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Attention-deficit/hyperactivity disorder: An integrated developmental psychopathology and Research Domain Criteria (RDoC) approach☆

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ABSTRACT

Attention-deficit/hyperactivity disorder (ADHD) is characterized by heterogeneous behaviors and symptoms, developmental trajectories, and treatment response. Isolating intermediate phenotypes that are superior to current DSM-based nosology in order to explain such heterogeneity is integral to enhancing etiological theory, improving clinical assessment, predicting treatment response, and developing tailored treatments. To this end, this review provides an integrated developmental psychopathology and National Institute of Mental Health Research Domain Criteria (RDoC) approach to ADHD. In particular, associations between ADHD and RDoC domains of cognition (specifically working memory) and positive valence (reward anticipation/delay/receipt) are discussed. These domains are examined across behavioral and neurocircuitry levels of analysis and placed within a developmental context via examining associations among RDoC domains, relevant features of ADHD, and environmental correlates implicated across development. Limitations of the existing literature and proposed future directions are explored. Importantly, future work should focus on novel approaches that account for developmental shifts in functioning of relevant RDoC domains over time, as well as further examination of the interaction across RDoC domains and levels of analysis.

1. Introduction

DSM 5 and ICD-10-CM conceptualize attention-deficit/hyperactivity disorder (ADHD) as a categorical diagnosis involving symptoms of inattention, hyperactivity, and impulsivity, as well as cross-situational impairment [1]. ADHD has a prevalence of 7.8 to 11% [2] and is highly heterogeneous; such that, individuals with the disorder differ considerably in behaviors, presence of comorbid diagnoses, developmental trajectories, and treatment response [3,4]. An integrated developmental psychopathology (DP) and National Institute of Mental Health Research Domain Criteria (RDoC) framework may further improve ADHD etiological theory and tailoring of treatment, given the shifting clinical presentation of ADHD across development via interactions among biological predispositions, development, and environmental contexts [3–6].

2. National Institute of Mental Health's Research Domain Criteria initiative (RDoC)

RDoC attempts to address the limitations of existing diagnostic classification systems by providing a research-based framework for the investigation of mental disorders [5,7,8]. RDoC redirects the primary focus from behavioral features of disorders to the functioning of specific domains presumed to underlie these behavioral manifestations. These domains include: negative and positive valence, cognitive, social, and arousal/regulatory systems [5,7,8]. RDoC proposes examining these domains across levels of analysis including: molecular, genetic, cellular, neurocircuits, behavioral, and beyond [5,7,8].

The RDoC framework has been preliminarily applied to research relevant to ADHD (for examples, see [9,10]), and emerging work is beginning to evaluate its relevance to related behavioral manifestations such as conduct problems [10] and sluggish cognitive tempo (for a review, see [11]). However, much of the work in ADHD has compared youth with ADHD to typically developing youth on a single RDoC domain at a single level of analysis, thereby, failing to integrate across multiple domains or levels of analysis, as well as failing to consider the dimensional nature of the disorder, comorbidity, development, and environment [12–14].

3. Developmental psychopathology (DP)

While RDoC is a relatively new approach, the discipline of DP spans four decades [15] and has the goal of integrating models from a variety of fields (e.g., genetics, neuroscience, psychology, and systems theory) to inform investigations of the developmental pathways relevant to typical and atypical development [15]. These developmental pathways are reciprocal and transactional [15]. Additionally, DP places equal

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weight across underlying systems, including environmental factors, emphasizing the complex interplay among levels of analysis and systems [12,16]. A DP approach is generally congruent with RDoC, as both center on examining relevant domains across units of analysis, favoring the use of a dimensional approach [17]. However, neither development nor environmental levels of analysis are specifically included in the current RDoC framework [5,7,8,18]. A DP approach is of critical importance in the understanding of ADHD, given its chronic course, changes in the presentation of ADHD across the lifespan [3,4], as well as developmental changes in the RDoC domains commonly implicated in ADHD.

4. Integrating across DP and RDoC in ADHD

An integrated DP and RDoC approach is important to the study of ADHD because ADHD: 1) is classified in DSM 5 as a neuro*developmental* disorder [1], 2) is characterized by heterogeneous symptoms reflecting extremes of rates of behaviors with a relatively normal distribution within the general population [19,20], 3) is associated with symptoms that are common in other disorders (e.g., ADHD symptom of "often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort" is relatively indistinguishable from similar symptoms of major depressive disorder or generalized anxiety disorder [1]), 4) is commonly comorbid with other disorders (greater than 65% of youth with ADHD have a second diagnosis [21]), 5) has symptom presentations that vary as a function of development, as well as gradual symptom remission generally occurring across development [3,4,22], and 6) is associated with core RDoC domains which change and develop across the lifespan [5,7,8,18].

Below we illustrate the importance of an integrated DP and RDoC approach to ADHD by considering two RDoC domains relevant to ADHD with an eye toward several of the guiding principles of a DP approach. An examination of each of the domains and subconstructs of RDoC previously implicated in ADHD is beyond the scope of this review and, as a result, we focus on cognitive systems and positive valence systems, specifically, working memory and reward anticipation/delay/receipt. These sub-constructs have been routinely implicated in ADHD and examined across development. Specifically, several theories of ADHD etiology and heterogeneity hypothesize a prominent role for impaired cognitive and reward processes. These include Barkley's Self-Regulation Theory (focusing on deficits in response inhibition and self-regulation [23]), Rapport's Working Memory Model (focusing on deficits in working memory [24]), Sonuga-Barke's Dual Pathway Model (focusing on deficits in executive function and reward/motivation [25]), as well as Nigg's Multiple Pathway Model (focusing on deficits in executive function, approach motivation/reward, and avoidance motivation [26]).

Importantly, a comprehensive review of each of the RDoC levels of analysis implicated in ADHD is also beyond the scope of this review. Here, we focus on behavioral manifestations, as well as neural circuits/functioning, as much of the literature spans these levels of analysis. We conclude with a discussion on the paucity of work integrating across comorbidity, continuous symptoms, development, RDoC domains and levels of analysis. We call for future inquiry utilizing an integrated DP and RDoC approach to improve understanding of ADHD.

4.1. Cognitive systems

4.1.1. Broad conceptualization

RDoC's cognitive systems domain involves multiple processes related to information processing, including the constructs of attention, cognitive control, declarative memory, language, perception, and working memory [5,7,8,18]. Working memory has been implicated in ADHD both in theoretical and empirical work [24,27–29].

4.1.2. Working memory

Working memory reflects a higher-order, limited capacity cognitive system for the temporary storage and maintenance of information for the purposes of directing behavior toward a goal [30]. RDoC ascribes several subconstructs to working memory including: active maintenance, flexible updating, limited capacity, and interference control [18]. There is substantial evidence for developmental improvements in working memory from the age 4 to approximately age 13 in typically developing youth [31]. Further, working memory is associated broadly with activation in the prefrontal cortex [32] with distinct associations between phonological short-term memory and left temporal and parietal regions [33,34] and between visuospatial short-term memory and prefrontal and parietal cortices [35]. In addition to ADHD, WM deficits have also been implicated in other conditions, such as autism spectrum disorders [36]. Further, a recent study provides evidence that working memory impairment portends both a liability for general psychopathology and a specific risk for externalizing behavior problems with non-significant associations with internalizing behavior problems [37].

4.1.2.1. Behavior. Empirical work utilizing computerized tasks has consistently identified deficits in working memory among individuals with ADHD across development [27–29,38]. With regard to an integrated DP and RDoC approach, the preschool and elementary years represent a period of time where increased environmental demands (e.g., school) are likely to interact with both typical and atypical neurodevelopment resulting in increased recognition of symptoms of ADHD [39]. For example, environmental changes result in increased demands on multiple cognitive systems, including rapidly developing working memory systems among typically developing youth [40]. While prior work has demonstrated worse working memory functioning in preschool-aged youth with ADHD, these effects have been smaller in magnitude than those observed in school-age youth which may reflect the fact that the working memory system has not yet matured sufficiently to detect between-group differences in this domain [41,42].

Investigations of working memory among elementary-aged youth with ADHD span the last two decades with results consistently demonstrating that ADHD is associated with substantial deficits (ES = 0.43 to 1.06) in both visuospatial and verbal working memory [27,28]. Notably, estimates of the prevalence of working memory deficits among elementary-aged youth with ADHD range from 30.1% to 98% [29,43]. With regard for the need of an integrated DP and RDoC approach, discrepancies in these estimates likely reflect multiple factors, including: true heterogeneity in cognitive function, task variability, as well as ADHD symptom composition, biological sex, comorbid diagnoses, developmental considerations, and diagnostic rigor [29].

In line with an integrated DP and RDoC approach, when symptoms are examined continuously, there tend to be stronger associations between working memory and inattentive relative to hyperactive/impulsive symptoms among both preschool- and elementary-age youth with correlation coefficients ranging from −0.17 to −0.28 [44,45]. These associations also emerge in the general population with stronger associations between both verbal and visuospatial working memory with inattentive symptoms ($r = -0.18$ to -0.25) and smaller, albeit significant, associations between verbal working memory and hyperactivity/impulsivity ($r = -0.12$ to -0.14) [46].

Substantially less is known regarding the extent to which WM deficits are present in adolescents and adults with ADHD [3,22,47]. Meta-analytic evidence of deficits in working memory among young adults with ADHD reveal somewhat smaller effect sizes than those observed in childhood across verbal (ES = 0.44 to 0.56) and visual memory (ES = 0.49) [48,49]. Demonstrating the benefits of an integrated DP and RDoC approach, recent longitudinal work has identified a potential role for improved visuospatial working memory in the remission of symptoms of inattention across the transition from childhood to adolescence among youth with ADHD [50]. This work highlights

the potential role of working memory in the shifting developmental course of the disorder.

Consistent with and integrated DP and RDoC approach, initial conceptualizations of the WM model of ADHD hypothesized a mediating role for WM such that early changes in genetics and neurobiological functioning result in deficits in WM functioning which culminate in adverse behavioral and functional (e.g., academics, social) outcomes [24]. Experimental support for this hypothesis has been obtained through objective measures of inattention (e.g., direct observations) and hyperactivity (e.g., actigraphy) while simultaneously manipulating WM demands [51]. Further, mediation analyses have demonstrated a similar mediating role for WM on impulsivity [52]. However, recent evidence for substantial heterogeneity in cognitive dysfunction in ADHD suggests instead a potential moderating role for WM with respect to functional outcomes and treatment response [53]. Additional work is needed to examine whether cognitive subgroups are relevant to differences in symptomatology and/or treatment response. The identification of nested heterogeneity of cognitive dysfunction across both children with ADHD and typically developing children highlights the potential transdiagnostic nature of WM deficits [14]. However, little work to date has examined these relationships along a continuum or compared youth with ADHD to youth with other disorders (e.g., anxiety, depression). Longitudinal work examining the relationship between behavioral data collected from cognitive tasks and data collected from parent-, teacher-, and self-report is necessary to clarify how these associations may change over the course of development.

4.1.2.2. Brain circuitry. Multiple brain regions have been implicated in the pathophysiology of ADHD with some demonstrating greater activation (e.g., default mode network, somatomotor, visual) and others demonstrating reduced activation (e.g., frontoparietal, ventral attention, right somatomotor, and putamen) relative to individuals without the disorder [11]. Notably, Cortese and colleagues (2012) demonstrated that a pattern of hypoactivated frontoparietal functioning persists into adulthood. Further, longitudinal studies examining developmental changes in cortical maturity from early childhood into adolescence have documented an approximately two to three-year delay in cortical thickening in children with ADHD relative to those without the disorder [54]. Decreased cortical thickening appears to be significantly associated with symptoms of inattention and hyperactivity in the general population [55]. Additionally, expected developmental increases in cortical thinning during adolescence were evaluated in relation to symptoms of hyperactivity and impulsivity from a dimensional perspective among non-clinic referred youth, which revealed that slowed cortical thinning was associated with greater symptoms of hyperactivity and impulsivity [56]. Collectively, this evidence provides additional support for conceptualization of ADHD along a continuum rather than as a discrete diagnostic entity.

With respect to working memory functioning and associated neurobiological functioning in children with ADHD, Massat and colleagues [57] utilized fMRI to evaluate regions associated with working memory performance in children with ADHD relative to children without ADHD. While they failed to find significant between-group differences in task performance, they identified reduced activation in children with ADHD across multiple neuroanatomical regions associated with working memory performance including occipital, inferior parietal cortex, caudate nucleus, and cerebellar regions. Surprisingly, no differences were identified in activation patterns in the prefrontal cortex; however, others have demonstrated reduced activation in left and right prefrontal regions in children and adults with ADHD during working memory tasks [58,59]. Notably, during working memory tasks, children with ADHD have also been shown to demonstrate increased activation of the medial prefrontal cortex - a region of the brain implicated in the default mode network - relative to children without the disorder [58]. The default mode network is considered a task-negative network which must be adequately suppressed by individuals during performance on cognitive tasks in order to maintain ongoing successful task execution and has been implicated heavily in recent etiological theories of ADHD [60,61]. This evidence highlighting neuroanatomical correlates of working memory and demonstrable hypoactivation of regions among individuals with ADHD are consistent with models implicating working memory in ADHD. Important to an integrated DP and RDoC approach, additional work is needed to clarify the extent to which the structure and function of these regions evolve over development by utilizing longitudinal designs with samples including children and adolescents as most work has involved cross-sectional comparisons. Additionally, future work attempting to integrate theoretical models of ADHD would benefit the field. For example, while default mode network (DMN) impairment is presumed to result in the behavioral manifestations of ADHD, little work examining the role of DMN in impaired WM performance has been conducted in an attempt to better understand the potential role of WM in this relationship.

4.2. Positive valence systems

4.2.1. Broad conceptualization

According to RDoC, positive valence systems are responsive to positive or approach-based motivational situations [5,7,8,18]. This domain is divided into several constructs and sub-constructs, including: reward responsiveness (e.g., reward anticipation, initial response to reward/reward receipt, reward satiation), reward learning (e.g., probabilistic and reinforcement learning, reward prediction error, habit), and reward valuation (e.g., reward probability, delay, and effort) [5,7,8,18]. We focus on reward anticipation, receipt, and delay.

4.2.2. Reward anticipation, receipt, and delay

The sub-constructs of reward anticipation, reward receipt, and reward delay are related, but distinct, and theorized to involve some of the same underlying neural circuitry [5,7,8,18]. RDoC describes reward anticipation as processes that are associated with the ability to anticipate or represent a future incentive [5,7,8,18]. In contrast, initial response to reward or reward receipt is described as processes evoked by the initial presentation of a positive reinforcer [5,7,8,18]. Finally, reward valuation delay are processes by which the value of a reinforcer is computed as a function of the reinforcers magnitude and the time expected prior to its delivery [5,7,8,18].

Recent work has conceptualized these elements of reward functioning as “wanting” and “liking”, representing reward or incentive salience (i.e., related to both anticipation and delay) and hedonic impact of receiving the reward or incentive, respectively [62]. The nucleus accumbens and ventral pallidum appear to be implicated in both liking and wanting; however, sub-regions of these circuits appear to be cued to opioid, endocannabinoid, and GABA-benzodiazepine systems associated with liking [63–66], while others appear to be influenced by mesocorticolimbic-dopamine-related systems associated with wanting [65,67].

Of note, evidence from both human brain imaging and animal models suggest that there is elevated responsiveness to rewards and incentives during adolescence, and impulse control is still relatively immature during this time [98]. This work reveals differential functioning of meso-limbic systems, implicated in reward processing, and prefrontal control systems during adolescence as compared to childhood and adulthood [98]. As described below, this developmental pattern may be exacerbated among individuals with ADHD [99].

4.2.2.1. Behavior. Several theories and much empirical work support the role of impaired reward processing as a key deficit in ADHD [25,68–70]. ADHD has been repeatedly demonstrated to be associated with a preference for small immediate over larger delayed rewards, as well as steepened discounting function when anticipating future rewards [71–75]. This has been supported via performance on laboratory and

computerized tasks. For example, meta-analytic work (e.g., [41]) has demonstrated medium associations between ADHD and delay aversion ($r = 0.38$) among preschool-age youth.

Disruption in reward and incentive processing has also been implicated in studies of ADHD in elementary-aged youth [76,77]. Numerous studies with this age-range have used delay tasks, which give individuals repeated choices between a small reward now and a large reward later. Youth with ADHD typically demonstrate a preference for immediate rewards more so than typically developing youth [78–83]. Additionally, among elementary-aged youth, the preference for immediate rewards is positively associated with inattention [84].

Important to an integrated DP and RDoC approach, despite the substantial evidence for preference for small, immediate rewards among individuals with ADHD, several studies suggest a need for special considerations in interpreting these results. For example, adolescents with ADHD have been shown to display steeper discounting of delayed *hypothetical* rewards of $100, but not $1000, when delays were between one month and 10 years [85]. Additionally, an association between continuous measures of ADHD hyperactivity/impulsivity symptoms (but not inattention symptoms) and discounting gradients has been reported among college students when rewards were *real*, but not hypothetical [86]. In contrast, when using actual (small $0.10) rewards with short (30 s) delays, prior work has identified no difference in delay discounting in children and adolescents with ADHD and matched controls [87]. However, in a separate sample of children and adolescents with and without ADHD, steeper delay discounting was observed among youth with ADHD combined presentation compared to typically developing youth when delays were up to 1 min [75]. Finally, a study of elementary aged youth with and without ADHD demonstrated that ADHD is associated with a steeper delay gradient when contemplating *hypothetical* delayed rewards (up to $10, delays up to 180 days); however, these results were not fully independent of child IQ [88]. Thus, future work may benefit from continuing to consider whether rewards and delays are real or hypothetical, as well as the length of delay utilized when designing studies to assess reward anticipation and delay among youth with ADHD. Further, in line with an integrated DP and RDoC approach, characteristics of participants such as age, IQ, symptoms, and comorbidity should be considered.

4.2.2.2. Brain circuitry. With respect to brain circuitry associated with reward processing impairments among individuals with ADHD, neuroimaging studies have revealed that the nucleus accumbens exhibits atypical functioning and/or functional connectivity among individuals with ADHD [89–93]. One prior study revealed that among elementary-aged youth with ADHD, functional connectivity differed from typically developing youth between the nucleus accumbens and regions in the default mode network, cortical regions important in cognitive control, posterior insula, and thalamus [89]. Further, among children with ADHD, disruptions in connectivity between the nucleus accumbens and anterior prefrontal cortex (PFC) and ventromedial PFC were associated with impulsive decision making on a delay discounting task. Individuals with ADHD have also been shown to exhibit reduced activity in these regions during reward anticipation and delay [13,92,94,95], as well as heightened activity in the ventral striatum/nucleus accumbens upon receipt of reward [90]. For example, adolescents with ADHD have been shown to demonstrate reduce activation in the ventral striatum during reward anticipation, which was associated with parent-rated hyperactive/impulsive symptoms [92]. These results are in line with prior theory by Volkow and colleagues (2011 [96]) which proposes that impulsive behavior is characterized by atypical sensitivity to reward cues and anticipation of reward. Important to an integrated DP and RDoC approach, this model was initially developed in the context of addiction and substance abuse research; however, it fits well with models of ADHD, and has clear relevance, given that: 1) children with ADHD are at an increased risk of addiction in adolescence and adulthood and 2) ADHD and addiction are associated with dysfunction in mesolimbic-dopaminergic systems related to reward anticipation and delay, which may help to explain the comorbidity between these disorders [93,94,96,97].

5. Limitations of prior literature and future directions

As noted above, there are several limitations to existing ADHD research, which may be addressed through the adoption of an integrated DP and RDoC approach. Some of these limitations include that the bulk of prior work has: 1) compared youth with ADHD to typically developing youth on a single RDoC domain, 2) compared youth with ADHD to typically developing youth at a single level of analysis, 3) failed to consider the dimensional nature of the symptoms of the disorder, 4) failed to consider the role of comorbidity, and 5) failed to consider the role of development and the environment [12–14]. We examine each of these limitations and call for future work to address these gaps in the literature below.

5.1. Consideration of single RDoC domains

The majority of prior work examining etiological mechanisms underlying ADHD has been focused on a single domain, and as such, has failed to consider the interaction of domains among youth with ADHD. Substantially less work has focused on the intersection across domains such as cognition and positive/negative valence. One example illustrating the importance of considering multiple RDoC domains in the study of ADHD is that of irritability. Irritability is increasingly recognized as an important influence in child psychopathology that cuts across existing diagnostic categories [77] and is characterized by "proneness to anger" [98]. Although irritability has been emphasized in disruptive mood dysregulation disorder (DMDD) and oppositional defiant disorder (ODD) in DSM 5, most children who meet criteria for DMDD also meet criteria for ADHD [99–102]. Importantly, over development, irritability has also been associated with the development of mood and anxiety disorders [98,101,103–106]. Thus, the presence of such a class of behavior may help to explain comorbidity of both externalizing (ODD) and internalizing (anxiety, mood) pathology in individuals with ADHD [98,107–109]. Importantly, irritability appears to be influenced by multiple RDoC domains, including cognitive systems and positive and negative valence [98,107–109]. Specifically, irritability is believed to be normally distributed among youth in the general population [98,107–109], and data suggest that irritability is associated with deficient reward learning, elevated sensitivity to reward receipt and omission (all positive valence), as well as maladaptive orienting to, interpreting, and labeling of threat (all negative valence), as well as deficits in cognitive control and regulation [98,107–109]. Thus, the consideration of multiple RDoC domains across development will be important to the study of ADHD.

5.2. Consideration of single RDoC levels of analysis

Despite the adoption and incorporation of multiple levels of analysis (e.g., neuroimaging, behavioral) when examining RDoC domains of relevance (e.g., positive/negative valence, cognitive systems) to ADHD, these levels of analysis continue to be examined mostly in isolation. Emerging work in this area has initially begun to propose integration across these domains while integrating neurobiological evidence from a transdiagnostic lens. For example, Holroyd and Umemoto (2016 [110]) present an integrative model in which they hypothesize that dysfunctions primarily in the anterior cingulate cortex (ACC) underlie disruptions in positive and negative valence systems in the form of difficulties appropriately processing rewards which extends to performance in cognitive domains and ultimately culminates in many of the behavioral manifestations observed in various forms of psychopathology (e.g., depression, OCD, ADHD). Future work evaluating the veracity of this model and/or others like it while simultaneously

incorporating changes in these areas over the course of development are likely to provide a greater understanding of the mechanisms underlying disorders such as ADHD.

5.3. Categorical focus and comorbidity

Prior work examining the etiological underpinnings of ADHD has focused on ADHD as a categorical disorder, there by ignoring the continuous distribution of ADHD symptoms in the general population, as well as comorbid diagnoses and symptoms. Examples provided earlier of the evaluation of specific neuroanatomical regions associated with specific domains of functioning (e.g., working memory) and their corresponding associations with symptoms of the disorder (e.g., inattention, hyperactivity/impulsivity) are consistent with between-group comparisons between children with ADHD and typically developing populations. However, there is a critical need for additional work examining these associations along a continuum in the general population. The emergence of more sophisticated analytic approaches such as machine learning and community detection algorithms have identified similar clusters of heterogeneity in cognitive [14] and temperament [111] domains in children with ADHD relative to typically developing children using multiple domains of analysis (e.g., behavioral, neurobiological, psychophysiological) representing a first step in this direction. Despite these advances, more work is needed to evaluate whether similar latent groups are present in other forms of psychopathology, as well as what clinical utility these may have with respect to assessment and treatment of psychopathology.

5.4. Cross-sectional approach to a developmental disorder

Prior work examining etiological underpinnings of ADHD has been cross-sectional, addressing a single developmental period, while ignoring the role of environmental context and development. A developmental approach is of critical importance in the understanding of ADHD, given its chronic course, changes in the presentation of ADHD across the lifespan [3,4], as well as developmental changes in the RDoC domains implicated in ADHD. A recent example of a longitudinal study examining the reciprocal influence of developmental changes in brain and behavior along a continuum examined neuroanatomical development over two years in a population-based cohort of children [112]. The association between the externalizing and internalizing dimensions of behavior as assessed by the Child Behavior Checklist (CBCL) and subcortical development were evaluated between the ages of 8 and 10 years. The results of this study demonstrated a significant contribution of elevated ratings of internalizing or externalizing scores to slower changes in subcortical development but not the reverse (i.e., subcortical development contributing to changes in internalizing or externalizing scores). This study highlights the potential reciprocal influence of brain and behavior while also providing an example of a longitudinal approach to examining these relationships. Innovations in data sharing, multisite data collection, and big data analytics are likely to accelerate the pace of these developments and several approaches incorporating these approaches, such as the ADHD-200 Consortium [113] and the Adolescent Brain Cognitive Development (ABCD) Study [114], provide a compelling framework for addressing these limitations. Incorporation of larger, more heterogeneous samples are likely to provide a greater understanding of how these domains relate to psychopathology broadly and ADHD specifically.

With respect to developmental trajectories of ADHD symptoms, of children with ADHD in childhood 50–70% continue to have a diagnosis during the transition to adolescence [72,115,116]. While some youth appear to remit, others experience persistent problems and serious negative outcomes, including drug abuse, school dropout, criminality, and antisocial behavior [22,117–119]. Further, in the transition from adolescence to adulthood, an additional 25–50% experience a remission of symptoms [47]. Importantly, it is well-established that across development hyperactive and impulsive symptoms are more likely to remit, while inattentive symptoms are more likely to remain stable [119]. However, the determinants and correlates of this developmental divergence in symptoms remain poorly understood and additional longitudinal work is critical to addressing this gap in the literature. An integrated DP and RDoC approach could help clarify the determinants of such changes in ADHD symptoms with development, as there are also normative developmental changes in these behaviors across development [120,121]. Specifically, hyperactive and impulsive behaviors normatively decline across adolescent development [4,116,122]. This normative decline may be due to the maturation of several key neural networks [123], and a combined DP and RDoC approach would allow for the examination of both typical and atypical development of these networks along with genetic and environmental influences as they contribute to shifts in the behavioral and symptom profile of ADHD across development.

Finally, an integrated DP and RDoC approach will require longitudinal designs to examine developmental changes in functioning in key domains, across levels of analysis; however, an important caveat here is that developmentally-sensitive and appropriate measures of several RDoC domains have yet to be developed and/or may not be reliability associated with one another at different periods of development [18]. Thus, potential limitations related to the measurement of each of these constructs are relevant to consider when adopting a DP framework. Specifically, instruments that are appropriate for one age group (e.g., preschool) may not adequately capture the construct of interest in older individuals given brain maturation and developmental shifts in RDoC domains over the course of development. Thoughtful and novel approaches will be necessary to adequately capture construct-related variance within the context of longitudinal designs.

6. Conclusion

In the current review, we utilize sub-constructs of the RDoC domains of cognition (i.e., working memory) and positive valence (i.e., reward anticipation, reward receipt, and reward delay), at the behavioral and neurocircuitry levels of analysis, to illustrate the utility of an integrated DP and RDoC approach. Critically, while substantial work has implicated both working memory and disruptions in reward processing in ADHD, as evidenced by significant between-group differences in children with ADHD relative to typically developing children, more recent work raises significant questions regarding their role in the disorder. For example, recent work adopting an RDoC dimensional approach to working memory impairment and symptoms of the disorder suggests a similar association with symptoms of inattention and hyperactivity/impulsivity [46] in typically developing youth indicating a potential lack of specificity with respect to these deficits in ADHD and points to a need for additional work incorporating more diverse samples (e.g., comorbidities and other disorders).

Developmental differences in the magnitude of deficits in working memory and reward processing among individuals with ADHD are present and may help to explain persistent disruptions in corresponding behavior and neurobiological functioning. This highlights the need for additional longitudinal work to identify what role these domains may play in the expression (and potential remission) of the disorder over time. Finally, models of ADHD diverge significantly with respect to their conceptualizations of how these domains contribute to the disorder and whether or not they mediate or moderate functioning in this population. This has resulted in the majority of the literature examining these domains in isolation rather than attempting to integrate domains such as cognition and positive valence systems. Future developmental work taking an integrative approach to these domains when assessing behavioral functioning and neurobiological correlates are likely to further our understanding of their mechanistic role in the disorder's expression, as well as potentially enhance their clinical utility with respect to assessment and treatment.

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