Adult ADHD

Concluding Thoughts

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ABSTRACT: This concluding paper raises some final questions and issues that the authors feel should receive more emphasis in future research on ADHD in adults. One significant problem for our field is the upward extension of child-based models and approaches without proper adaptation to adults. With adults differing patterns of comorbidity and symptom heterogeneity pose new conceptual, diagnostic, and treatment challenges. As an illustration, we review ten common presenting complaints in adults and their link to the underlying core ADHD deficits of hyperkinesis, inattention, and impulsivity. While these core symptoms are often overt problems in children, in adults subtler executive dysfunction appears. Even though the growing consensus is that ADHD is a disorder of executive functions (EF), the details of the EF/ADHD connection remain unclear and may be far more complex in adults. That complexity is mirrored in the widening anatomic representation of EF, extending beyond the frontal lobes into the subcortex and other nonfrontal regions. More research will be needed to follow the developmental trajectory of executive dysfunction in ADHD over the life cycle and tie this to the developmental neuropsychology of EF. Psychosocial context and nongenetic familial influence are also critical variables that need greater consideration when characterizing and measuring ADHD symptoms in adults. Finally, until we have reached consensus on adult subject selection, we may not be able to enhance diagnostic rigor or expand our conceptual framework for understanding the underlying pathophysiology of ADHD in adults.

KEYWORDS: ADHD; Development; Adult psychopathology; Executive functioning; Frontal lobes.

The preceding papers have given us historical underpinnings and varied perspectives on a disorder often characterized by the popular press as being the "diagnosis du jour." To the contrary, the scholarship of our contributing authors clearly demonstrates

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that ADHD is a behavioral marker for a complex neuropsychiatric syndrome, or syndromes, that truly debilitates many young (and not-so-young) adults. After reading this volume, there should be no doubt that this is a serious condition that fully deserves the increased attention it is receiving from the medical and scientific communities. Naturally, many questions remain. We would like to close this volume with a discussion of a few issues that we believe are likely to attract more research energy in the future. These topics, although diverse, share a common theme: Keeping a broad outlook and thus avoiding the pitfall of rushing to draw premature conclusions and oversimplify our concepts.

HETEROGENEITY AND THE COMPONENTS OF ADHD

A fitting start is to ask whether we are describing a single entity, whether genetic or acquired, when we speak about "ADHD." Much suggests we are not. ADHD-related neuropathology appears to cluster in variable combinations. Denckla[1] has suggested that this variability in expression of different symptoms in ADHD may reflect dysfunction in different regions of the frontal-subcortical loop. While the symptoms of ADHD can be the result of acquired encephalopathy,[2] the more usual etiology is familial.[3] Yet, it is far from clear that the acquired and inherited forms share the same pathophysiology. Moreover, where the condition is inherited, we do not know whether we are dealing with a restricted range of genotypes with many different phenotypes, or multiple gene clusters. In this volume, Comings[4] and Mirsky and Duncan[5] have each suggested different genes underlying ADHD. Others have described a separate genetic basis for inattentive and hyperactive-impulsive subtypes.[6] On the other hand, a recent study at Harvard looks to nongenetic causes to explain symptom heterogeneity.[7] Given genetic and neurobehavioral heterogeneity, some speak of an ADD/ADHD spectrum, rather than a single diagnosis (see Denckla[8] on children and Ratey and Johnson[9] on adults). Perhaps the original "minimal brain dysfunction" label, while overly general and somewhat pejorative, came closer to recognizing the broad range of conditions under consideration.

We may ultimately understand this variability by examining the functional connections between ADHD core symptoms. The evolution of the DSM definitions of these disorders, with the shifts in relative importance of core symptoms, reflected the growing recognition that inattention, impulsivity, and hyperactivity are not universally coupled. In its most recent volume, the DSM-IV[10] includes three subtypes (Predominantly Inattentive, Predominantly Hyperactive-Impulsive, and Combined), but no one suggests that this nosology is final.[7] In particular, one recent study argues that the Inattentive and Combined subtypes are the only valid ones,[11] and it is well known that impulsivity can exist without hyperkinesis, especially in ADHD adults. As we study these disorders more closely throughout the life cycle, we will likely find other ways in which core symptoms uncouple. Research in adults will certainly grapple more and more with these questions.

The example of uncoupling of impulsivity/hyperactivity illustrates this fertile frontier of study. Does it follow that inattention can take different forms, as either an impulsive variant or one more cognitively based (or even a combination of the two)? That is, does inattentive behavior in some patients reflect distraction secondary to

poor impulse control (perhaps orbital-frontal)? For others (or at other times) does inattention reflect poor alerting or orienting of attention in line with right hemisphere attention distribution models?[12–14] Or can poor attention performance be due to dysfunction in subcortical and limbic circuits underlying motivation? More controversial, is the primary deficit in ADHD really related to attention at all? Is "ADHD" correctly defined by a symptom (Inattention) which may not be present universally? In fact, one large meta-analytical study of ADHD children failed to find primary deficits in attention.[15] If inattention per se is not a core cognitive symptom, what then underlies "inattentive" behavior? Related to this, can a dysexecutive syndrome exist without inattention, impulsivity or hyperkinesis? Would this still be identified as ADHD? Ultimately, how do we conceptualize ADHD in the presence of cognitive and behavioral heterogeneity? Many reports in the child literature at the time of the publication of DSM-IV re-conceptualized ADHD as a multidimensional disorder. This approach clearly will be useful in resolving these analogous issues in adults.

Comorbidity contributes to heterogeneity and poses additional conceptual challenges, both construct (regarding the definition of ADHD) and clinical (regarding diagnosis and treatment). Is ADHD with a comorbid condition simply ADHD plus other disorders, or are these bona fide ADHD variants? For example, Comings[4] has argued that Tourette's syndrome (TS) is really a form of ADHD. TS has further been conceptualized as a fronto-subcortical circuit disorder,[16] involving the basal ganglia and related structures.[17] Different clinical subtypes of TS and/or ADHD may reflect different levels of dysfunction in the executive regulatory role of the cortex over subcortex.[17] Are ADHD and TS the same disorder or examples of several possible related corticostriatal syndromes?[17,18] In adults, a number of acquired, behavioral disorders have been described by Cummings[19] that also reflect disruption in three parallel frontostriatal circuits (e.g., dysexecutive behavior reflecting dysfunction in the dorsolateral prefrontal loop, disinhibited behavior reflecting dysfunction in the orbito-frontal loop, and inertia reflecting dysfunction in the mesial-limbic loop). Several of these behavioral disorders bear a striking resemblance to ADHD and again suggest shared neuropathology.

Exploring heterogeneity in adults with ADHD will require more attention to the methodology we use to identify our research subjects. Adult studies will continue to stand on the shoulders of child studies, with their advanced experimental designs, using sophisticated technology such as functional MRI[20] and elegant psychological tasks such as visual-spatial cueing, saccadic eye tracking tasks, covert orienting tasks and behavioral go-no-go tasks[21–24] to elucidate brain function in ADHD. However, many of these studies may be limited by the use of broad behavioral measures for identifying research subjects (e.g., DSM IV criteria for ADHD, subtype and symptom variants often are not specified). As we point out elsewhere,[25] strict adherence to the DSM IV criteria may not be the most appropriate tool for diagnosing and identifying potential ADHD research subjects in adulthood. Until we have reached consensus on adult subject selection, we may not be able to enhance diagnostic rigor or expand our conceptual framework for understanding the underlying pathophysiology.

THE COMPLEXITY OF PSYCHOSOCIAL CONTEXT

Psychosocial context is another critical variable that needs greater consideration when characterizing and measuring ADHD symptoms. ADHD is a genetic disorder, which means index patients often live with others similarly affected. In fact, we know that at least 25% of children diagnosed with ADHD have a parent with the diagnosis[3] and that more than 50% of adults with ADHD will have a child with the diagnosis.[7] This may be why parent-child interactions are more problematic in families of children with ADHD.[26] Mothers of ADHD children have more negative perceptions of their own childhood,[27] as well as more depression.[28] This may carry over into their parenting, especially in a child with similar symptoms.[29] The so-called "ADHD-family," defined as a family with one or more ADHD parents and an affected child,[29] has unique difficulties around organization, setting and keeping routines, day-to-day supervision, stress tolerance, mood stability, compliance with treatment recommendations, etc. These may be an outgrowth of current and residual functional deficits in the ADHD parent, which may interact with and secondarily affect the ADHD child[29] and perhaps worsen his/her prognosis.

Different manifestations of ADHD symptomatology may result in different psychosocial problems. The bulk of prospective follow-up studies of adults diagnosed with ADHD as children predict a future plagued by substance abuse, involvement with the law, educational and occupational under-attainment.[30–32] Yet, there appear to be mitigating factors. Studies have reported that the worst outcomes may be in the small number of subjects who persist with the full-blown syndrome.[31] Perhaps these adult patients were at the worst end of the spectrum of severity during childhood. Others have indicated that while ADHD adolescents are at considerable psychosocial disadvantage,[32,33] they do improve by young adulthood. In one study, young adults with childhood ADHD reported more psychological distress and ongoing mental health treatment than non-ADHD controls, but the groups did not differ in their rates of legal difficulties, eventual educational attainment, and occupational achievement.[33] Thus, many managed to overcome some of the difficulties which may have been present in high school.

Clearly, both biology and sociology are sources of considerable diversity in clinical presentation. It will be our challenge to keep both ends of the conceptual spectrum in mind as the field moves forward.

ADHD AS A DYSEXECUTIVE SYNDROME: RELEVANT ISSUES

There appears to be a growing consensus that ADHD is a fundamental disorder of executive functions (EF). Even as we crystallize our thinking around this very powerful notion, it is essential to not oversimplify the many complex interrelationships. This is exemplified in the ongoing discussion of what the construct means and where in the brain it resides.

History of the EF Concept

The term "executive function" has become shorthand for many processes (motor and mental) by many different names. Terms often used interchangeably include

self-reflection, self-regulation, self-control, behavioral inhibition, planning, forethought, delay of gratification, anticipatory set, future orientation, working memory, planning, set shifting, selecting, dividing and sustaining attention, affect regulation, resistance to distraction, flexibility, and metacognition. The construct itself was born in the late 1970s and early 1980s, emerging in both the literatures on information processing and clinical neuropsychology. Each discipline developed an understanding of "control functions" to suit their own explanatory principles (see Eslinger[34] for an historical review), often at different levels of abstraction.

For Butterfield and Belmont,[35] who introduced the term from the information processing perspective, EF was exemplified when "a subject spontaneously changes a control process or sequence of control processes as a reasonable response to an objective change in an information processing task" (p. 244). From this perspective there were three essential components underlying such flexibility of responding: task analysis, strategy control, and strategy monitoring. Interestingly, these closely resemble four levels of problem-solving behavior proposed by Luria[36,37] which form the core of many current definitions of EF. These include: 1) analysis of task features, 2) generation of alternative solutions, 3) formulating flexible motor programs to achieve solutions, and 4) evaluation of outcome of programs by using error feedback.[36]

Similar to the information processing approach, clinical neuropsychologists speak of EF as the abilities underlying implementation and regulation of goal directed behavior. Lezak, in introducing the concept to neuropsychology, referred to EF as those behaviors necessary for fully independent, socially responsible and effective living.[38] In her scheme, the components of EF were fundamental processes such as starting, stopping, shifting, as well as sequencing, planning, self-awareness and foresight—that which Lezak termed the "how" and "whether" of actions.[39] She explicitly separated these control functions from reasoning capacities, such as abstraction and concept formation. Again consistent with Luria, the four major classes of EF defined by Lezak[39] include formulation of goals, planning, execution to attain goals, and effective performance of these goals.

The EF concept was particularly organizing and influential, leading to expanding bodies of research and theory in each intellectual school (information processing and neurobehavioral, respectively). Rapid construct development alone could have been a source of confusion regarding the meaning of EF. The quandary may have been worsened by converging paths between the cognitive and the neurological traditions (see Eslinger[34]). This has led to the present state of affairs where EF has been used to denote every thing from "initiate, sustain, inhibit/stop and shift,"[40] to "separation of affect, prolongation, internalization, and reconstitution,"[41] "managerial knowledge units,"[42] "working memory or remembering to remember,"[43] "coordinator of cognitive and metacognitive processes,"[44] and "rule flexibility, rule generation, rule understanding, rule following,"[45] to name but a few.

Despite such epistemological considerations, three child neuropsychologists have relied on models of EF to understand ADHD and other childhood developmental disorders. As central to the EF problems in ADHD, Denckla[46] highlights deficits in goal-oriented modulation between inhibitory and initiation functions. We clearly see the influence of Luria's[36] model in her definition of EF as a "cognitive module consisting of effector output elements involving inhibition, working memory, and organizational strategies necessary to prepare a response" (pp. 283).[17] By contrast, Barkley[47,48]

asserts that the core deficit in ADHD is one of disinhibition. He too posits four executive functions that underlie behavioral inhibition: working memory, private speech, emotional control, and reconstitution (of sets of behaviors). Finally, Pennington,[43] has defined EF as the ability to maintain an appropriate problem-solving set for attainment of a future goal, emphasizing deficient working memory as the core dysexecutive issue in ADHD.

Thus the above authors emphasize understanding ADHD in terms of its EF deficits with somewhat different profiles. Despite the compelling face validity of the EF/ADHD link, however, the relationship remains unclear. This lack of clarity is further complicated by the ambiguities surrounding the meaning of the EF construct and the parameters of the ADHD diagnosis itself, as highlighted in our discussions above. Yet, if we consider EF as the matrix of abilities necessary for the execution of socially and temporally effective and organized behavior (in keeping with its original neuropsychological meaning), we can begin to more accurately describe and study component brain mechanisms which contribute to the breakdown of these behaviors in ADHD. These may well involve interactions between elementary neurobehavioral and higher cognitive functions. Treating ADHD as a unitary diagnosis masks important individual or subtype differences.

Is EF in ADHD a Frontal Lobe Deficit?

Another area of investigation that may run the risk of arriving at premature conclusions is the growing research effort to locate the brain structures underlying ADHD. As a part of this endeavor, the field has deliberated the location of EF and whether this would lead us closer to our goal. The historical debate boils down to the importance of the frontal lobes for EF. Although, a detailed treatment of the link between EF and the frontal lobes is beyond the scope of this paper (for excellent texts, see Stuss and Benson,[50] Perecman,[51] Miller and Cummings,[52] and Krasnegor, *et al*.[53]), we shall briefly highlight some points pertinent to our discussion.

Within neuropsychology, EF has traditionally become tied to the regulatory function of the frontal lobes, particularly the lateral convexity of the prefrontal cortex. At minimum as it relates to ADHD, we believe this to be a narrow view. There is little doubt that the frontal lobes are essential for uniquely human behaviors such as making decisions, staying on task, being flexible, correcting errors, solving new problems, and overcoming inertia. However, at the very least, the subcortical web subserving the frontal lobes is equally critical to proper function. Classical neuropsychology informs us that persons suffering damage to this circuitry have difficulty developing new strategies in response to environmental contingencies, as well as difficulties in impulse control.[36,37] But EF extends beyond even this elaborate system. Indeed, Lezak's original description of EF involved behavior mediated by areas outside the frontal cortex, including subcortical regions and the right hemisphere.[38] Clearly, EF depends on far more than an intact prefrontal cortex.

The link between EF and ADHD originated with the observation that children with ADHD share many features with adults suffering brain damage. Early authors noticed similarities in the behaviors seen in children with hyperactivity and those seen in adults with frontal lobe damage.[54–57] Later authors, using neuropsychological testing, reported EF deficits in children with attentional problems.[58–66] Some authors have reported the presence of a "frontal lobe syndrome" in children with

ADHD,[67] while others have concluded that there is no clinical utility in using tests of frontal lobe functioning in the diagnosis of these children.[68] More recently, adult studies have also interpreted EF deficits as reflecting frontal dysfunction in ADHD.[69–71] We have already discussed the difficulty with automatically linking EF dysfunction with frontal lobe dysfunction per se. The same caution applies when discussing EF, frontal lobes, and ADHD. Indeed, while recent imaging studies provide evidence of frontal and striatal involvement in children and adults (reviewed in Giedd[72]), cerebellar, posterior and right hemisphere findings have been reported as well.[73–74]

Development, EF, and ADHD

Many authors, including Barkley[75] and Denckla[17] have articulated that becoming an adult involves increasing development of and reliance on EF. Barkley lists a number of developmental tasks of adulthood as examples of this: increases in organization and self-sufficiency, reflectivity, objectivity, responsibility, planning and concern for the future, independence, social skills with concomitant decreases in immediate gratification.[71] In essence, over time the emerging adult becomes more future-oriented rather than confined to the present. This closely parallels Denckla's assertion that, through development, EF enables the child to become more goal-directed. Denckla also emphasizes that while the source of the EF dysfunction in ADHD may be subcortical, the prefrontal cortex may have a substantial role in symptom reduction in adults.[17] By implication, both Barkley and Denckla are describing the reduction in "stimulus bound" behavior, which is another frontally mediated capacity sometimes included under the umbrella term of EF. Is ADHD then best conceptualized as a delay in frontal cortical development, as some believe? While there is appeal in this formulation, our discussion above regarding multiple representations of EF in the brain suggests that such a model would be incomplete or even misleading. We believe that a particularly significant problem for our field may be the upward extension of child-based models and approaches without proper adaptation to adults.

UNIQUELY ADULT PROBLEMS

Despite the richness of the child's psychological landscape and the difficulties encountered by children with ADHD, the adult with this diagnosis faces even more complex and varied problems. These difficulties stem in part from the deficits in EF discussed above. Understanding the functional difficulties encountered by ADHD adults is limited by our incomplete grasp of the unfolding of ADHD over the lifespan. Adult ADHD researchers will need to closely examine developmental and psychosocial factors, as well as control for the various methodological caveats discussed previously (especially sample characteristics). A number of our authors have touched on the common functional concerns that are most relevant to the ADHD adult and which may dominate their life trajectories and clinical presentations. These merit a second look.

Substance abuse, antisocial behavior and even criminality are significant and well-known adult outcomes reviewed in this volume[76,78] and elsewhere.[31,32] As

adult ADHD is a continuation of childhood ADHD, it might be argued that these are the most likely residua of the childhood ADHD core symptoms, especially poor impulse control.[78] It should be emphasized, however, that these are not universal outcomes and may be more closely associated with other, albeit poorly delineated, predictors (e.g., poor parenting, comorbid Conduct Disorder, and/or ADHD combined type). Yet other common symptoms are also prominent (if less dramatic) in the life of the ADHD adult. For example, sleep dysregulation is a frequent but less well-recognized symptom of ADHD[79] that may become more obvious when one has a job and a family. Hormonal fluctuations are especially relevant for women with ADHD, as they move through menarche, monthly cycles, pregnancy, and menopause. It is quite possible that ADHD symptom expression may be more variable in females as a consequence of such fluctuations.[80] Women may become fully symptomatic only at certain estrogen levels. The literature regarding estrogen and cognition, as well as its role as a neurotrophin, bears on this.[81,82]

It is quite likely that undetected (thus untreated) ADHD is common in adults seeking psychotherapy for mood disorders, anxiety, or general problems in functioning.[85] To the best of our knowledge, there are no studies of base rates of ADHD among adults seeking generic outpatient psychotherapy. Moreover, adults with ADHD may often be misdiagnosed by mental health professionals who are not familiar with the diagnosis, and therefore do not consider it.[25,85,86] Listed below are ten frequent complaints presented by adults seeking evaluation for ADHD.[86] They illustrate the difficulty clinician's encounter in assessing and treating these patients:

- difficulty in finding and keeping jobs,
- performance on job below level of competence,
- inability to perform up to intellectual level in school,
- inability to concentrate,
- lack of organization,
- inability to establish and maintain a routine,
- poor discipline,
- depression, low self-esteem,
- forgetfulness or poor memory, and
- confusion, trouble thinking clearly.

As can be seen, none of the complaints imply overactivity, a symptom that children with ADHD typically outgrow by adulthood. About one-third of the complaints are cognitive, such as inability to concentrate, forgetfulness, and confusion. Thus, subjective cognitive manifestations of ADHD clearly are still present in adulthood. Notably, another third of the complaints address difficulties in self-regulation (e.g., lack of organization, inability to establish and maintain a routine, poor discipline). During childhood such organizational tasks are commonly supported by parents and teachers, and are therefore less of a central issue for an ADHD child. By contrast, during adulthood, without other supervising adults to act as external regulators (or what Denckla has referred to as "the prosthetic frontal lobes"), deficits in self-regulation become more obvious. Moreover, the parent with ADHD may now also

be called upon to act as the external regulator of their child (with or without ADHD), and thereby find their own regulation abilities even more drained. The remaining complaints appear to be derivative of both the residual cognitive and the (more evident) self-regulation issues. These take the form of: 1) problems at work (difficulty finding and keeping jobs, performance on jobs below level of competence, inability to perform up to intellectual level at school), and 2) reactive emotional distress (depression, low self-esteem). Compared to adults without ADHD, those with the disorder have more unstable marriages, unsatisfactory work histories, car accidents, as well as interpersonal and social problems.[87] Many of these may be an additional outgrowth of the variety of self-regulation difficulties discussed above.

The above complaints presumably represent the ways in which adults manifest the underlying core ADHD deficits: hyperkinesis, inattention, and impulsivity. These core symptoms are often seen in overt behavior and learning problems in children. In adults, however, subtler dysexecutive issues emerge, as these complaints show. As we have discussed, the link between executive dysfunction and conventional core ADHD deficits remains unclear for both children and adults, but in adults this connection may be even more complex.

THE HORIZON

In conclusion, we have argued that EF is a central concept in understanding the real world difficulties encountered by adults with ADHD and may underlie much of the disabling aspect of the disorder. Yet we caution that the meaning of EF is extremely ambiguous, and the conclusion that the frontal lobes are implicated is not complete. The next generation of progress in this field will illuminate many of these discussions and will certainly spark others we cannot imagine as yet. This is an exciting field due in no small part to the considerable controversy, media attention and the concomitant, very real implications for society.

In this paper, we have highlighted that issues of heterogeneity, comorbidity, etiology, and diagnostic classification in adults must be resolved for us to approach the "true" state of affairs. While the field advances, we must not lose sight of the fact that adults with ADHD may also number among the most dynamic members of our society. The positive consequences of ADHD have not been systematically studied, but it might be argued that ADHD qualities such as high energy, novelty seeking, and risk taking often transform into exuberance, curiosity, and creativity. We hope that a better understanding of core deficits, including change over development and interactions in the brain, will enable clinicians and families to properly support, challenge, and channel the natural assets of children with ADHD so that they may develop into optimally effective and productive adults.

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