds greater support for right versus left hemispheric involvement in ADHD.[27]

Although response inhibition and working memory are the EF weaknesses most often discussed in theories of ADHD, meta-analyses indicate decrements of moderate magnitude in other EF domains as well. Willcutt et al.[20] found impairments of moderate magnitude (ds = 0.43–0.69) for measures of planning (Tower tests), organization (Rey-Osterreith Complex Figure [ROCF]), set shifting (Wisconsin Card Sorting Test [WCST]), impulsivity (continuous performance test [CPT] commissions), and processing speed that includes a set-shifting component (Trails B). Frazier and colleagues[28] similarly found moderate weighted mean effect sizes for Trails B and CPT omissions and commissions (0.55–0.59) but slightly lower effect sizes for the WCST (0.35) and the ROCF (0.24). In their article, nonexecutive measures yielded a smaller overall effect size (0.39) compared with executive measures (0.58), suggesting some specificity of an EF deficit in ADHD; however, they and others also found moderate decrements in processing speed (0.40–0.65),[19,28] vigilance (i.e., CPT omissions; 0.50–0.64),[19,20,28] and overall intellectual functioning (0.61),[28] causing some researchers to question whether deficits in ADHD extend beyond the executive domain (e.g., Boonstra et al.,[19] Frazier et al.[28]).

Heterogeneity Within ADHD

Despite the well-replicated EF weaknesses in ADHD subjects, variability between studies has been noted in conceptual reviews (e.g., Pennington and Ozonoff[8]) and has been statistically supported for a variety of measures in several meta-analyses,[19,26,28] suggesting that it is not simply due to sample error. Recently, researchers have also noted variability within ADHD samples that is evident when examining whether EF measures can be used to diagnose ADHD. Data on male[29] and female[11] youth as well as adults[13] have indicated that many measures of EF have good positive predictive power for ADHD but poor negative predictive power. That is, abnormal scores on EF measures are generally predictive of the diagnosis; however, normal scores on a particular EF measure, or even a combination of measures,[29] cannot rule ADHD out. This pattern is due to the fact that not every person with ADHD is impaired on every test and that some individuals with ADHD perform within the normal range on all or most measures.

Even the well-replicated response inhibition weakness is only present in a subset of individuals with ADHD. For example, Crosbie and Schachar[30] found that only 40% of their ADHD sample fell in the impaired range on the SSRT. Similarly, Nigg and colleagues[31] found that only half of the ADHD Combined-Type subjects assessed at different ADHD research centers across the United States exhibited SSRT scores that surpassed the 90th percentile of controls. In this analysis, no other individual neurocognitive measure examined was impaired in more than 50% of ADHD subjects. Percent of subjects that surpassed the 90th percentile cutoff on other tests (including the Stroop, Trails B, CPT commissions, and the variability of reaction time [RT] on the stop signal test) ranged from 48% to 16% at different research sites. In the Nigg et al. study[31] and another recent paper,[32] aggregating tests to assess a general EF deficit still only identified a subsample of ADHD cases.

Potential Moderators of Neuropsychological Heterogeneity

Although neuropsychological heterogeneity within ADHD has not been extensively acknowledged or studied,

the literature raises several possible factors that may be associated with variability of performance on EF measures.

Family history. Two research groups have shown an association between a family history of ADHD and EF impairment. Crosbie and Schachar[30] found that ADHD children with poor inhibition on the stop signal test had a significantly higher rate of familial ADHD (48%) compared with a normal-inhibition ADHD group (19%) and controls (8%). Seidman et al.[33] also found that youth with ADHD who had a family history of ADHD performed more poorly on subtests of the Stroop and WCST than youth with ADHD who did not have a family history of the disorder.[12,33] These reports raise the possibility that familial and nonfamilial cases of ADHD differ neuropsychologically. Further work is needed to determine whether such differences are qualitative or quantitative.

Comorbid disorders. The presence of comorbid disorders may exacerbate or modify the neuropsychological profile of youth with ADHD. Several studies (e.g., Willcutt et al.,[14] Seidman et al.,[34] Lazar and Frank,[35] Rucklidge and Tannock[36]) have shown that individuals with ADHD with comorbid learning disorders have greater EF deficits than individuals with ADHD alone. However, data from meta-analyses are mixed. On the Stroop, van Mourik et al.[22] found that children with ADHD alone had better Word and Color Naming scores than individuals with reading disorders (with or without ADHD) but worse interference scores. Martinussen et al.[26] found that comorbid reading and language disorders explained some of the variance among studies in spatial but not verbal working memory domains. Additionally, these authors found greater effect sizes for different domains of spatial working memory in studies that controlled for reading and language.

Neuropsychological studies of other comorbidities in ADHD are fewer in number. The handful of studies of youth with ADHD and comorbid anxiety disorders suggest that the comorbid subgroup shows less severe deficits in response inhibition than ADHD children without anxiety[37] but more severe deficits on working memory tasks.[38,39] Although there have been more neuropsychological studies of ADHD plus conduct disorder, meta-analyses have not found support for comorbid conduct disorder as a moderator of response inhibition in ADHD.[16,17]

DSM-IV subtypes. It has been hypothesized that different patterns of EF weaknesses might distinguish between ADHD Inattentive (ADHD-I) and Combined subtypes (ADHD-C)[40]; however, meta-analyses do not provide clear support for neuropsychological differences between these subtypes. Willcutt et al.[20] found no significant differences between ADHD-C and ADHD-I on any EF measure (mean d = 0.09 ± 0.10), and Lijffijt et al.[17] found no effect for subtype with regard to SSRT. In contrast, van Mourik et al.[22] found that ADHD-I showed greater deficits in interference control than ADHD-C or ADHD Hyperactive/Impulsive type (ADHD-H/I; d = –0.35). Yet, the small number of studies targeting ADHD-H/I and/or symptoms of hyperactivity/impulsivity have failed to show expected EF deficits.[41–44] Thus, further investigation of cognitive impairments differentially associated with inattentive and hyperactive/impulsive symptom dimensions is warranted.

Developmental differences. Although adolescents are underrepresented in the ADHD literature, studies suggest similarities across preteen and teenage years (e.g., Seidman et al.[45]). Adults are less well studied than youth but seem to show EF impairments as well[19,21]; however, some differences with child samples have emerged in meta-analyses. Schoechlin and Engel[46] found minimal impairments on measures of planning and abstract problem solving in adults with ADHD, possibly due to ceiling effects of the tasks or to the most impaired adults not being available for assessment.[21] Lijffijt et al.[17] also found that although children and adults showed moderate to high decrements on the SSRT, adults showed greater discrepancy between baseline RT and SSRT, which the authors argue is the best measure of response inhibition. Nonetheless, given the small number of neuropsychological studies of adults, differences across adult and child samples require further confirmation. Finally, preschool-aged children with ADHD have received minimal attention, with 1 such study documenting EF impairments[47] and 2 failing to find them in this age group.[48,49] Because most of the available data are cross-sectional, longitudinal studies are needed to better understand the course of neuropsychological impairments within ADHD across the life span.

Normal-Range Performance

Although the above discussion highlights factors that may contribute to the neuropsychological variability within ADHD samples, it does not address the fact that many individuals with ADHD do not exhibit deficits on any EF measure. This section discusses possible reasons for this normal-range performance.

Executive function measures may not always capture frontal system impairments. One possibility is that EF measures are imperfect indicators of frontal impairment or the latent construct of EF due to either (1) measurement error or (2) compensatory mechanisms that allow some individuals to use alternative cognitive resources to solve "frontal" system tasks. Among the factors that may introduce error into the measurement of EF weaknesses is low sensitivity (for a full discussion of these factors, see Doyle et al.[50]). Because many measures of EF were developed to assess the effects of a significant cerebral insult in adults,[8] such tests may not capture mild cognitive impairments occurring within the context of development. Since individuals with EF deficits are highly responsive to external structure,[51] the structured testing situation may also

mask less severe impairments.[52] These possibilities imply a range of severity of EF impairments in ADHD, with EF measures capturing the more impaired end of the distribution.

Compensatory mechanisms that allow some individuals to recruit other cognitive resources to solve tasks that would normally engage frontal circuits may also explain normal-range performance. Neuroimaging studies of patients with other disorders[53,54] provide evidence of this phenomenon and suggest that such compensatory mechanisms are vulnerable to disruption.[55] Although this possibility has not been studied extensively in ADHD, Bush and colleagues[56] found that both ADHD adults and controls experienced an interference effect on a counting version of the Stroop test, but controls activated the anterior cingulate cortex when performing the task, while those with ADHD activated the insula. These data require replication; yet, the fact that performance was equivalent across groups suggests alternative pathways for problem-solving.

Executive function deficits may not be the core deficit in some or all ADHD cases. A second possibility is that EF deficits may not be the core or only causal deficit underlying ADHD. Impairments in state regulation and delay aversion are interesting candidate deficits to consider in ADHD, because their association with the disorder is supported by theory and data and because they may relate to the neuropsychological heterogeneity within ADHD samples. Due to space constraints, we describe these constructs briefly and refer the readers to recent reviews for further details.[57,58]

Sergeant[59] has proposed the cognitive-energetic model of ADHD in which impairments on tasks requiring effortful control of attention and executive processes could be due, in part, to deficiencies in activation, arousal, and effort that control the allocation of cognitive resources rather than impaired cognitive resources per se. Consistent with this theory is evidence that the rate of presentation of stimuli affects ADHD subjects differently than controls, with slow rates of presentation related to poor performance, potentially due to underarousal.[59] Thus, it has been suggested that the slower inhibitory process found in studies of the stop signal test may reflect an arousal problem rather than an inhibition problem per se.[60] One potential index of such state regulation difficulties is variability of RT, a measure of the consistency of the speed of a response after a stimulus. As reviewed by Castellanos and Tannock,[23] RT variability is one of the most replicated deficits in ADHD. Yet, RT variability may not be universal within ADHD. In Nigg and colleagues' study of heterogeneity,[31] only half of ADHD subjects from different research sites fell in the impaired range on RT variability on the stop signal test, despite a relatively large effect size overall (Cohen's $d = 0.8$). Thus, these data suggest that arousal/energetic factors are clearly important to consider in conjunction with EF deficits as a neurocognitive mechanism in ADHD but are unlikely to account for all ADHD cases.

Delay aversion is a construct grounded in an animal model of altered reinforcement and extinction processes.[61] Based on this model, Sagvolden and colleagues[61] posit that goal-directed behavior in youth with ADHD requires frequent, potent reinforcers proximal to the behavior being reinforced. If such reinforcers are lacking or distal, inattention and motor impulsivity occur. Consistent with this model, Sonuga-Barke and colleagues[62] have shown that children with ADHD exhibit aversion to delay, showing preferences for smaller, immediate rewards compared with larger, delayed rewards. Solanto et al.[63] found that measures of inhibitory control and delay aversion were not correlated in ADHD subjects; however, the 2 measures together identified the majority of ADHD cases in a discriminant function analysis. Based on these and other data, Sonuga-Barke[64] has proposed a dual pathway model of ADHD involving both EF and delay aversion. Although further data are needed to determine whether the predictions of this model are borne out, this theory marks an important contribution to the field as the first formal model of neuropsychological heterogeneity in ADHD.

SUMMARY AND IMPLICATIONS: NEUROPSYCHOLOGICAL HETEROGENEITY OF ADHD

The literature supports the association between ADHD and deficits in response inhibition, working memory, and broadly conceived domains of EF. Yet, data also reflect neuropsychological variability within ADHD, with factors such as family history of the disorder, comorbidity, symptom dimensions, and developmental stage potentially associated with differential performance on EF measures. Moreover, the small proportion of individuals with ADHD who show normal-range EF performance raises questions of whether non-EF deficits, such as impairments in state regulation and delay aversion, underlie symptoms of ADHD as well. Thus, this disorder may be best understood as a neuropsychologically heterogeneous condition. While it is possible that measurement error accounts for some of the observed variability, true neuropsychological heterogeneity would be consistent with the phenotypic heterogeneity of ADHD (e.g., symptom-based subtypes and various comorbid presentations), the disorder's likely genetic heterogeneity,[65] and the heterogeneity found across ADHD neuroimaging studies.[6]

Behavioral genetic data provide further support for the notion that EF deficits are etiologically linked to ADHD but do not represent the single underlying deficit in the disorder. Because ADHD is highly heritable, if EF weaknesses were the primary deficit that gave rise to ADHD symptoms, family, twin, and adoption studies would be

expected to reveal significant familial/genetic overlap between ADHD and performance on EF measures. Although the limited literature on this topic suggests that some of the same familial and genetic influences on ADHD also influence impairments on EF measures, the magnitude of the shared familial/genetic influences is low to moderate,[50] suggesting that either a significant proportion of these influences on ADHD differ from those on EF measures or else that some factor (e.g., measurement error or heterogeneity) is limiting the detection of the shared influences. The fact that aggregating neuropsychological measures often slightly increases the magnitude of familial/genetic overlap suggests that some measurement error exists but that it is unlikely to be the sole reason for the modest overlap.[50]

Given these data, ADHD researchers should move beyond the search for a single, core cognitive deficit to formally study the nature of the neuropsychological heterogeneity in ADHD. What remains to be better understood, in addition to the impact of the potential moderating variables discussed above, is whether there are separate and unique pathways to ADHD (e.g., some individuals with EF deficits and some with delay aversion, as hypothesized by Sonuga-Barke[58]) or whether there is a pool of overlapping risk factors that contribute variably to all cases of ADHD.

Documenting this heterogeneity is important from a clinical perspective. The fact that individuals with ADHD do not show a consistent profile of EF impairments renders neuropsychological testing inappropriate as a diagnostic tool.[29] Importantly, normal-range performance on EF measures should not be used to rule out ADHD if careful diagnostic interviewing and behavioral rating scales support the diagnosis. Clinicians may need to educate families and school personnel as to the reasons behind good performance to prevent benign test scores from undermining pursuit of appropriate treatment and academic supports. Nonetheless, neuropsychological testing of individuals with known or suspected ADHD offers other clinical benefits, including identification of strengths and weaknesses that can be helpful for school or career planning. Recently, Biederman et al.[32] showed that youth with ADHD with impaired scores on 2 or more EF measures had higher rates of repeated grades and placement in special educational classes than individuals with ADHD who did not meet this definition of EF impairment. This finding was recently replicated in a sample of adults (J. Biederman, M.D.; C. Petty, M.A.; R. Fried, Ed.D.; et al., manuscript submitted) in which impairments also extended to the occupational domain. Thus, neuropsychological testing may identify individuals within ADHD who are at particularly high risk for adverse outcomes and who may require additional/specialized behavioral, pharmacologic, or educational interventions.

In addition to their clinical implications, neuropsychological impairments may be promising targets for molecular genetic studies of ADHD.[50] For conditions that are likely influenced by multiple genetic and nongenetic factors, biologically based phenotypes that lie in the pathway from genes to behavior (i.e., "endophenotypes") may provide a more powerful target for molecular genetic studies than the disorder as a whole. Because EF impairments partially index the familial/genetic liability for ADHD, they may be useful for identifying at least some of the genes that confer susceptibility to ADHD or the chromosomal regions that harbor them. In turn, expression studies may serve to further elucidate the pathophysiology of the disorder, including potential heterogeneous processes and differences and commonalities between ADHD and other neurodevelopmental disorders that also show EF impairments.[8] Thus far, the use of EF measures as ADHD endophenotypes is just beginning to be explored.

CONCLUSION

Although elegant theories have emphasized specific EF deficits as underlying ADHD, careful examination of the empirical literature suggests neuropsychological heterogeneity within the disorder. Formal recognition and further investigation of this heterogeneity are essential for clinical purposes and have the potential to further our understanding of pathophysiologic processes, which, in turn, will engender novel prevention and intervention strategies.

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