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Improving Outcomes for Youth with ADHD: A Conceptual Framework for Combined Neurocognitive and Skill-Based Treatment Approaches

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent and chronic mental health condition that often results in substantial impairments throughout life. Although evidence-based pharmacological and psychosocial treatments exist for ADHD, effects of these treatments are acute, do not typically generalize into non-treated settings, rarely sustain over time, and insufficiently affect key areas of functional impairment (i.e., family, social, and academic functioning) and executive functioning. The limitations of current evidence-based treatments may be due to the inability of these treatments to address underlying neurocognitive deficits that are related to the symptoms of ADHD and associated areas of functional impairment. Although efforts have been made to directly target the underlying neurocognitive deficits of ADHD, extant neurocognitive interventions have shown limited efficacy, possibly due to misspecification of training targets and inadequate potency. We argue herein that despite these limitations, next-generation neurocognitive training programs that more precisely and potently target neurocognitive deficits may lead to optimal outcomes when used in combination with specific skill-based psychosocial treatments for ADHD. We discuss the rationale for such a combined treatment approach, prominent examples of this combined treatment approach for other mental health disorders, and potential combined treatment approaches for pediatric ADHD. Finally, we conclude with directions for future research necessary to develop a combined neurocognitive + skill-based treatment for youth with ADHD.

Keywords

ADHD; cognitive training; working memory; attention; treatment; skills; combined treatment

Attention-deficit/hyperactivity disorder (ADHD) is a complex, neurodevelopmental disorder affecting brain, behavior, and cognition for an estimated 3% to 7% of U.S. school-aged children at an annual cost of illness of over \$42 billion (Pelham et al., 2007; APA, 2013).

Given the enormous societal costs of ADHD, there is a critical need to develop efficacious interventions that affect the immediate impairments and adverse long-term outcomes associated with ADHD. In the present review, we briefly summarize the benefits and limitations of currently available interventions and argue that combined approaches – interventions combining next-generation neurocognitive training with conceptually-matched skill-based training – may improve outcomes for children with ADHD. Our call for novel, combined interventions for children with ADHD is based on four interrelated assumptions:

1. Novel interventions are needed to improve short- and long-term outcomes for children affected by ADHD. Extant evidence-based treatments (i.e., behavioral and pharmacological) portend moderate to large magnitude improvements in ADHD behavioral symptoms and some areas of functional impairment, but do not appear to exert long-term benefits, generalize into non-treated settings, or sufficiently improve functional impairments and executive functioning.
2. Underdeveloped neurocognitive/executive functions, particularly in specific components of working memory and sustained attention, appear to be more prevalent in ADHD than previously estimated. These developmentally impaired neurocognitive processes are strongly associated with – and may be causal factors underlying – ADHD behavioral symptom expression and key areas of functional impairment.
3. Neurocognitive training is a promising avenue for improving these neurocognitive functions, but extant approaches have generally not targeted the neurocognitive mechanisms and processes most strongly associated with ADHD behavioral and functional difficulties due to both inadequate potency and target misspecification.
4. Through targeted improvements at the neuronal/structural level, next-generation neurocognitive training may provide the cortical foundation to improve children's ability to fully benefit from adjunctive, skill-based approaches intended to ameliorate the behavioral, academic, and interpersonal manifestations of the complex interactions between underlying neurocognitive impairments and the child's environment. Importantly, despite potential direct benefits of neurocognitive training plus adjunctive skill-based approaches, maximal outcomes will likely require adult-mediated (e.g., parent, teachers, etc.) supportive instruction and behavioral skill practice in context.

In the following sections, we briefly review the current evidence base for ADHD treatments for youth. Following this review, we discuss the pathophysiology of ADHD with a specific focus on neurocognitive deficits. We then briefly review the current state of the neurocognitive training literature followed by a discussion of combined neurocognitive + skill-based treatment approaches for schizophrenia, an area of empirical investigation that may offer insights into the potential utility of combined approaches for the treatment of ADHD. Finally, we discuss the potential for combined neurocognitive + skill-based treatment approaches for ADHD as well as considerations for future treatment research in this area.

1. Novel Interventions are Needed for Children with ADHD

Numerous RCTs and meta-analytic reviews have documented the short-term benefits of extant pharmacological and behavioral interventions for improving oppositional behavior and overt ADHD behavioral symptoms, as well as some aspects of peer, family, and academic functioning (Dupaul, Eckert, & Vilardo, 2012; Evans, Owens, & Bunford, 2013; Fabiano et al., 2009; Rajwan, Chacko, Moeller, 2012; van der Oord, Prins, Oosterlaan, & Emmelkamp 2008). At the same time, the limitations of these evidence-based treatments are being increasingly recognized (Antshel & Barkley, 2008; Chacko et al., 2013a; Halperin & Healey, 2011) and strongly call for novel interventions to improve outcomes for children and families affected by ADHD. For example, these treatment approaches have not been shown to have long-term benefits, and both practical and theoretical issues limit their utility and potency. While stimulant medication is relatively easy to implement and often provides rapid therapeutic benefit, a significant minority of youth with ADHD do not respond to stimulant medication (10–30%; Goldman, Genel, Bezman, & Slanetz, 1998) or experience significant side effects that prohibit continued use (< 10%; Graham & Coghill, 2008). Additionally, stimulant medications appear less effective for young children with ADHD (Greenhill et al., 2006) and may result in an increased rate of side effects (Wigal et al., 2006). Parental perceptions of stimulant medication's impact on overall health and preference for alternative (non-medication) treatments also limit the use of and compliance with stimulant medication (Chacko, Newcorn, Feirsen, & Uderman, 2010) – by some accounts, up to 58% of parents refuse stimulant medication for their ADHD children (Krain, Kendall, & Power, 2005). Finally, stimulant medication effects are present only when the medication is taken, suggesting that medication regimens must be continued indefinitely and/or combined with additional interventions to provide maximal benefits.

Behavioral interventions, in contrast, are often more difficult to sustain over long durations, are generally more costly, and, arguably, may be less effective than stimulant medications—particularly for the core symptoms of ADHD (MTA Cooperative Group, 1999; Sonuga-Barke et al., 2013). Moreover, although there are exceptions (e.g., Mikami, Lerner, Griggs, McGrath, & Calhoun, 2010), the effects of behavioral interventions do not appear to generalize to non-targeted settings or non-targeted behaviors (see Rajwan, et al., 2012 for a discussion of this issue), and there may not be enough community-based therapists trained in behavioral interventions for ADHD (AAP, 2011). Lastly, limited data suggest the potential for iatrogenic effects during behavioral treatment (Barkley, Guevremont, Anastapolous, & Fletcher, 1992; Lee, Niew, Yang, Chen, & Lin, 2012) — an understudied area of investigation (Antshel & Barkley, 2008).

In addition to these treatment-specific limitations, there are several limitations shared by both stimulant medications and behavioral interventions. First, neither approach is associated with clinically significant gains in academic achievement (Langberg & Becker, 2012; Raggi & Chronis, 2006; van der Oord et al., 2008), with nonsignificant changes for medication and small magnitude benefits ($ES = 0.19$) for behavioral interventions (van der Oord et al., 2008). Second, although efficacious for treating behavioral symptoms, these interventions do not normalize behavior for a significant number of youth with ADHD. As an example, Swanson and colleagues (2001) found that despite intensive, relatively long-

term stimulant medication and behavioral treatment, one-third to two-thirds of youth with ADHD did not evince clinically significant improvements in the Multimodal Treatment of ADHD Study (MTA, 1999). Moreover, maintenance of acute treatment gains is understudied for some psychosocial interventions (e.g., classroom contingency management; DuPaul et al., 2012) and appears to be attenuated for behavioral parent training (e.g., Lee et al., 2012) and stimulant medication (Jensen et al., 2007; Molina et al., 2009). In fact, some studies of children with ADHD have demonstrated that withdrawal of psychosocial (Chronis et al., 2004) and pharmacological interventions (Chronis, Pelham, Gnagy, Roberts, & Aronoff, 2003) results in deterioration in child functioning within minutes to a few hours. Lastly, data suggest limited longer-term benefits of stimulant and behavioral interventions, even when applied intensively for both school-age and preschool children (Molina et al., 2009; Riddle et al., 2013).

It appears that the benefits of stimulant medication and psychosocial interventions are acute and time-limited, and do not fully address key areas of functional impairment such as academic underachievement, social and familial functioning, and executive dysfunction (discussed below). Given the chronic nature of ADHD (Kline et al., 2012), extracting maximum benefits of current evidence-based treatments will require them to be applied intensively, across key developmental periods (preschool, school age, adolescence) by key individuals (parents and teachers) over extended durations. Although possible (Chronis et al., 2001), it is unlikely that this approach is feasible given that even short-term adherence to these evidence-based treatments is challenging (Chacko et al., 2010; Witt, 1986).

In summary, novel interventions are needed to improve short- and long-term outcomes for children and families affected by ADHD. Extant evidence-based treatments (i.e., behavioral and pharmacological) demonstrate moderate to large magnitude improvements in ADHD behavioral symptoms and some areas of functional impairment, but do not appear to exert long-term benefits or significantly improve academic, executive, and social functioning.

2. ADHD and Underdeveloped Neurocognitive Functioning

In light of these significant limitations, some have posed a more fundamental obstacle (Antshel and Barkley, 2008; Halperin and Healey, 2011; Rapport, Orban, Kofler, & Friedman, 2013): Current evidence-based treatments are not theoretically derived to address the underlying pathophysiology of, or compensatory mechanisms associated with recovery from ADHD. As argued by Antshel and Barkley (2008), deficits in response to contingency management or low levels of neurotransmitters (e.g., dopamine) – the foci of behavioral and stimulant medication treatments, respectively – are not central to the pathophysiology of ADHD. As such, the acute, time- and setting-limited effects of behavioral interventions and stimulant medications are not surprising. Once these interventions have been terminated, lack of change in the underlying neurobiological substrate (Rubia et al., 2013) or neurocognitive performance (Dovis et al., 2012; Jarrett, 2013) may be the reason for the observed rapid return of pre-treatment symptoms/impairments. Importantly, this is not to say there is no role for these interventions in the treatment of ADHD. However, the failure of current interventions to show both generalized and long-term improvements in children with ADHD may be due in part to developing treatments based on a limited appreciation of the

disorder's etiology and pathophysiology. As such, interventions that more principally address the pathophysiology of ADHD and/or compensatory mechanisms associated with recovery from ADHD are needed.

In this section, we argue that underdeveloped neurocognitive functions, particularly in specific components of working memory and sustained attention, appear to be more prevalent in ADHD than previously estimated. These developmentally impaired neurocognitive processes appear to both directly and indirectly influence ADHD behavioral symptom expression and key areas of functional impairment.

The search for novel, malleable neurocognitive treatment targets has led to the development of several conceptual models (Table 1). Neurocognitive functions have assumed a prominent role in most of these models, although the etiological primacy and relevance of particular deficits varies considerably from model to model. For example, some models ascribe a causal role to underdeveloped neurocognitive/executive functions (Barkley, 1997; Rapport et al., 2008; Rapport, Chung, Shore, & Isaacs, 2001; Sonuga-Barke, Bitsakou, & Thompson, 2010). Other models describe executive functioning impairments as correlates of the disorder (Castellanos et al., 2005) or outcomes of impairments in more basic processes (Sagvolden, Johansen, Aase, & Russell, 2005). Finally, some models hypothesize that executive functioning impairments are unrelated to core ADHD behavioral symptoms (Halperin & Schulz, 2006), but rather serve ontogenetic compensatory mechanisms (Rajendran et al., 2013). Additional differences across models reflect the specific executive/neurocognitive functions implicated in the disorder. For example, the Rapport et al. (2001) model posits a key role of working memory central executive processes, whereas Sonuga-Barke and colleagues (2010) conclude that inhibition, temporal processing, and motivation – but not working memory – are interrelated pathways to ADHD behavioral symptoms. While reconciling similarities and differences among these conceptual models is beyond the scope of the current review, we have included a brief summary in Table 1 to note that disparate hypotheses regarding ADHD etiology, mechanisms, and processes will necessarily result in selection of different neurocognitive training targets.

Identifying the specific neurocognitive functions that are underdeveloped in ADHD is critical for treatment development to the extent that these deficits contribute to the symptoms and functional impairments of children with ADHD (Rapport et al., 2001). According to the clinical model of psychopathology, interventions aimed at improving suspected causal mechanisms of ADHD should produce the greatest level and breadth of therapeutic change (National Advisory Mental Health Council's Workgroup, 2010; Rapport et al., 2001). Conversely, those aimed at peripheral symptoms are expected to show limited generalization upward to core features, and only minimally affect non-targeted peripheral features. Thus, novel interventions are more likely to be successful if they target aspects of neurocognitive functioning that are not only deficient in ADHD but also causally related to the primary behavioral, academic, and social difficulties associated with the disorder.

In their recent meta-analysis of the cognitive training literature, Rapport and colleagues (2013) reviewed evidence for and against links between specific neurocognitive functions and ADHD behavioral/ functional impairments. In reviewing these literatures, Rapport and

colleagues (2013) provided inchoate evidence linking specific ADHD behavioral symptoms and functional impairments with specific neurocognitive impairments. In particular, the reviewed evidence implicated specific (e.g., sustained attention) rather than generalized attention deficits and significantly underdeveloped central executive working memory abilities. Although it is clear that children with ADHD are a heterogeneous group (Nigg & Casey, 2005) who demonstrate impaired performance on tasks intended to measure a wide range of neurocognitive functions (e.g., Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), we concur with the Rapport et al. (2013) summary and argue that, from our perspective, interventions targeting central executive working memory and sustained attention may offer the best opportunity to positively impact core ADHD symptoms and functional impairments. The relative importance of these two neurocognitive functions was supported by a substantial evidence base documenting that many, if not most, children with ADHD display impairments in these areas (Rapport et al., 2013; Willcutt et al., 2012). More importantly for our purposes, however, these specific neurocognitive functions have been linked repeatedly with important behavioral and functional outcomes for children with ADHD.

In relation to behavioral symptoms, experimental evidence suggests that underdeveloped central executive abilities may explain ADHD-related impairments in objectively measured attention (Kofler, Rapport, Bolden, Sarver, & Raiker, 2010) and hyperactivity (Rapport et al., 2009). Although independent replication is needed, these studies provide emergent evidence for a causal role of working memory in both attention deficits and hyperactivity due to their experimental design, systematic manipulation of working memory demands, and concurrent measurement of the differential effects of this manipulation on attentive behavior and actigraph-measured hyperactivity for children with and without ADHD. Similarly, underdeveloped central executive processes are associated with impaired performance on neurocognitive measures of impulsivity (Raiker, Rapport, Kofler, & Sarver, 2012), response variability (Kofler et al., 2014) and behavioral disinhibition (Alderson, Rapport, Hudec, Sarver, & Kofler, 2010). With regards to functional impairments, central executive abilities strongly predict social problems (Kofler et al., 2011), and early verbal and visual memory abilities appear to be better predictors of long-term academic achievement than early attention problems (Sarver et al., 2012). Finally, underdeveloped working memory (Kofler et al., 2011) and other executive functions (Huang-Pollock, Mikami, Pfiffner, & McBurnett, 2009) appear to be important factors in ADHD-related peer relational difficulties, suggesting that improving these neurocognitive functions may be a critical first step to improving social functioning for these children.

Similarly, sustained attention abilities predict objective and subjective reports of classroom behavior (Brocki, Tillman, & Bohlin, 2010; Epstein et al., 2003; Rapport et al., 1987), academic performance (Molina et al., 2009; Rapport et al., 1994), special education placement, and comorbid learning disabilities (Faraone et al., 1993). To our knowledge, however, no study has investigated the role of neurocognitive processes in family functioning, despite evidence that these processes are associated with most if not all other key areas of ADHD-related behavioral and functional impairments (Rapport et al., 2013).

In contrast to central executive and sustained attention deficits, the Rapport (2013) review and meta-analysis concluded that there is limited evidence supporting inhibition, set shifting, short-term memory (the “memory” component of working memory), and other cognitive components of attention as credible targets for ADHD neurocognitive training. While meta-analyses have shown evidence for between-group differences (i.e., ADHD vs. controls) on tasks intended to assess these neurocognitive functions (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), these deficits are often smaller in magnitude than sustained attention and central executive working memory deficits. Further, there has been significant variability in the measurement of these processes, and in some cases, outcome variables have been broader indices that do not adequately isolate specific neurocognitive components (Alderson, Rapport, & Kofler, 2007; Lijffijt, Kenemans, Verbaten, & van Engeland, 2005). For example, multiple meta-analyses using more fine-grained measurement approaches have concluded that inhibition processes may be intact in ADHD (Alderson et al., 2007; Lijffijt et al., 2005), suggesting that targeting this core executive function may exert minimal benefits. Likewise, the short-term memory (working memory storage/rehearsal) processes targeted by extant cognitive training interventions (Chacko et al., 2013b; Gibson et al., 2011) are not significantly associated with behavioral symptoms (Kofler, Rapport, Bolden, Sarver, & Raiker, 2010), other aspects of neurocognitive functioning (Alderson et al., 2010), or peer relational difficulties (Kofler et al., 2011; Huang-Pollock et al., 2009). Finally, the evidence base was insufficient to draw conclusions regarding the role of set shifting (cognitive flexibility) in ADHD (Rapport et al., 2013). Other meta-analyses have also shown that problems in set-shifting, if present, are often smaller in magnitude than deficits such as sustained attention and working memory (Willcutt et al., 2012).

In summary, underdeveloped neurocognitive functions – particularly in specific components of working memory and sustained attention – appear to be more prevalent in ADHD than previously estimated. These developmentally impaired neurocognitive processes appear strongly associated with – if not causal mechanisms underlying – ADHD behavioral symptoms and key areas of functional impairment. It is important to acknowledge, however, that significant differences are apparent across studies and ADHD conceptual models (Table 1), and that these differences will necessarily lead to different intervention targets, outcome measures, and criteria for training efficacy.

3. The Promise of Neurocognitive Training

In the current section, we argue that neurocognitive training is a promising avenue for improving these underdeveloped neurocognitive functions, but that currently available training programs have generally not targeted the neurocognitive mechanisms and processes most strongly associated with ADHD behavioral and functional difficulties due to both inadequate potency and target misspecification.

Considerable research has been conducted in recent years to elucidate the impact of extant treatments on neurocognitive functioning for children with ADHD. While these efforts are not surprising given the proposed centrality of neurocognitive functions in ADHD pathogenesis, the findings may be somewhat unexpected. Collectively, our reading of this literature is that neither medication nor behavioral interventions significantly improve

executive functioning for children or adults with ADHD (Advokat, 2010; Rapport et al., 2013; Jarrett, 2013). For example, psychostimulant medications appear to improve basic (non-executive) cognitive processes such as attention and response speed, whereas their impact on tasks with a prominent executive component, such as central executive working memory, is considerably more limited (Bedard, Jain, Hogg-Johnson, & Tannock, 2007; Epstein et al., 2006; Kobel et al., 2009; Rhodes, Coghill, & Matthews, 2006). Although understudied, data also suggests that behavioral interventions do not result in improvements in executive functioning (Jarrett, 2013). The improvements in attention and gross motor activity observed with psychostimulants and incentivized behavioral interventions likely reflects the impact of these treatments on arousal-regulating mechanisms needed to activate executive functioning-supporting structures in the brain (Cortese et al., 2012). Longitudinal fMRI evidence, however, reveals a 3–5 year delay in the development of these same prefrontal/frontal regions in children with ADHD relative to typically developing children (Shaw et al., 2007). Activating these regions is thus unlikely to improve executive or academic functioning, given the underdeveloped cortical structures themselves and the executive functions these structures support (Rapport et al., 2013).

Given these findings, researchers have adopted three conceptually distinct approaches to treating underdeveloped neurocognitive functions in children with ADHD: Cognitive therapy, compensatory strategies, and neurocognitive training (Rapport et al., 2013). Cognitive therapy, however, appears to be ineffective for treating ADHD symptoms in children with ADHD (Abikoff, 1991; Toplak, Connors, Shuster, Knezevic, & Parks, 2008; Washington State Institute for Public Policy, 2012). In addition, only one study to date has investigated a classroom-based compensatory approach. This approach, which focused on identifying and restructuring curricula to decrease working memory demands, failed to find significant academic or neurocognitive benefits relative to control groups (Elliot, Gathercole, Alloway, Holmes, & Kirkwood, 2010).

The third approach, neurocognitive training, involves directly training neurocognitive functions through repeated practice. These approaches typically involve computer-based, automated training exercises designed to strengthen deficient neurocognitive functions. A central tenet of these programs is that extensive practice, repetition, and feedback will result in lasting, measurable improvement in the neural substrates that support the targeted neurocognitive functions. By engendering improvements at the neuronal level, these training gains are expected to generalize to improvements in other areas of functioning known to depend on these same neural networks (Klingberg, 2010). This is a critical assumption of neurocognitive training programs that differentiates it from CBT-based approaches that teach regulatory and/or problem solving strategies (Rapport et al., 2013).

Two recent meta-analyses have examined the efficacy of neurocognitive training for children with ADHD (Rapport et al., 2013; Sonuga-Barke et al., 2013). Both meta-analyses suggest that the benefits of existing neurocognitive training protocols on ADHD symptoms are minimal, and that previous claims of significant benefits were likely attributable to Hawthorne/expectancy effects. For example, Sonuga-Barke and colleagues (2013) reviewed 6 neurocognitive training studies and found no significant benefits on ADHD symptoms as rated by blinded observers (Cohen's d 95% CI = -0.24 to 0.72 , indicating no effect).

Similarly, Rapport and colleagues (2013) reviewed 25 ADHD neurocognitive training studies. They found that training short-term memory resulted in significant, medium magnitude improvements in short-term memory (Cohen's $d = 0.63$, 95% CI = 0.46 to 0.80), whereas targeting aspects of attention or multiple neurocognitive functions did not significantly improve the targeted neurocognitive functions (95% CIs included 0.0 indicating no effect). Further, the Rapport (2013) meta-analysis found that neurocognitive training, regardless of training target, had no discernable benefits on blinded behavioral ratings of ADHD symptoms or objective measures of academic achievement.

One of the most striking findings from the Rapport et al. (2013) meta-analysis was the incongruence between the neurocognitive training targets and the empirical literature. None of the included studies targeted working memory (although 68% claimed to do so), and most of the studies targeting sustained attention/vigilance also targeted multiple additional attention processes. Rapport and colleagues (2013) hypothesized that the inefficacy of extant protocols may be attributable to poor potency – that is, the limited time spent training impaired neurocognitive processes due to target misspecification and/or time spent training neurocognitive functions that are not likely impaired in most children with ADHD.

Although the results of these meta-analyses are disappointing, they provide clear guidance for the development of next-generation neurocognitive training protocols that may have the potential for lasting improvements in behavior and functioning for children with ADHD. For example, the Rapport et al. (2013) meta-analysis reported significant treatment-related improvements in short-term memory across eight ADHD studies, with benefits remaining apparent for up to 6 months in the three studies reporting follow-up data. These findings provide solid “proof of concept” that neurocognitive functions are amenable to intervention for this population and suggest optimism regarding next-generation neurocognitive training approaches for these children. The finding that improvement in short-term memory did not translate into improved behavioral or academic functioning is not surprising and adds to experimental evidence indicating that short-term memory deficits in ADHD are minimally related to ADHD behavioral symptoms or functional impairments (e.g., Raiker et al., 2013). In contrast, if central executive processes are similarly amenable to intervention, the basic science research to date suggests that we should see measureable improvements in behavior and academic potential. This is a critical area of future empirical investigation.

In summary, extant neurocognitive training approaches have not been shown to improve ADHD symptoms and related functional impairments. This lack of efficacy may be due to mis-specification and/or low potency of these neurocognitive training approaches. More specifically, extant neurocognitive training approaches may not have intensively targeted the neurocognitive mechanisms and processes most strongly associated with ADHD behavioral and functional difficulties. Next-generation neurocognitive training that intensely targets core underdeveloped neurocognitive functions most closely related to ADHD holds promise for improving not only these core neurocognitive deficits but also the varied functional outcomes associated with these deficits. Clearly, considerable research is required to develop such next-generation neurocognitive training and to determine the efficacy of such approaches.

4a. Combined Next-Generation Neurocognitive + Skill-Based Treatment Approaches

In the following section, we argue that improving neuronal/structural functioning via next-generation neurocognitive training may provide the cortical foundation upon which adjunctive, skill-based approaches can ameliorate the behavioral, academic, and interpersonal manifestations of the complex interactions between underlying neurocognitive impairments and the child's environment. Benefits of this combined intervention approach is likely maximized when the combined intervention is applied within the context of adult-mediated (e.g., parents, teachers, etc.) supportive instructional and behavioral skills practice in context.

Collectively, we view the basic science and neurocognitive intervention literature as suggesting great promise for improving neurocognitive functioning for children with ADHD. The extent to which these approaches can help these children 'catch up' to their peers, however, remains unclear. For example, longitudinal fMRI investigations reveal a 3–5 year delay in the maturation of prefrontal cortical regions associated with central executive working memory functioning (Shaw et al., 2007). In addition, age-appropriate neurocognitive functioning may be best conceptualized within a developmental framework as a necessary but not sufficient component for successful outcomes in important areas of behavioral, peer, family, and academic functioning. For example, peer relational difficulties are apparent in a majority of children with ADHD (de Boo & Prins, 2007; Huang-Pollock et al., 2009). Although central executive functioning is critical for dynamic social decoding (Phillips, Tunstall, & Channon, 2007) and is significantly associated with social problems for children with ADHD (Kofler et al., 2011), it is one of myriad factors influencing social functioning. Social cognitive factors (Marton, Wiener, Rogers, Moore, & Tannock, 2009; Sibley, Evans, & Serpell, 2010), the relative stability of peer interactional patterns in classroom settings (Stormshak, Bierman, Bruschi, Dodge, & Cole, 1999), impulsive, hyperactive, and inattentive behavior (Kofler et al., 2011), reputation among peers (Bickett & Milich, 1990), and social performance inconsistency (de Boo & Prins, 2007) will likely all need to be addressed if lasting improvements in interpersonal functioning are to be realized. We view the relation between improved neurocognitive functioning and functional outcomes in ADHD as akin to the relation between corrective lenses and reading: Glasses allow children with farsightedness to see the printed words and benefit from classroom instruction, but the glasses themselves do not teach children to read (Rapport et al., 2001). Similarly, improving central executive and/or sustained attention abilities is expected to result in improved *potential* due to the improved cortical foundation, but changing the trajectory of ADHD-related interpersonal difficulties and academic underachievement will likely require targeted, individualized, skill-focused interventions. Importantly, this combined intervention will likely require adult-mediated, supportive instruction and behavioral skill practice to remediate and further support specific skills that were not mastered previously due to neurocognitive limitations. This hypothesis is consistent with extant neurocognitive training studies suggesting no significant benefits on standardized academic achievement measures (Rapport et al., 2013), but some improvement in performance on unstandardized academic tasks (e.g., math worksheets; Kerns, Eso, &

Thomson, 1999; Shalev, Tsai, & Mevorach, 2007). Similarly, Huang-Pollock and Karalunas (2010) found that children with ADHD had difficulty learning a new task under high but not low cognitive load conditions, suggesting that improving or normalizing central executive abilities may provide the foundation for improved learning when combined with developmentally appropriate instruction.

As noted by Rapport et al. (2001), targeting neurocognitive/neurobiological mechanisms may be a critical component in the treatment of ADHD given the downstream effects on symptoms and functional domains. From an early intervention perspective, these neurocognitive vulnerabilities are likely to be present at an early age, and may precede and predict the development of psychopathology (Nigg, 2006). In turn, early intervention has significant implications for reducing future impairment, since early remediation of such deficits may buffer against the development of symptoms and functional impairments as a child develops socially, emotionally, and cognitively. For example, early underdeveloped working memory abilities are associated with decreased learning and processing of new material in academic settings (cf. Sarver et al., 2012), which may result in accumulated delays in achievement over time that may eventually manifest as a specific learning disorder (e.g., reading disability). As such, we hypothesize that early intervention utilizing a neurocognitive intervention targeting working memory deficits in younger children combined with evidence-based emergent literacy skills interventions may be an optimal approach to preventing the onset of reading disorder. In the remainder of this section, we briefly highlight recent literature in schizophrenia which has focused on combining neurocognitive training with skill-based interventions.

Augmented effects of combined neurocognitive + skill-based interventions in schizophrenia: Potential parallel for ADHD

Similar to ADHD, schizophrenia is a neurodevelopmental disorder associated with deficits in multiple neurocognitive functions as well as associated functional impairments. For example, individuals with schizophrenia have been shown to have deficits in neurocognitive domains including working memory, processing speed, and attention (Green & Nuechterlein, 2004). Moreover, individuals with schizophrenia have significant social, occupational and independent living impairments (Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006; Green, Kern, & Heaton, 2004; Wiersma et al., 2000). Although there are clear qualitative and quantitative differences between schizophrenia and ADHD, a link between the neurocognitive deficits associated with each disorder and multiple areas of functional impairment (Bowie et al., 2006; Green, 1996; Green et al., 2004; Green, Kern, Braff, & Mintz, 2000) provides a useful framework for discussing the potential benefits of combined neurocognitive + skill-based approaches.

There have been considerable efforts in the field of schizophrenia to target both neurocognitive deficits and skills deficits through distinct neurocognitive, skill-based, and combined interventions. Interestingly, over years of refinement, neurocognitive interventions for schizophrenia have been shown to reliably improve neurocognitive functioning; however, studies suggest limited impact of these interventions on functional outcomes (McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007). In contrast, skill-based

approaches (e.g., social skills training; vocational training) have a long history for the treatment of functional impairments in schizophrenia, but do not affect neurocognitive functioning and result in only moderate skill improvements that often do not persist (Bowie, McGurk, Mausbach, Patterson, & Harvey, 2012). However, when neurocognitive interventions are combined with evidence-based psychosocial skill-based interventions (e.g., vocational therapy), there appears to be greater transfer of effects to functional outcomes for adults with schizophrenia that persists over time (McGurk et al., 2007; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011).

Although a comprehensive review of this literature is beyond the scope of this paper, we focus on a recently completed randomized clinical trial of a combined neurocognitive + skill-based intervention for schizophrenia as an exemplar of the potential for combined intervention approaches. Bowie and colleagues (2012) evaluated the effects of a computerized neurocognitive intervention, a skill-based intervention, and combined neurocognitive + skill-based intervention for adults with schizophrenia. The 12-week neurocognitive intervention included computer-based cognitive exercises and therapist support in developing, implementing, and evaluating cognitive strategies during everyday life. The 12-week skill-based intervention focused on using props and role playing with the therapist to support competence in social skills and independent living. The combined intervention included both interventions. Importantly, in each intervention condition, therapists were utilized significantly to help support acquisition and implementation of the neurocognitive strategies and skills learned during treatment within the participants' everyday life. Outcomes of this study focused on clinical symptoms, neurocognitive functioning (i.e., reasoning, problem solving, processing speed, verbal memory, and working memory), social competence, analog assessments of functional competence, and real-world functional outcomes (interpersonal relationships, activities, work skills) at post-treatment and 12-week follow-up assessments.

Results of this study demonstrated specificity of effects for the individual interventions and augmentative effects for the combined intervention. The skill-based intervention led to improvements in social competence, analog assessments of functional competence, and real-world work skills, but did not improve clinical symptoms or neurocognitive outcomes. In contrast, neurocognitive treatment led to significant benefits on neurocognitive outcomes but did not improve social competence and had limited effects on functional outcomes. The combined intervention, however, led to improvements in neurocognitive outcomes, social competence, analog assessments of functional competence, as well as real-world community activities and work skills. Importantly, the effects of the combined intervention were generally greater than those observed for the separate skill-based and neurocognitive interventions.

Collectively, this seminal RCT demonstrated a clear additive benefit of combining neurocognitive training with skill-based interventions for the treatment of schizophrenia and the importance of adult-mediated (e.g., therapist) support in utilizing and practicing acquired skills in context. Although there are clearly differences between adults with schizophrenia and children with ADHD (e.g., developmental differences, pathophysiology and course of the disorders), we argue that the evidence found in the schizophrenia literature, as well as

emerging evidence in depression (e.g., Richey et al., 2013; Siegle et al., in press; Siegle, Ghinassi, & Thase, 2007) and anxiety (e.g., Amir & Taylor, 2012; Shechner et al., 2013), offer reason for optimism regarding the potential benefits of combined neurocognitive + skill-based approaches with adult-mediated supportive instruction and behavioral skill practice in context. Importantly, however, our hypotheses remain speculative at this time, and the utility of neurocognitive + skills-based approaches for addressing the needs of youth with ADHD is unknown. With that caveat in mind, we describe below potential combinations of neurocognitive + skill-based approaches that may offer benefits for youth with ADHD.

4b. Combined Next-Generation Neurocognitive and Skill-Based Treatment Approaches: Potential Intervention Pairings and Hypothesized Additive Benefits in ADHD

“Next-generation” neurocognitive interventions: Improving neurocognitive training specificity and potency

Although there is currently lack of empirical research on combined neurocognitive + skill-based approaches for ADHD, we focus here on conceptual issues and arguments for psychosocial treatments that may complement existing and future neurocognitive training programs.

In our view, the first step toward efficacious neurocognitive + skill-based approaches will be development of next-generation neurocognitive training protocols with improved validity, specificity, and potency. Although initial research indicates that extant neurocognitive training interventions improve some aspects of neurocognitive functioning (Chacko et al., 2013b; Gibson et al., 2011; Rapport et al., 2013), much work remains to be done to fine-tune such interventions so that they more clearly target and improve key underlying neurocognitive deficits (Shipstead, Redick & Engle, 2012; Rapport et al., 2013). For example, multiple, independent investigations reveal that existing neurocognitive training interventions intended to train working memory appear to target short-term storage/rehearsal rather than central executive deficits (Chacko et al., 2013b; Gibson et al., 2011; Rapport et al., 2013). Novel interventions are needed to more specifically target what we believe to be the core neurocognitive deficits for many if not most children with ADHD: sustained attention and central executive working memory deficits¹.

Matching neurocognitive training protocols with skill-based approaches

In addition to improving the specificity and potency of ADHD neurocognitive training protocols, future research should carefully consider the specific skills training programs that best pair with specific neurocognitive training protocols to maximize benefits for children

¹As discussed previously, our reading of the ADHD neurocognitive literature suggests that central executive working memory and sustained attention may be key intervention targets due to the magnitude of observed impairments and links to ADHD behavioral symptoms and functional impairments. Alternate models, however, hypothesize that targeting other/additional processes may provide maximum benefits (Table 1), and issues of within-group heterogeneity and equifinality (Nigg, 2005) will need to be considered when adapting training protocols for individual children (Epstein & Tsal, 2010). Regardless of intervention target(s), we echo cognitive methodologists' calls for demonstrating proof of concept and training task validity – that the tasks impact their intended training target – via experimental studies prior to advancing to clinical trials (cf. Shipstead et al., 2012).

with ADHD. Overall, it will be important to consider the linkage between specific neurocognitive functions and particular functional deficits, since this linkage will help to determine which neurocognitive + skill-based combination might result in the greatest effects. In other words, optimal pairing is likely to involve (a) identifying the neurocognitive mechanisms and processes involved in a specific functional skill (e.g., peer interactions), and (b) combining targeted skills training with neurocognitive training that strengthens the underlying mechanisms and processes upon which these skills depend within the context of adult-mediated supportive instruction and behavioral skill practice. Importantly, our perspective is that despite potential direct benefits of neurocognitive training, maximal outcomes will likely require adult-mediated (e.g., parent, teachers) supportive instruction and behavioral skill practice in context. This may be especially true for children given the important role adults have in supporting children in learning and effectively implementing skills in key contexts (i.e., home, school, peer interactions).

Given that neurocognitive training involves an attempt to change a developmental trait (i.e., the child's neurocognitive functioning), initial intervention attempts might include combining neurocognitive training with more child-oriented skills training programs. For example, evidence-based skills training programs are available for children with ADHD who have academic skills deficits (Evans, Schultz, DeMars, & Davis, 2011; Langberg, Epstein, Becker, Girio-Herrera, & Vaughn, 2012). Given the strong relation between academic achievement and neurocognitive abilities such as sustained attention and central executive working memory (cf. Sarver et al., 2012), pairing central executive/sustained attention training with academic skills training in the context of supportive teacher-mediated instruction and guided skill practice might portend additive effects and improve transfer of laboratory-based gains to more naturalistic settings (i.e., classrooms). Similarly, given the relationship between organizational skills and ADHD neurocognitive deficits in central executive working memory and sustained attention (Barkley et al., 1997; Willcutt et al., 1995), we hypothesize that pairing central executive /sustained attention training with organizational skills training (e.g., Abikoff et al., 2012) in the context of supportive parent and teacher-mediated instruction and guided skill practice would result in optimal improvement in organizational impairments for youth with ADHD.

In addition to academic and organizational skills training, social skills training is another promising intervention that may benefit from a combined approach. On the surface, this recommendation may appear counterintuitive – why would we expect efficacy by combining next-generation neurocognitive intervention with a largely ineffective treatment? However, we hypothesize that the inefficacy of social skills training (Evans et al., 2013) may be due to underdeveloped executive functioning-related cortical structures needed to support dynamic social interactions (Huang-Pollock et al., 2010; Kofler et al., 2011). Recent conceptualizations suggest that social difficulties in ADHD may be a performance problem rather than a skills deficit (de Boo & Prins, 2007). Thus, we hypothesize that improving specific neurobiological substrates critical for complex social interactions may allow children with ADHD to benefit from (currently ineffective) skill-based approaches that emphasize behavioral practice. For example, recent research suggests that working memory and related executive functions play an important role in social functioning for children with ADHD (Huang-Pollock et al., 2010; Kofler et al., 2011). In addition, developmental

research points to working memory as a key factor in dynamic social decoding (Phillips et al., 2007), suggesting that improving these neurocognitive functions may improve the ability to quickly and accurately process social cues and more consistently demonstrate prosocial behaviors during complex social interactions in children with ADHD (Sibley et al., 2010). Moreover, to maximize potential outcomes, parent- and teacher-mediated guided and supportive behavioral practice of social skills in context will likely be required. As the literature suggests, the most effective social skills interventions require active adult instruction and support for children to use social skills in context (e.g., Mikami et al., 2010; 2013). Alternatively, if social problems in ADHD result entirely from performance rather than skills deficits, improving the underlying neurocognitive substrate through next-generation neurocognitive intervention may improve social performance without the need for a combined approach. However, given the relative stability of peer interaction patterns and the relative inexperience of youth with ADHD with aspects of positive peer relationships (e.g., developing close friendships), adding parent- and teacher-mediated supportive behavioral practice of social skills in context (cf. Mikami et al., 2010; 2013) to next-generation neurocognitive interventions may maximize training benefits.

The hypothesized benefits of combined neurocognitive + social skill-based treatments remain speculative, however, and empirical research is needed to test the extent to which (a) underdeveloped neurocognitive functions serve as a suppressor effect against social skills training efficacy, (b) social impairment is related to a skill deficit or a performance deficit, and (c) combining targeted neurocognitive training + social skills treatment within the context of adult-mediated instruction and behavioral practice in context results in improved social functioning for children with ADHD.

Finally, although considered a behavior management approach rather than a training-based approach (Evans et al., 2013), parent training may provide a supportive environment wherein the potential benefits of neurocognitive interventions may be fully realized. Arguably, strengthening neurocognitive functioning in youth with ADHD may naturally improve family/home-based functional outcomes, such as complying with multi-step directions and completing chores that require a myriad of executive and non-executive neurocognitive functions including sustained attention, active rehearsal, and working memory updating and dual-tasking, among others. However, it is likely that these outcomes will be maximally improved when parents are taught to implement strategies to further support their child through environmental contingencies (i.e., developing incentive systems, organizing environmental antecedents and consequences for targeted behaviors via behavioral parent training). There is considerable research attesting to the benefits of supportive parenting behavior to maximize child competency, even in otherwise healthy (e.g., neurocognitively intact) children (Collins, Maccoby, Steinberg, Hetherington, & Bornstein, 2000). As such, pairing neurocognitive interventions with parent training may address within-child as well as broader parent, family, and home environment contingencies that influence children's family/home-based functional impairments. As an example, a recent preliminary study of a combined neurocognitive (i.e., sustained attention) and evidence-based parent training intervention with children in Head Start suggests that the combination of these interventions results in more comprehensive effects on child

competencies and challenging behavior compared to either intervention alone (Neville et al., 2013).

Hypothesized effects of combined treatment approaches

The specific effects of combined interventions will largely be based upon the unique pairing of the neurocognitive and skill-based interventions. There are, however, general hypotheses regarding the impact of these combined treatment approaches that can be gleaned from the existing ADHD literature, parallels from other areas (e.g., schizophrenia), and the assumption that newly developed (“next-generation”) neurocognitive interventions will more precisely and potentially impact core neurocognitive factors associated with ADHD and related impairments.

In line with existing evidence, skill-based interventions alone are not expected to improve underlying neurocognitive functions (Advokat, 2010; Rapport et al., 2013; Jarret, 2013), whereas next-generation neurocognitive interventions are expected to offer immediate and longer-term benefits at the neurocognitive level. This latter assertion is speculative but grounded in meta-analytic data demonstrating training-related improvements in some aspects of neurocognitive functioning (e.g., short-term memory), with sustained benefits over (relatively) short durations (i.e., 6 months; Rapport et al., 2013). Additionally, we expect skill-based interventions to continue to evince intervention-specific functional benefits in the short-term (Evans et al., 2013; Fabiano et al., 2009; Rajwan et al., 2012); however, clinically significant benefits will likely not be observed for many youth (Swanson et al., 2001) and longer-term outcomes are likely to be minimal (Lee et al., 2012; Jensen et al., 2007; Molina et al., 2009). To the extent that next-generation neurocognitive treatments demonstrate improved specificity and potency, we hypothesize that neurocognitive improvements following these interventions will result in significant improvement in associated functional impairments. However, because youth with ADHD may demonstrate poor mastery of necessary skills to maximize competence in functional areas (e.g., academic achievement), next-generation neurocognitive interventions will share limitations with current evidence-based interventions in that clinically significant benefits will likely not be observed for many youth. However, as observed in combined neurocognitive + skill-based treatment approaches for schizophrenia (e.g., Bowie et al., 2012), we hypothesize that combining next-generation neurocognitive interventions with conceptually-matched, skill-based interventions will result in both neurocognitive and functional improvements (effect of the individual interventions themselves), but, importantly, the statistical and clinical effects of combined interventions will be significantly greater than either intervention alone and will result in greater sustained benefits over time. These effects may likely be maximized through adult-mediated supportive instruction and behavioral skills practice in context.

In summary, we believe that combining next-generation neurocognitive treatments with conceptually-matched, skill-based treatments has the potential to address several limitations of current treatments. Next-generation neurocognitive interventions may provide the cortical foundation to improve children’s ability to benefit from adjunctive, skill-based approaches. The combination of these approaches, particularly when skills are further

practiced in context with the direct support of adults, is therefore expected to ameliorate behavioral, academic, and interpersonal manifestations of the complex interactions between targeted neurocognitive impairments and environmental demands. Although the benefits of similar approaches in the treatment of other mental health disorders (e.g., schizophrenia) offer a promising model for ADHD treatment, the benefits of combined approaches for ADHD are speculative and will require substantial efforts in developing next-generation neurocognitive interventions and determining how best to combine these training programs with skill-based interventions.

Summary and Future Directions

In the current review, we argue that combined neurocognitive + skill-based interventions in the context of adult-mediated supportive instruction and behavioral skills practice in context may result in additive benefits for children with ADHD to the extent that training components are selected based on empirical evidence of (a) impairments in the targeted neurocognitive functions, (b) impairments in the targeted aspects of peer, family, and academic functioning, and (c) functional associations between the targeted neurocognitive functions and the targeted behavior/skill (i.e., successful execution of the targeted skill is associated with the brain regions targeted by the neurocognitive training). We conclude that, for many ADHD behavioral symptoms and functional impairments, central executive working memory and sustained attention may be the neurocognitive functions most likely to meet these criteria. At the same time, we acknowledge significant differences across ADHD conceptual models, the need for continued investigation to establish the strength of the relations between specific neurocognitive factors and various functional impairments in youth with ADHD, the need to consider heterogeneity and equifinality when tailoring interventions to individual children, and the need for additional proof of concept and validity testing as prerequisites for clinical trials. In this final section, we briefly review some additional issues that will need to be considered if combined neurocognitive + skills training approaches are to improve outcomes for children with ADHD.

Consideration of additional issues such as developmental level, treatment settings, participants, and duration will be critical for optimal development and implementation of combined approaches. For example, neurocognitive interventions will likely need to be adapted based on developmental considerations including child age, their particular pattern of neurocognitive strengths and weaknesses, and the timing of developmentally sensitive periods for neural development. Currently, the neurocognitive + skill-based intervention literature is dominated by studies of adult participants, so it is unclear whether and how such approaches can easily translate to children and adolescents. At the same time, we argue that the increased neuroplasticity characteristic of the child and adolescent developmental periods (e.g., Garon, Bryson, & Smith, 2008) may allow for potentially greater gains in functioning for children relative to adults. More empirical research is needed, though, to support this contention. Modifying combined interventions for use with children might involve the nature of the training environment (e.g., more child friendly), task complexity, and maximum treatment dosage the child or adolescent can realistically complete. Further developmental considerations include the degree of expected neural plasticity and timing of brain development. Such considerations may maximize benefits by implementing

neurocognitive training during sensitive periods associated with more rapid neural growth. For example, neurocognitive functions begin to emerge in infancy but undergo substantial growth and differentiation during the preschool period and again during adolescence (cf. Garon et al., 2008). Given this developmental pattern, intervening during such sensitive periods may maximize the benefits of neurocognitive training interventions. It should be noted, however, that prefrontal cortical areas implicated in working memory and other important neurocognitive functions continue to develop throughout early adulthood, and cognitive training studies of older adults suggest lifelong neuroplasticity and ability to improve key neurocognitive functions such as processing speed, perceptual reasoning, and memory (Ball et al., 2002).

Moreover, it will be important to consider a range of practical issues that might affect treatment fidelity, feasibility, acceptability, efficacy, and dissemination. For example, existing laboratory- and clinic-based neurocognitive interventions include parent coaches for treatment delivered in a home setting, teacher training aides for treatments delivered in school settings, or therapist-aided intervention approaches, and their inclusion complicates interpretation of treatment outcomes that rely on unblinded child behavior ratings (Sonuga-Barke et al., 2013). Although an advantage of computerized interventions is the ability to standardize treatment delivery, adherence to training procedures remains a challenge when utilizing paraprofessionals. Further, such treatments often involve treatment delivered daily or near-daily, making such interventions very intensive and time consuming. Additional research is needed to better understand how to maximize the feasibility and acceptability of such approaches. For example, researchers have begun to utilize smartphones and similar devices for the delivery of neurocognitive training (Enock & McNally, 2012). While these smartphone-based interventions have some challenges, they also offer unprecedented opportunities for dissemination, given that nearly half of American mobile phone subscribers utilize smartphones (Nielsen, 2011).

Finally, given the recent movement towards personalized medicine (National Advisory Mental Health Workgroup Report, 2010) and a greater understanding of the diverse developmental pathways to ADHD (Nigg, 2005), it may be beneficial for future studies to identify subtypes of youth with ADHD based on their specific neurocognitive profiles and tailor neurocognitive training and/or combined approaches to these specific subgroups (e.g., NIH RDOC criteria). For example, some research suggests that those with more impaired neurocognitive processes may benefit the most from neurocognitive training (Diamond & Lee, 2011). In addition, measurement of pre-treatment neurocognitive deficits may help to further tailor treatment (Epstein & Tsal, 2010).

Improved identification of specific neurocognitive impairment profiles at the individual level may be valuable in better tailoring treatment for individuals with ADHD. While this goal is aspirational, we urge caution during treatment development. It will be necessary to develop target-specific neurocognitive protocols and demonstrate their validity and near-transfer efficacy prior to adding that protocol to our armamentarium for use in combined and/or individually tailored treatment packages. Such an approach to demonstrating proof-of-concept prior to testing combined treatments is critical to advance both the neurocognitive training and combined treatment literatures. As noted in multiple empirical

and theoretical reviews of extant neurocognitive training programs, there are a host of conceptual, methodological, and practical issues to consider when developing and evaluating neurocognitive training programs (Chacko et al., 2013a; Shipstead, et al., 2012). Such issues are not unique to neurocognitive training, however, as recent reviews suggest that unblinded ratings may have inflated previous estimates of non-pharmacological treatment efficacy for ADHD behavioral symptoms (Sonuga-Barke et al., 2013). In addition to greater consideration of the underlying pathophysiology of ADHD, future treatment studies will need to utilize more rigorous methodological and measurement approaches to more accurately evaluate the efficacy of next generation neurocognitive and combined neurocognitive + skill-based treatment approaches.

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Table 1

Attention-deficit/hyperactivity disorder (ADHD) etiological models with testable predictions regarding neurocognitive training

Model	Model description of ADHD	Probable Neurocognitive Intervention Targets	Representative publications
Attentional Lapse Models	Models vary from DSM-5 Clinical Model (core attention deficit in ADHD) to attention deficits attributable to alternate processes/mechanisms (see models below)	One or more attention processes	Leth-Steensen et al. (2000)
Behavioral Inhibition Model	A core deficit model wherein deficits in behavioral inhibition (stopping pre-potent/ongoing responses and interference control) result in four areas of executive dysfunction that collectively result in ADHD behavioral symptoms.	Behavioral inhibition	Barkley (1997, 2001)
Cognitive Neuroenergetic / State Regulation Deficit Model	Decreased ATP production and inadequate lactate supply from deficient astrocyte functioning cause depletions in energetic resources associated with activation and effort. These depletions result in performance variability, which in turn impacts performance on executive functioning tasks. Executive functions interact with primary impairments in effort and activation via both top-down and bottom-up processes to result in the behavioral features of ADHD.	Response variability Information processing efficiency Attention, Inhibition (due to assoc. with energetic dysfunction) Activation and/or effort	Russell et al. (2006/2013); Sergeant (2005)
Default Mode Network Model	A multiple pathway model that hypothesizes that disruptions in cortico-striato-thalamo-cortical neuroanatomical circuitry—consisting of ‘hot’ and ‘cool’ regions—contribute to functional behavioral and cognitive differences in ADHD. Rhythmic, periodic interruption of resting state (“default mode”) brain waves into task-positive networks during task engagement result in ADHD inattentive behavior.	Unclear; Response variability?	Castellanos et al. (2005); Castellanos & Tannock (2002); Sonuga-Barke & Castellanos (2007)
Dynamic Developmental Model	A core deficit model that hypothesizes that reduced dopaminergic functioning causes narrower reinforcement gradients and altered extinction processes in normal behavior-consequence relationships. These deficient dual processes contribute to core ADHD symptoms and behavioral variability, which vary based on context, task, and function. Executive dysfunction, particularly disinhibition, is viewed as an outcome of these altered reinforcement and extinction processes.	Unclear; Training to widen reinforcement gradients?	Sagvolden et al. (2005)
Subcortical Deficit Model	A developmental model that hypothesizes that ADHD is caused by subcortical neural dysfunction that manifests early in ontogeny, remains relatively static throughout life, and is not associated with the remission of symptomatology. Executive dysfunction does not cause ADHD symptoms, but developmental growth in executive functions facilitates recovery.	Working memory manipulation Note: only expected to benefit patients with major allele homozygosity in two DRD1 polymorphisms; may be more beneficial later in development	Halperin & Schulz (2006); Halperin et al. (2008); Trampush et al., 2014
Tripartite Pathway Model	A multiple pathway/equifinality model in which ADHD symptoms are caused by deficits in one or more dissociable cognitive (behavioral inhibition, temporal processing) and/or motivational (delay aversion) processes.	Behavioral inhibition, temporal processing, and/or delay aversion dependent on patient's particular pattern of impairments	Sonuga-Barke (2010)

Model	Model description of ADHD	Probable Neurocognitive Intervention Targets	Representative publications
Working Memory Model	A core deficit model that views inattention, hyperactivity, and impulsivity as phenotypic/behavioral expressions of the interaction between neurobiological vulnerability and environmental demands that overwhelm these children's impaired working memory. Associated features of ADHD arise through direct effects of impaired working memory, or indirect effects of impaired working memory through its impact on core behavioral symptoms	Central executive working memory (updating, dual-task/ manipulation, serial reordering) Note: Expected to benefit ~80% of children with ADHD with CE WM deficits	Rapport et al. (2001/2008) Rapport et al., 2013