Development and Psychopathology (2021), **33**, 1803–1820
doi:10.1017/S0954579421000900

CAMBRIDGE UNIVERSITY PRESS

Special Issue Article

Longitudinal network model of the co-development of temperament, executive functioning, and psychopathology symptoms in youth with and without ADHD

Sarah L. Karalunas[1], Dylan Antovich[2], Patrick K. Goh[3], Michelle M. Martel[3], Jessica Tipsord[2], Elizabeth K. Nousen[2] and Joel T. Nigg[2]

[1]Department of Psychological Sciences, Purdue University, West Lafayette, Indiana, USA; [2]Department of Psychiatry & Behavioral Neuroscience, Oregon Health & Science University, Portland, Oregon, USA and [3]Department of Psychology, University of Kentucky, Lexington, KY, USA

Abstract

Attention-deficit hyperactivity disorder (ADHD) is a common, chronic, and impairing disorder, yet presentations of ADHD and clinical course are highly heterogeneous. Despite substantial research efforts, both (a) the secondary co-occurrence of ADHD and complicating additional clinical problems and (b) the developmental pathways leading toward or away from recovery through adolescence remain poorly understood. Resolving these requires accounting for transactional influences of a large number of features across development. Here, we applied a longitudinal cross-lagged panel network model to a multimodal, multilevel dataset in a well-characterized sample of 488 children (*n*ADHD = 296) to test Research Domain Criteria initiative-inspired hypotheses about transdiagnostic risk. Network features included Diagnostic and Statistical Manual of Mental Disorders symptoms, trait-based ratings of emotional functioning (temperament), and performance-based measures of cognition. Results confirmed that ADHD symptom domains, temperamental irritability, and working memory are independent transdiagnostic risk factors for psychopathology based on their direct associations with other features across time. ADHD symptoms and working memory each had direct, independent associations with depression. Results also demonstrated tightly linked co-development of ADHD symptoms and temperamental irritability, consistent with the possibility that this type of anger dysregulation is a core feature that is co-expressed as part of the ADHD phenotype for some children.

Keywords: ADHD, executive functioning, longitudinal network, RDoC, temperament, transdiagnostic risk

(Received 1 March 2021; revised 30 June 2021; accepted 30 June 2021)

Attention-deficit hyperactivity disorder (ADHD) is a common, chronic, and impairing disorder characterized in the official Diagnostic and Statistical Manual of Mental Disorders (DSM) scheme by age-inappropriate levels of inattention and/or hyperactivity–impulsivity (APA, 2013). Yet presentations of ADHD and clinical course are highly heterogeneous. Whereas some children with ADHD show a seemingly full remittance of symptoms by adolescence or early adulthood, many, if not most, continue to experience clinically impairing ADHD symptoms (Biederman, Petty, Clarke, Lomedico, & Faraone, 2011; Sibley et al., 2012; Willoughby, 2003). ADHD is also a risk factor for a range of serious subsequent complications. It appears very early in development and conveys 50% to 300% increased risk for problems across the life span ranging from depression to conduct problems to substance use and even shortened life span (Bussing, Mason, Bell, Porter, & Garvan, 2010; Erskine et al., 2016; Franke et al., 2018; Groenman, Janssen, & Oosterlaan, 2017; Kessler et al., 2014, 2006; Lee, Humphreys, Flory, Liu, & Glass, 2011).

Despite substantial research efforts, both (a) the secondary co-occurrence of ADHD and complicating additional clinical problems and (b) the developmental pathways leading toward or away from recovery through adolescence remain poorly understood. One possibility is that the core symptoms domains of ADHD – inattention and hyperactivity–impulsivity – are early emerging risk features that directly convey risk for later problems. Alternatively, ADHD symptoms may operate via indirect influences – inattention contributing to academic failure that in turn increases risk for depression and conduct problems. A third possibility is that features outside of traditional symptom domains, such as weaknesses in executive functioning (EF) or anger regulation, may convey transdiagnostic risk for multiple problem domains including both ADHD and co-occurring symptoms of disruptive behavior disorders and depression (Beauchaine & Tackett, 2020; Macdonald, Goines, Novacek, & Walker, 2016; McTeague, Goodkind, & Etkin, 2016). Resolving these (nonmutually exclusive) hypotheses requires accounting for transactional influences of a large number of features across development. Here, we apply a longitudinal network model to a theoretically

Author for Correspondence: Sarah Karalunas, Purdue University, 703 3rd Street, West Lafayette, IN 47907; E-mail: skaralunas@purdue.edu

Cite this article: Karalunas SL, Antovich D, Goh PK, Martel MM, Tipsord J, Nousen EK, Nigg JT (2021). Longitudinal network model of the co-development of temperament, executive functioning, and psychopathology symptoms in youth with and without ADHD. *Development and Psychopathology* **33**, 1803–1820. https://doi.org/10.1017/S0954579421000900

justified set of diagnostic and transdiagnostic features spanning DSM symptoms, trait-based ratings of emotional functioning (temperament), and performance-based measures of cognition (executive function) to address how ADHD and co-occurring problems unfold over time.

Network perspective on problem co-occurrence

Historically, categorical, DSM-oriented perspectives have suggested that symptoms of ADHD (and other disorders) arise from latent disease entities that cause sets of symptoms (Kendler, 2009; McNally, 2020). Co-occurring problems in this framework are viewed as "comorbid" because of the implication that they arise from distinct, independent disease entities. This Kraepelinian framework and the related DSM perspective has of course received ample challenge (Kendler & Engstrom, 2018; Wakefield, 2016). Symptoms and disorders cluster hierarchically into a fairly constrained number of domains (Achenbach, 1966, 2020; Caspi et al., 2014; Lahey et al., 2008; Olino et al., 2018; Smith, Atkinson, Davis, Riley, & Oltmanns, 2020). Similar symptoms also appear as indicators of multiple disorders – for example, concentration problems appear as a symptom in both ADHD and depression (and other disorders as well). Unsurprisingly, comorbidity is the rule rather than the exception.

In ADHD, as many as 60% of children experience a co-occurring condition across the life span, with ADHD frequently the first condition to emerge (Kessler et al., 2006a). Because ADHD diagnosis often precedes full onset of other conditions, it is often viewed as a liability for secondary psychopathology (Kessler et al., 2006a). Evidence suggests it does in fact serve as a causal step toward both depression (Riglin et al., 2020; Stern et al., 2020) and conduct disorder (Beauchaine, Hinshaw, & Pang, 2010). However, the specific pathways by which this risk is conveyed remain unclear.

One conceptualization, popularized over the last decade, comes from network theory (Borsboom & Cramer, 2013; Fried et al., 2017; McNally, 2016, 2020). From a network perspective, changes in symptoms across time result from patterns of co-activation among the symptoms themselves. For example, inattention or hyperactivity–impulsivity may activate sleep problems, which in turn activates other symptoms of depression, leading to their commonly observed co-occurrence. The dynamics of the symptoms themselves constitutes the mechanisms of disorder co-occurrence.

Statistically, these hypotheses are tested via a partial correlation network model in which nodes (which correspond to variables) are connected by edges that reflect the partial correlation between two variables controlling for all other variables in the model. For example, if ADHD symptom domains "activate" (or cause) features of depression (or other co-occurring problems), this would be reflected in edges that directly connect these nodes in the network. Alternatively, connections may be indirect. For example, ADHD may activate oppositional defiant behaviors that in turn activate depression symptoms, which would be reflected in short overall path lengths from ADHD to depression but only via indirect paths. Thus, network approaches offer an analytical tool for understanding the unique direct and indirect associations between large sets of interrelated features. They are ideal for testing hypotheses about how specific features characterizing one disorder, such as inattention and hyperactivity–impulsivity, are related to multiple other domains of psychopathology. Figure 1 conceptually depicts some of the common metrics used to assess longitudinal network structure. Figure 2 depicts hypothetical examples of how different relationships between ADHD, oppositional defiant disorder (ODD), and depression would appear in a network analysis.

DSM symptom networks

The majority of network studies of psychopathology to-date have focused on relationships among DSM symptoms, either within or between disorders (Contreras, Nieto, Valiente, Espinosa, & Vazquez, 2019; Robinaugh, Hoekstra, Toner, & Borsboom, 2020). The observed symptom networks are often densely connected with many edges between nodes. Unsurprisingly (Achenbach, 1966, 2020), symptoms tend to cluster broadly into internalizing, externalizing, and attention problems domains in networks based on both youth self-report (Boschloo, Schoevers, van Borkulo, Borsboom, & Oldehinkel, 2016; Funkhouser, Chacko, Correa, Kaiser, & Shankman, 2020) and parent-report symptom ratings (McElroy, Shevlin, Murphy, & McBride, 2018; Rouquette et al., 2018). Studies also consistently find moderate to strong connections between symptoms in different domains (Contreras et al., 2019). Of particular interest for ADHD, studies of both child- and parent-reported symptom network configuration in middle childhood identify inattention, specifically, as a central feature with strong, direct connections to other internalizing and externalizing features (Boschloo et al., 2016; Funkhouser et al., 2020; Rouquette et al., 2018). However, other studies in early to middle childhood using maternal report of symptoms have placed other domains more central in the psychopathology network (McElroy et al., 2018).

In a cross-sectional network (one in which all features in the network are measured at the same time) the edges are undirected (for review see McNally, 2020). Thus, cross-sectional studies may identify inattention as a central feature but cannot clarify whether inattention exerts influence on other symptoms or if other symptoms exert influence on inattention. From a developmental perspective, the difference between these interpretations is critical. Further, cross-sectional networks rely on *between-person* associations that may or may not accurately reflect the *within-person* covariation of features (McNally, 2020). A longitudinal design can address both limitations.

The recently developed cross-lagged panel network model (CLPN) combines a network approach with a traditional cross-lagged model (Funkhouser et al., 2020; Rhemtulla, van Bork, & Cramer, 2020). Estimates for both incoming and outgoing edges can be estimated controlling for all other incoming or outgoing paths, including autoregressive effects, thus isolating the direction of influence and clarifying the causal structure relating the features over time. Using this approach, recent longitudinal studies in community-based samples in middle childhood suggest inattention causally influences the development of other internalizing and externalizing symptoms across time based on both parent- and child-report (Funkhouser et al., 2020; Rouquette et al., 2018). However, it is unclear if this pattern holds for clinical range problems. Additional studies in clinical populations can clarify whether causal structure varies based on the range of symptom severity present in the sample (Hoffman et al., 2019).

Incorporating the benefits of the RDoC perspective

Important explanatory power can also arise from inclusion of other domains related to psychological dimensions. National

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

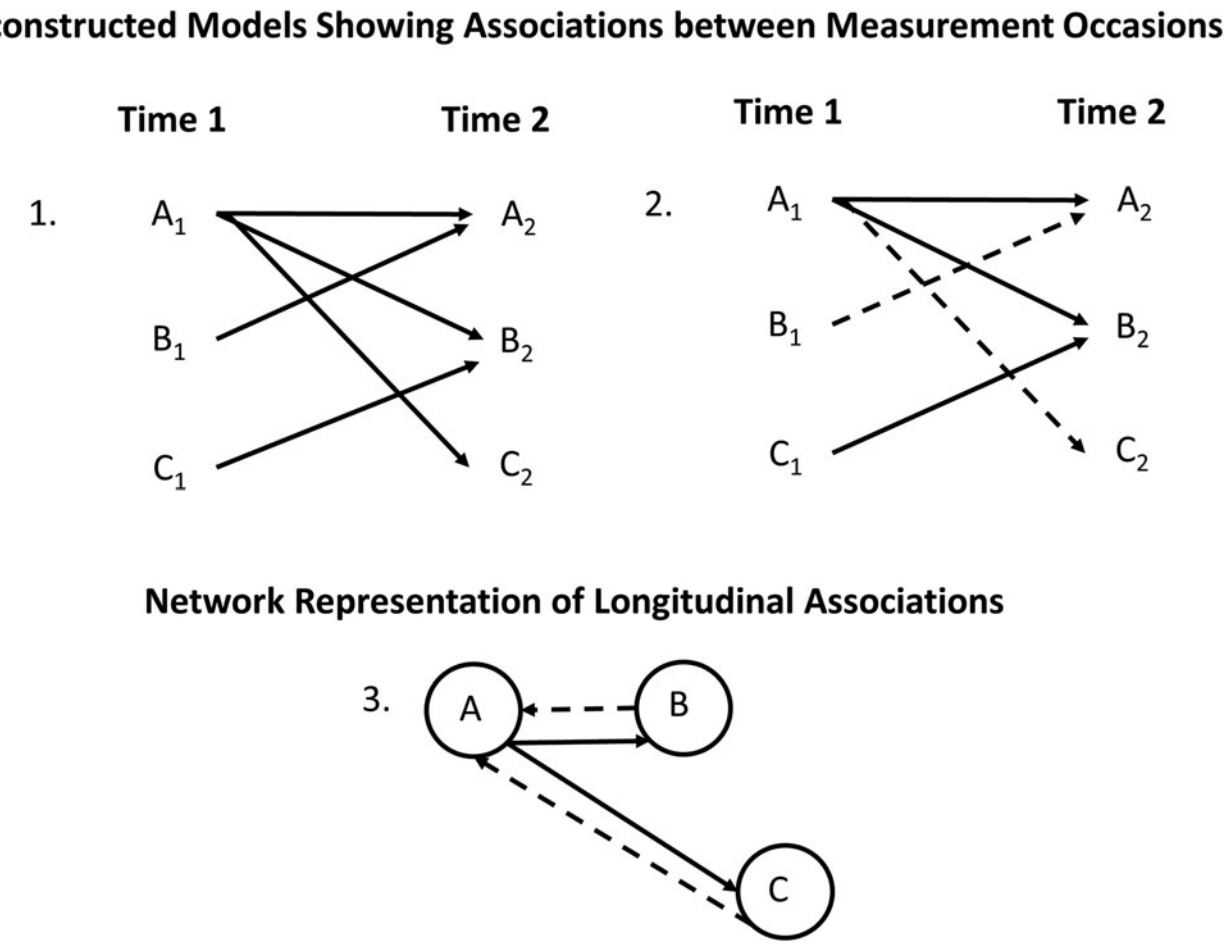

Figure 1. Shows how longitudinal associations are captured in a network framework. **Panel 1** depicts hypothetical edges between three variables (A, B, C) measured at two time points. Variable A has *outgoing edges* to itself (the autoregressive path), B, and C. *Outgoing strength* for A is equal to the sum of the edge weights from A1 to B2 and A1 to C2. Variable A has incoming edges from itself (autoregressive path) and B. The *incoming strength* for A is equal to the edge weight from B1 to A2. In models used here, the autoregressive path is omitted when computing *outgoing* and *incoming strength*. Variable A has high *closeness centrality*. It has direct connections (short paths) to all other nodes. Variables B and C would have lower closeness centrality because they require longer paths to get to some other nodes. For example, variable B has a direct connection to A but an indirect connection to C (i.e., that path requires two edges: B1 to A2, A1 to C2). **Panel 2** highlights the edges contributing to the indirect path from B to C using dotted lines. Edge weight also plays a role in determining path length with stronger associations resulting in shorter paths. In conventional representation of longitudinal networks, the multiple measurement occasions are not explicitly shown. Instead, outgoing and incoming paths are represented as directional arrows. In **panel 3**, solid arrows contribute to A's outgoing strength (A1 to B2 and A1 to C2) and dotted lines to its incoming strength (B1 to A2 and C1 to A2). Note that for B and C, solid lines would contribute to incoming strength and dotted lines to outgoing strength.

Institute of Health (NIH)'s Research Domain Criteria (RDoC) initiative is one example of efforts to re-conceptualize psychopathology via the study of dimensionally measured psychological or biological features that extend beyond traditional DSM symptom domains (Cuthbert & Insel, 2010; Insel et al., 2010) and may cut across traditional disorder categories. For example, although they are not part of formal diagnostic criteria, differences in emotion regulation and executive function are commonly observed in both ADHD and other disorders, suggesting they may be transdiagnostic risk factors that influence multiple forms of psychopathology. Thus, the co-occurrence of ADHD with factors such as disruptive behavior disorders and depression may not reflect a direct influence of ADHD symptoms on other symptoms but instead implicate transdiagnostic risk factors that convey shared risk for multiple disorders. In a network model, this would be reflected in direct pathways from these transdiagnostic features to multiple psychopathology domains with few or no connections directly between the disorder symptoms themselves. Longitudinal network approaches offer an ideal analytic tool to test this possibility but have not yet been applied in studies of developmental psychopathology, despite calls for studies that address multilevel, multimodal conceptualizations of disorder (Beauchaine & Hinshaw, 2020; Thomas & Sharp, 2019) and incorporate developmental perspectives into RDoC (Mittal & Wakschlag, 2017).

Emotional functioning

Within ADHD, expansion to domains outside of the core symptoms has proven fruitful for describing the heterogeneous developmental pathways observed within the disorder. One expansion has included use of trait-based measures of emotional functioning operationalized from a temperament perspective (Bates, Goodnight, & Fite, 2008; Clark, 2005; Rothbart & Ahadi, 1994). Domains of temperament functioning align with the positive and negative valence system domains of RDoC, and provide an optimal trait-based assessment that may be complementary to state-based assessments of RDoC constructs (Patrick & Hajcak,

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

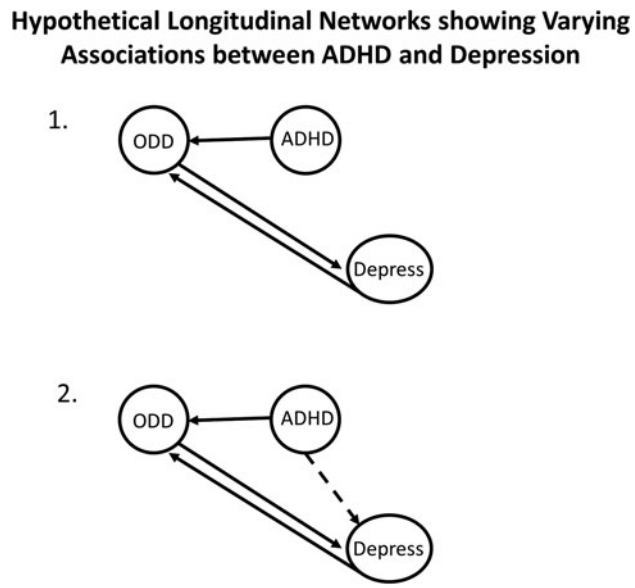

Figure 2. Provides a hypothetical example of the network conceptualization of problem co-occurrence using fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnoses. In **panel 1**, attention-deficit/hyperactivity disorder (ADHD) has a direct outgoing edge to oppositional defiant disorder (ODD). ADHD predicts developing ODD symptoms over time. ODD and depression have direct, bidirectional edges, they each contribute to each other over time, potentially suggesting linked co-expression of these symptoms. In contrast, ADHD and depression influence each other only indirectly via their associations with ODD. In this example, ODD has the highest closeness centrality because of short paths (direct connections) to all other features. In **panel 2**, an additional direct connection exists between ADHD and depression (dotted line), indicating that ADHD independently predicts both ODD and depression, suggesting ADHD plays a direct causal role in developing depression. Here, both ADHD and ODD would have high closeness centrality, while depression would have lower closeness centrality because its only direct connection is to ODD.

2016). A major benefit, from an RDoC perspective, is that temperament traits are measured via standard, easily obtained self-report but are hypothesized to be related to neurobiological features that can be studied at other levels of analysis as well (Whittle et al., 2008; Whittle, Allen, Lubman, & Yücel, 2006).

Work in young children (Martel, 2016), school-age children (Karalunas et al., 2014; Karalunas, Gustafsson, Fair, Musser, & Nigg, 2019), and young adults with ADHD (Martel, Goth-Owens, Martinez-Torteya, & Nigg, 2010; Smith & Martel, 2019) converge on the importance of affective features, including dysregulation of both positive and negative affect (Karalunas & Nigg, 2019; Nigg, Karalunas, Feczko, & Fair, 2020a). Recent theory posits high negative affect, especially irritability, as a causal factor in the development of ADHD symptoms (Gagne & Hill Goldsmith, 2011; Nigg et al., 2020a; Nigg, Sibley, Thapar, & Karalunas, 2020c). Other perspectives suggest affective dysregulation is a manifestation of ADHD and should be considered a core feature of the disorder for some children (Karalunas et al., 2019; Nigg et al., 2020b). From a network perspective, these possibilities can be untangled by looking for either unidirectional or bidirectional effects between these features (the former suggesting a specific longitudinal pathway and the latter suggesting closely linked co-expression over time).

Further, emotional heterogeneity, particularly high negative affect and irritability, may increase vulnerability to other co-occuring problems, such as oppositional defiant behavior and depression, via both direct and indirect pathways (Karalunas et al., 2014, 2019; Martel, 2016; Muris, Meesters, & Blijlevens, 2007; Rutter & Arnett, 2020; Smith & Martel, 2019). Recent evidence from network studies suggest that irritability may serve as a key bridge between multiple forms of DSM psychopathology when considering self-reported symptoms in adolescence (Madole, Rhemtulla, Grotzinger, Tucker-Drob, & Harden, 2019; McElroy et al., 2018). However, the direction of relationships remains unclear. Traditional cross-lag models suggest irritability is a stronger prospective predictor of internalizing symptoms than the other way around (Savage et al., 2015), but longitudinal network findings accounting for other domains of psychopathology suggest the opposite (depressed mood as a cause of developing irritability over time) or find bidirectional relationships that are more consistent with co-expression than directional causality (Madole et al., 2019). Support emerged in one study of short-term longitudinal change in the Adolescent Brain Cognitive Development sample that youth-reported irritability more strongly predicted developing impulsivity symptoms than the other way around (Funkhouser et al., 2020). However, relationships may vary by age (Karalunas & Nigg, 2019; McElroy et al., 2018), and additional studies using parent-report of both irritability and ADHD symptom are needed given challenges with youth report of these domains (Du Rietz et al., 2016; Sibley et al., 2012). In addition, most studies thus far have focused on overt aggression or composite measures of DSM-based ODD symptoms that do not differentiate irritability from other types of oppositional and defiant behavior, although such distinctions are likely to be important (Cardinale et al., 2021; Vidal-Ribas, 2021). Relationships also require further analysis in clinical samples, particularly given evidence that network structure may be less informative for psychopathology when too few "cases" are included in the sample (Hoffman et al., 2019).

Executive function

Cognitive systems are a major domain of interest for RDoC, as well as for understanding the progression of ADHD symptoms and co-occurring problems over time. Numerous alterations in cognitive development are apparent in ADHD (Kofler et al., 2013; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Among the most consistently identified are weaknesses in working memory and inhibition (which often though not always co-occur Karalunas & Nigg, 2019), as well as slow and/or variable reaction times (Bergwerff, Luman, Weeda, & Oosterlaan, 2017; Fair et al., 2012), which may reflect arousal-related deficits in attention (Aston-Jones & Cohen, 2005; de Gee et al., 2020; Karalunas & Huang-Pollock, 2013; Karalunas, Huang-Pollock, & Nigg, 2012; Murphy, Vandekerckhove, & Nieuwenhuis, 2014). Yet the role of cognitive impairments in ADHD symptom development and secondary comorbidity development has seen insufficient empirical study (Karalunas & Nigg, 2019; Nigg et al., 2020a). The evidence to date appears strongest for a direct role of working memory. Development of working memory in childhood and early adolescence follows a parallel trajectory of change in ADHD symptoms (Karalunas et al., 2017). However, examining the effects of working memory in the context of other putative causal factors is necessary.

In addition, the cognitive weaknesses observed in ADHD are commonly associated with multiple forms of psychopathology (Bloemen et al., 2018; Karalunas et al., 2018; Martel et al., 2017; White et al., 2017), yet it is not clear how strongly these impairments are correlated with disorders when ADHD is also controlled (Nigg et al., 2017). Thus, it remains unclear whether

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

cognitive impairments in ADHD are epiphenomenal, are directly related to ADHD symptom course, or potentially reflect a transdiagnostic mechanism that could explain changes in ADHD symptom expression with age (Biederman, Mick, & Faraone, 2000; Lahey, Pelham, Loney, Lee, & Willcutt, 2005; Larsson, Dilshad, Lichtenstein, & Barker, 2011; Van Lier, Der Ende, Koot, & Verhulst, 2007), as well as the heterogeneous trajectories for co-occurring clinical problems (Goodkind et al., 2015; Hawkey, Tillman, Luby, & Barch, 2018). Each would be reflected differently in network structure as described.

Crucially, while it is clear that some top-down regulatory functions are shared in EF and emotion regulation, the mechanistic relationship between the emotional functioning and cognitive domains remain poorly characterized, with some studies suggesting a direct relationship (e.g., poor EF causes poor emotion regulation) and common neurobiological mechanisms (Macdonald et al., 2016) and other studies suggesting they reflect orthogonal, interacting dimensions (Banaschewski et al., 2012) that may moderate relationships between psychopathology symptoms (Madole et al., 2019). A network approach is, in some ways, ideal for study of these cross-domain interactions. It can characterize the relationships among a broad number of diverse feature sets accounting for the influence of all other features. Yet studies have not yet applied a process-oriented network model to a broad multilevel feature set.

Current study

The current study applies a CLPN approach in a relatively large sample of children oversampled for ADHD between 7 and 15 years old. We build on prior network studies of psychopathology but substantively expand in several ways that align with an RDoC framework. We included a broad feature set that includes traditional symptom ratings, trait-based ratings of positive and negative valence systems, and performance-based measures of executive function. Although prior studies have looked at single level ratings data over time using this approach (e.g., Funkhouser et al., 2020), the present report is the first study that we are aware of that has applied a network approach suited to causal inference to a multiconstruct, multilevel dataset that extends to trait- and performance-based measures of relevant domains. Debate continues as to whether explanatory power in network analysis is best achieved by using individual symptoms/behaviors or composite constructs as input features. Ultimately, the optimal input features will depend both on the questions of interest and the domain being measured. Here, we preserve power for our primary questions about transdiagnostic causal dynamics by selecting a set of conceptually guided composite dimensions, rather than individual symptoms, in most cases. Justification for each input feature is incorporated into the relevant sections in the Method.

Consistent with prior DSM-based work, we expected a densely connected network with a large number of edges connecting features within- and across- disorders and domains. In response to recent calls to move beyond an exploratory application of the network approaches (Robinaugh et al., 2020), we focused on several specific hypotheses regarding network structure. First, we expected both ADHD symptom domains to be closely connected to other model features (i.e., high closeness) and to have high outgoing strength centrality with outgoing edges specifically linking ADHD to depression and ODD at later time points. This pattern would be consistent with inattention and hyperactivity–impulsivity serving as early emerging features that convey transdiagnostic risk for multiple pathologies over time, even when accounting for differences in other aspects of emotional functioning and cognition. We also hypothesized that temperamental irritability would be a central feature and a likely bridge feature connecting between domains (i.e., high betweenness centrality). We further hypothesized independent causal roles for irritability in worsening ADHD and depression symptoms over time (i.e., high outgoing strength with edges directly connecting irritability to ADHD and depression symptom domains rather than only indirect connections, again consistent with direct transdiagnostic risk). Finally, we hypothesized that working memory would be an important causal feature that predicted ADHD symptoms, particularly inattention (high outgoing strength with edges to inattention), and we sought to examine whether working memory also exerted independent influence on depression-related features. A major advance here over prior work suggesting similar associations is the ability to use a longitudinal network approach to examine directional paths while controlling for all other model features in order to isolate the specific unidirectional or bidirectional influences of interest.

Method

Participant enrollment

The enrolled sample included 673 children (ADHD $n = 415$) who enrolled in a longitudinal study and a parent or legal guardian. Children were between the ages of 7 and 12 years at initial entry into the study. Children were recruited via community volunteers and mass advertising. Children were followed annually. The current analyses use data from Years 1–3 of the ongoing longitudinal study, and included 488 children (nADHD = 296) who completed at least one of the measures used in the current analyses at all three years of assessment (additional information on missing data handling is described in that section below). Table 1 provides demographic characteristics by diagnostic group. Detailed information on retention in the overall cohort (Supplementary Table S1) can be found in the Supplemental Information (SI). Human participant protection procedures were approved by the local Institutional Review Board. A parent/legal guardian provided written informed consent, and children provided written assent. Behavioral ratings data were collected and managed using REDCap®, which provides a secure web-based and intuitive interface and export capabilities (Harris et al., 2009).

Diagnostic procedures

ADHD and all comorbid diagnoses were established via a multimethod, multi-informant, best-estimate diagnostic confirmation procedure. A parent/guardian, teacher, and child all completed nationally normed, reliable and valid standardized rating scales, including the Conners' Rating Scales (CRS-R, Conners, 2003), Strengths and Difficulties Questionnaire (SDQ, Goodman, 2001), and the ADHD Rating Scale (ADHD-RS, DuPaul, Power, Anastopoulos, & Reid, 1998).

The parent/guardian also completed a semi-structured clinical interview for DSM-IV diagnoses (the cohort was enrolled prior to DSM-5) (Kiddie Schedule for Affective Disorders and Schizophrenia [KSAD], Puig-Antich & Ryan, 1986). Child IQ was estimated based on a reliable and valid three-subtest short

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

Table 1. Sample demographics by diagnostic group

Variable	Overall	ADHD	Control
% Male	63.9%	70.6%	52.6%
Mean age at Y1 (years)	9.1 (1.5)	9.2 (1.5)	8.7 (1.4)
Mean IQ	111.4 (14.2)	108.7 (14.3)	116.2 (12.5)
% White & Non-Hispanic	80.5%	79.7%	80.9%
Median income range	$75,000–100,000	$50,000–75,000	$75,000–100,000
% with history of mood disorder at Y1	1.2%	1.4%	0.0%
% with anxiety disorder at Y1	16.4%	20.6%	8.7%
% with ODD at Y1	12.3%	18.9%	1.2%
% with conduct disorder at Y1	1.2%	1.7%	0.0%

Note: Y1 = Year 1; mood disorders includes fourth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) major depressive episode or dysthymia (*current* major depressive episode was exclusionary at baseline so totals reflect percent of children with history of mood disorder but not currently experiencing a major depressive episode); anxiety disorder includes separation anxiety, social phobia, and generalized anxiety disorder; ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder

form of the Wechsler Intelligence Scale for Children (WISC)-IV (Sattler & Dumont, 2004). Academic achievement was assessed using the Word Reading and Math Reasoning subtests of the Wechsler Individual Acheievement Test, 2nd edition (WIAT-II (Wechsler, 2002). Final ADHD and all comorbid diagnoses were made by a clinical diagnostic team. Their blind agreement was acceptable for ADHD diagnosis (kappas at all years >.88) and for other disorders with >5% base rate in the sample (all kappa >.70). Disagreements were conferenced for final diagnostic assignments.

Measures

Inattention and hyperactivity–impulsivity

Primary analyses included two latent variables reflecting the two ADHD symptom domains that were created based on parent-report measures of: (a) inattention (indicators were: ADHD Rating Scale inattention raw score, KSAD inattention symptom count, Conners' inattention raw score, and the Strengths and Weaknesses of Attention-Deficit/Hyperactivity-symptoms and Normal-behaviors [SWAN] Rating Scale inattention score) and (b) hyperactivity–impulsivity (indicators: ADHD Rating Scale hyperactivity–impulsivity raw score, KSAD hyperactivity–impulsivity symptom count, Conners' raw hyperactivity–impulsivity raw score, SWAN hyperactivity–impulsivity raw score, and the SDQ hyperactivity–inattention raw score). Treating ADHD as a continuous trait is consistent with evidence that symptoms reflect underlying correlated but distinct dimensions (Sturm, McCracken, & Cai, 2019). The selection of these composites follows extensive prior work in ADHD, including in the current sample (Nigg et al., 2020b), indicating a two-factor model fits the data well. Other ongoing work in this sample examines cross-sectional networks using individual symptoms to answer different questions. However, the most recent network studies of ADHD focused on clinical course prediction across domains suggest that little additional information is gained by inclusion of individual symptoms over composite measures given that symptoms have been selected over time via factor analytic studies to reflect unitary constructs (Preszler, Burns, Becker, & Servera, 2020; Silk et al., 2019).

Secondary analyses replaced parent-reported ADHD symptoms with teacher-reported ADHD symptoms. Teacher ratings were combined into two latent variables using the same indicators as described for parent report when available: (a) inattention (indicators were: ADHD Rating Scale inattention raw score, Conners' inattention raw score) and (b) hyperactivity–impulsivity (indicators: ADHD Rating Scale hyperactivity–impulsivity raw score, Conners' raw hyperactivity–impulsivity raw score. The SDQ hyperactivity–inattention raw score was allowed to cross-load on both the inattention and hyperactivity–impulsivity factors. The model fit the data moderately well at all years, albeit with slightly higher root mean square error of approximation (RMSEA) values than would be desirable (comparative fit index [CFI] .97–.98, Tucker–Lewis index [TLI] .88–.93, RMSEA .22–.27). Use of the reasonably well-fitting two-factor model here allowed us to easily compare networks based on parent and teacher ratings.

Oppositional defiant disorder

Parent-reported KSAD symptoms were used as indicators for two separate latent variables: (a) defiant/headstrong behavior and (b) angry/irritable mood with symptoms assigned based on how they are classified in DSM-5. Composite selection was guided by prior literature suggesting that ODD symptoms are best understood as two correlated but distinct dimensions of behavior (Burke et al., 2014; Stringaris & Goodman, 2009), as well as with recent network analyses suggesting network structure aligns with these latent variables (Preszler & Burns, 2019). Consistent with the literature, this model fit the data well (RMSEA = .043, CFI = .993, TLI = .995).

Depression

Children self-reported on symptoms of depression using the Children's Depression Inventory (CDI). At the time data collection was initiated for this longitudinal study (2009), the CDI was a widely used 27-item self-report questionnaire assessing features of depression in children and adolescents (Kovacs, 1985, 1992) and the CDI-2 had not yet been published. The original CDI was retained in original form over time to maximize sensitivity to detect change. Children rated items on a 0 to 2 scale. Items were combined into five subscales: (a) negative mood, (b) negative self-esteem, (c) interpersonal difficulties, (d) ineffectiveness, and (e) anhedonia. Scale reliabilities at all years were adequate (all alpha >.60).

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

Executive functioning

Children completed multiple measures of working memory and arousal/alertness. They also completed multiple measures of inhibitory control, but a single indicator is emphasized here (see Supplemental Information for additional details on all tasks). Tasks were used to create two latent variables: (a) working memory (indicators: WISC-IV digit span forward and backward raw scores, Cambridge Neuropsychological Test Automated Battery (CANTAB) spatial span backward number completed, and N-back 2-back accuracy) and (b) arousal (indicators: drift diffusion model drift rate (Ratcliff & McKoon, 2008; Wickens, 2002) and two versions of *d'* for the identical pairs continuous performance task). Latent variables were based on previously validated and well-fitting latent variable models used in this sample (Nigg et al., 2018).

Working memory measures captured both verbal and nonverbal working memory domains. Use of this composite factor score is consistent with findings that domain general processes are primarily implicated in ADHD (Fosco, Kofler, Groves, Chan, & Raiker, 2020) and in other forms of psychopathology (Huang-Pollock, Shapiro, Galloway-Long, & Weigard, 2017). Arousal indicators were derived via well-validated computational cognitive models (Ratcliff & McKoon, 2008; Wickens, 2002) that isolate parameters linked neurobiologically to noradrenergic neural systems (Aston-Jones & Cohen, 2005a; Aston-Jones & Cohen, 2005b). We included arousal here due to longstanding theories about the role of arousal in ADHD and our prior work in this sample linking arousal to ADHD genetic risk (Nigg et al., 2018).

Response inhibition is best conceptualized as multiple distinct cognitive processes, only some of which are impaired in ADHD. Here, response inhibition was measured using a single observed variable – the well-validated stop signal reaction time from a tracking version of the Logan Stop task. This measure captures a type of inhibitory control commonly impaired in ADHD, is based on a well-validated cognitive theory, and showed adequate reliability in our sample. While it could be combined with other measures of inhibitory control in our sample (e.g., Delis–Kaplan Executive Function System [DKEFS] Color Word), the factor loadings for the resulting latent variable are modest, consistent with the multifactorial nature of the construct.

Child temperament

A parent/guardian completed the Temperament in Middle Childhood Questionnaire (TMCQ, Simonds & Rothbart, 2004). Features included three TMCQ subscales measuring negative affect: (a) anger (referred to as irritability in the text here consistent with the widely used definition of irritability as "proneness to anger" Vidal-Ribas, Brotman, Valdivieso, Leibenluft, & Stringaris, 2016), (b) fear, and (c) sadness, as well as two measures related to positive affect dysregulation: (d) high-intensity pleasure (HIP) and (e) activity level. Feature selection follows prior theory (Rothbart, 2007, 2011; Rothbart, Sheese, & Posner, 2014) and is in line with prior work in this sample (Nigg et al., 2020b). All scales showed adequate reliability (Cronbach's α all > .80).

Item overlap

Temperament scales related to Effortful Control (Inhibitory Control, Attentional Control, Impulsivity) were excluded from analyses due to item overlap with ADHD ratings. The ADHD latent variables already included indicators that captured a full range of both clinical and nonclinical symptom levels. In contrast, we retained the Anger/Irritability and Sadness scales in full despite item overlap with ODD-related anger-irritability and depression-related sadness, respectively. Temperament rating scales capture a wider range of dimensional behavior as compared to the clinical symptom ratings on the ODD and Depression scales. Thus, retaining both measures specifically allowed us to address how the broader dimensional constructs were related to other features over time, a critical part of assessing transdiagnostic risk prior emergence of clinical-level syndromes. Nonetheless, we specifically de-emphasize discussion of direct relationships between ODD and temperamental irritability or depression and temperamental sadness due to item overlap.

Analysis plan

Data preparation and missing data

All data transformations and analyses were conducted in R (vers. 3.6.1). To facilitate comparison across variables with different scales, variables were converted to *z* scores. Missing data were handled in two ways. First, during latent variable creation, missing indicators were handled via full-information maximum likelihood procedures in MPLUS. Thus, anyone with at least one indicator for the construct received a latent variable score. Second, prior to conducting the network model analysis, remaining missing data (i.e., when all indicators of a construct were missing or measurement was not by latent variable) were imputed via random forest imputation implemented with the missForest package (vers. 1.4). This method imputes data iteratively by fitting a random forest model on the observed data to predict the missing data, repeating this process until a prediction performance stopping criterion is met. This nonparametric method has been used with other work utilizing CLPN models with psychological data (Funkhouser et al., 2020), and there is evidence that random forest imputation methods perform well when compared with other missing data methods (e.g., Waljee et al., 2013). Prior to the imputation, missingness within the selected sample of participants with data at all three time points ranged from 0% to 7% for Y1 variables, 0%–32% for Y2 variables, and 0%–15% for Y3 variables.

Cross-lagged panel networks

To examine associations among symptoms over time, a set of CLPN models were applied. We separately estimated: (a) the Year 1–Year 2 (Y1–Y2) network and (b) the Year 2–Year 3 (Y2–Y3) network. CLPN models allow the strength of the directional relationship between pairs of variables in a network to be assessed across time points while accounting for the effects of all variables at baseline, including autoregressive effects for the outcome variable (for recent examples of CLPN models, see Bernstein et al., 2019; Epskamp, 2020; Funkhouser et al., 2020). Thus, in the CLPN framework, edges reflect the directed, pairwise relationship between two nodes controlling for all other nodes at the first time point and any covariates. The edge weights can be interpreted similar to a regression coefficient in standard cross-lagged model. Age and sex were included as covariates in the models.

To reduce the likelihood of spurious edges in the network models, the resulting regression coefficients were adjusted using least absolute shrinkage and selection operator (LASSO) regularization, which helps prevent overfitting and reduces network complexity. The LASSO method shrinks small regression coefficients to zero based on a penalization value, lambda, determined through cross-validation. Thus, this method reduces the number of nonzero regression coefficients, which are used as edges for

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

the network model. The LASSO regularized regression and a 10-fold cross-validation were conducted using the glmnet package (vers. 3.0-2). Analyses for the current study utilized the lambda penalization value that minimized the mean cross-validated error. The regularized regression coefficients served as edge weights in the networks.

The directed networks were plotted with the qgraph package (vers. 1.6.5) using a force-directed layout based on the Fruchterman–Reingold algorithm. In this layout, node placement is determined by the strength of association between each node pair, with highly associated nodes generally appearing closer to each other in the graph.

Network reliability

We addressed reliability of network structure by estimating the stability of the Y1–Y2 and Y2–Y3 networks using a nonparametric bootstrap method implemented with the bootnet package (vers. 1.4.3). A set of 1000 bootstrap samples were drawn with replacement from the dataset and the network model was fit for each sample. This process provides both the mean value for each edge weight across all bootstrapped models and a confidence interval (CI) for that mean based on the range of edge weight values in the bootstrapped models (the 2.5th and 97.5th quantiles).

Comparison of networks

We compared the Y1–Y2 and Y2–Y3 networks by assessing the correlation between edge weights in the two networks, the percentage of edges that maintained the same direction (i.e., positive or negative), and correlation of centrality indices (Funkhouser et al., 2020). Given that we expect some relationships to change with development, we do not interpret this strictly in terms of network reproducibility but as descriptive information about network similarity.

Measures of centrality

Centrality measures were calculated to support interpretation of the CLPN model output using the qgraph package (vers. 1.6.5). A variety of centrality measures can be used to guide network interpretation. Because our hypotheses focus on identifying features that are strong predictors of worsening or remitting problems over time, we emphasize outgoing strength centrality in our interpretation. Outgoing strength is the sum of the absolute value of regression coefficients for all *outgoing* edges from a feature (i.e., all edges directed from a Y1 feature to any Y2 feature or from a Y2 feature to any Y3 feature; see Figure 1 for visual depiction). Thus, high outgoing strength identifies those features that have the most predictive power within the network, and the observed edges reflect the specific pathways driving the overall strength.

We also calculated closeness centrality (mathematically average shortest path between a given node and the remaining nodes in the network; Robinaugh, Millner, & McNally, 2016) and betweenness centrality (mathematically the sum of the number of times a feature appears on the shortest path between any other two features), as well as incoming strength (i.e., the sum of the absolute value of all incoming edges to a feature, indicating which features are most highly predicted within the network). Several of these metrics are depicted in Figure 1.

Centrality stability

Similar to edge weight stability, centrality measure stability was assessed using a bootstrap method in the bootnet package. To accomplish this, 1000 bootstrap samples were drawn using the case-drop method described by Eskamp and colleagues (Epskamp, Borsboom, & Fried, 2018). In this method, the stability of centrality measures is assessed by examining the maximum proportion of the sample that can be dropped while still maintaining a correlation between respective centrality values in the original versus bootstrapped samples with a 95% CI that does not fall below .7. The authors recommended a minimum cutoff for the centrality stability coefficient of 0.25 (Epskamp et al., 2018), and we do not interpret measures that fall below this cutoff.

Results

Network reliability

Y1–Y2 and Y2–Y3 networks are shown in Figure 3, and edge weights with 95% CIs are shown in Figure 4. A majority of non-LASSO penalized edges had bootstrapped CIs that did not cross zero, suggesting that the direction of relationships was reliable and can be interpreted. The CIs around the edge weights are relatively large, indicating there was significant overlap in the range of edge weights for each node pair across the bootstrapped samples. Therefore, interpretation of differences in the magnitude of individual edges should be made with caution. We focus interpretation on the presence/absence of edges rather than on comparison of edge strength. Correlations matrices with all incoming and outgoing edge weights are provided in Supplementary Table S2.

Centrality stability

Our primary centrality measure of interest – outgoing strength – had acceptable stability in both the Y1–Y2 (0.43) and Y2–Y3 networks (0.28). Closeness centrality had acceptable stability in the Y1–Y2 network (0.28) but rank order of coefficients was not stable in the Y2–Y3 network (0.13); we report these but interpret them with caution in the Y2–Y3 network. Incoming strength (Y1–Y2: 0.20; Y2–Y3: 0.00) and betweenness (Y1–Y2: 0.00; Y2–Y3:0.00) had poor stability in both networks and are not discussed further.

Closeness centrality

Closeness centrality indicates how closely connected a feature is to other features in the network via both direct and indirect paths. In the current analysis, it reflects outgoing-closeness, which is how closely a Year 1 feature is connected to all other Year 2 features. High closeness centrality in this context is often interpreted in terms of a feature's ability to efficiently influence other features (Bringmann & Eronen, 2018, caveats to interpretation are discussed in more detail in the Discussion). Closeness centrality is network dependent and thus interpreted in terms of rank order of features within a given network.

Consistent with hypotheses, ADHD symptom domains had the highest closeness centrality in the Y1–Y2 network and were among the top three features in closeness centrality in the Y2–Y3 network (with ADHD inattention retaining the highest closeness centrality but temperamental irritability rising above hyperactivity–impulsivity; see Figure 5). Hyperactivity–impulsivity and inattention each had outgoing edges connecting them to nearly all other network features in both the Y1–Y2 and Y2–Y3 networks.

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

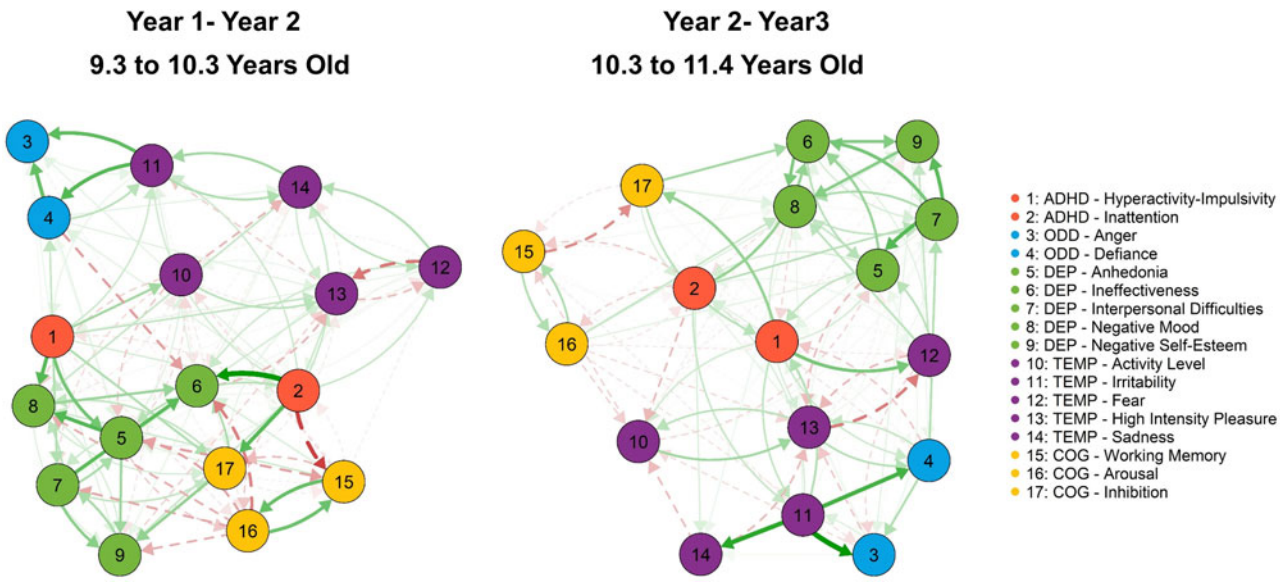

Figure 3. Shows the cross-lag panel networks for the year 1–year 2 and year 2–year 3 networks. Arrows indicate the directed effects from a feature at the first time point to another feature at the second time point controlling for all other network features. Thickness of the arrow is determined by the edge weight, with thicker arrows indicting higher absolute values for the partial correlation between features. Green solid arrows indicate a positive correlation between features and red dotted arrows denote a negative correlation between features. Color of the nodes indicate their domain: depression features (green), temperament features (purple), attention-deficit/hyperactivity disorder (ADHD) features (red), oppositional defiant disorder (ODD) features (blue), cognitive features (yellow).

Temperamental irritability was also among the most closely connected features. In the Y1–Y2 model, temperamental irritability had the fourth highest closeness centrality. In the Y2–Y3 network, temperamental irritability had the second highest closeness centrality (after only ADHD inattention). It had the highest outgoing strength of any feature in the Y2–Y3 network.

We did not make predictions about overall closeness centrality for working memory. Nevertheless, working memory emerged as one of the most closely connected features in the Y1–Y2 network (third highest closeness centrality after only the ADHD symptom domains); rank order fell relative to other features in the Y2–Y3 network.

Overall, ADHD symptom domains, temperamental irritability, and working memory were all closely connected features within the network suggesting they may efficiently influence multiple other domains, which is consistent with the conceptualization of transdiagnostic risk markers.

Outgoing strength

High outgoing strength identifies those features that have the most predictive power within the network. Outgoing strength metrics for all nodes are shown in Figure 5.

ADHD symptoms predict later ODD

We hypothesized that ADHD symptoms would have outgoing edges to both ODD-related and depression-related features. Results in the Y1–Y2 network were consistent with predictions that higher ADHD symptom severity temporally precedes and predicts worsening ODD over time. Both ADHD inattention and ADHD hyperactivity–impulsivity had outgoing edges to ODD anger and ODD defiance. Outgoing edges from ODD symptom domains to ADHD domains were not present in the Y1–Y2 network, suggesting a directed relationship from ADHD to ODD in this period. In the Y2–Y3 network, ADHD hyperactivity–impulsivity retained an outgoing edge to ODD defiance but other outgoing edges from ADHD domains to ODD domains were not present.

Overall, ADHD symptoms appear to have direct, causal influence developing ODD anger and defiance. Inattention and hyperactivity–impulsivity both play a role earlier in development, but the specific relationships between persistent hyperactivity–impulsivity and ODD defiance symptoms is most developmentally stable.

ADHD symptoms predict later depression

Regarding depression, ADHD hyperactivity–impulsivity and ADHD inattention each predicted multiple depression features, but hyperactivity–impulsivity uniquely predicted negative mood and interpersonal problems while inattention uniquely predicted ineffectiveness. Results confirmed hypothesized relationships between ADHD and depression but also suggest each symptom domain shows unique associations with specific depression features. In the Y2–Y3 network, a similar pattern emerged. ADHD inattention uniquely predicted ineffectiveness. ADHD hyperactivity–impulsivity unique predicted negative self-esteem. Overall, ADHD symptoms play a direct role in developing depression, with each ADHD symptom domain appearing to contribute via a unique pathway.

Bidirectional effects of temperamental irritability with ADHD and depression features

The hypothesized outgoing edges from irritability to depression (specifically interpersonal problems) and to both ADHD symptom domains were also present in the network. In the Y1–Y2 network, there was evidence of bidirectional effects; temperamental irritability predicted worsening ADHD and depression, but each of these features also had outgoing edges to temperamental irritability as well.

Results from the Y2–Y3 network were similar. In the Y2–Y3 network, temperamental irritability had outgoing paths to both

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

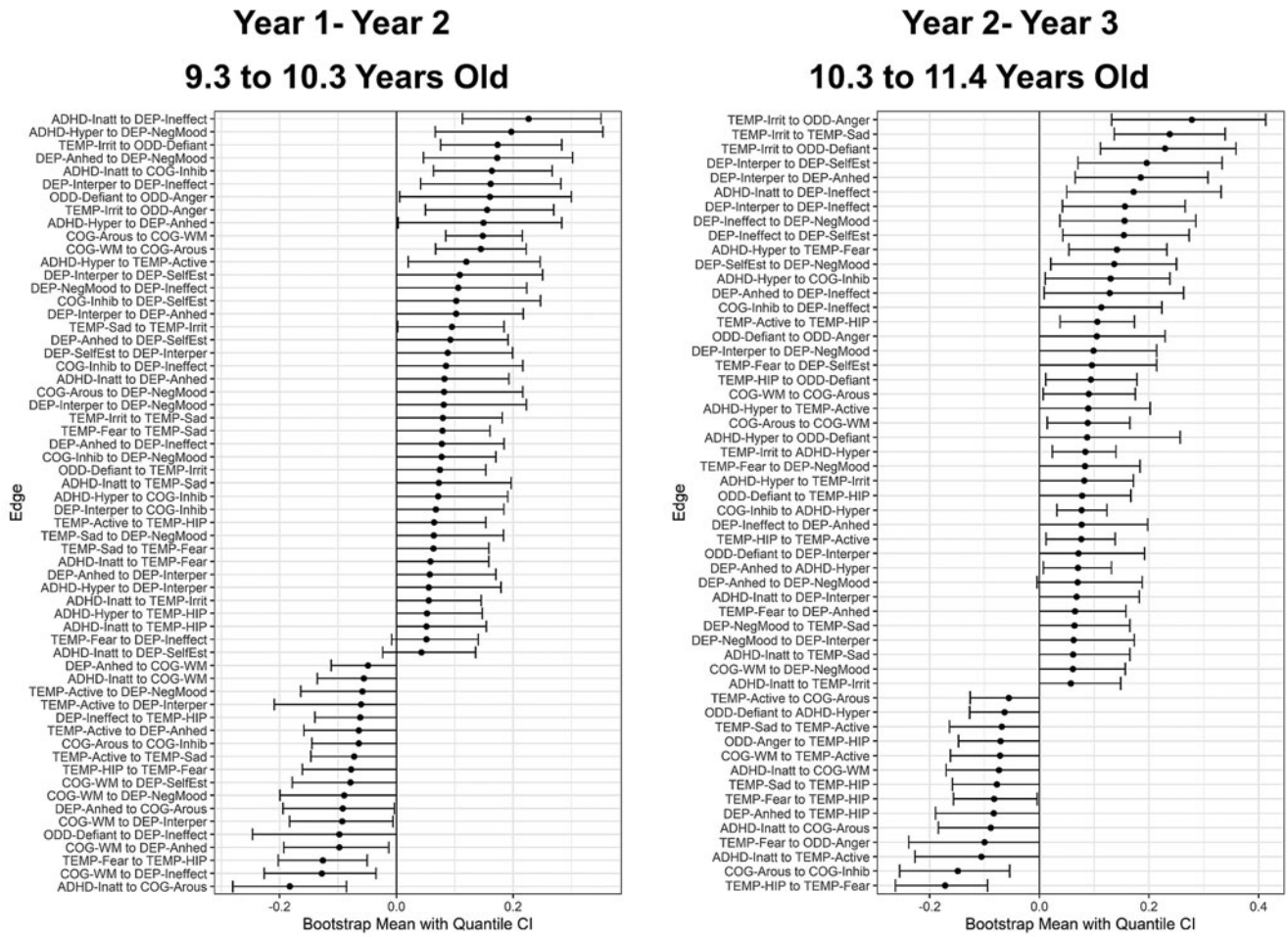

Figure 4. Shows edge weights from 1,000 bootstrapped samples with 95% confidence intervals (CIs) for all nonzero edges in the network. A majority of non-LASSO penalized edges had bootstrapped CIs that did not cross zero, suggesting that the direction of variable relationships was reliable and can be interpreted. The CIs around the edge weights are relatively large, indicating there was significant overlap in the range of edge weights for each node pair. Therefore, interpretation of differences in the magnitude of individual edges should be made with caution.

ADHD symptom domains and to aspects of depression (interpersonal problems and negative mood). Edges from the ADHD symptom domains to temperamental irritability in the Y2–Y3 network continued to support transactional influences; however, there were no edges from depression-related features to temperamental irritability. This pattern was consistent with edges observed for temperamental sadness. Temperamental irritability predicted temperamental sadness but the reverse was not true.

Overall, temperamental irritability and ADHD symptoms have bidirectional influence on each other consistent with tightly linked co-expression in middle childhood and early adolescence. Temperamental irritability and depression have bidirectional influences that may shift to unidirectional influence over development.

Working memory independently predicts ADHD and depression

As predicted, in the Y1–Y2 network, working memory had an outgoing edge to ADHD inattention. Working memory also had outgoing edges to all depression features. In the Y2–Y3 network, working memory retained moderate outgoing paths to ADHD inattention and multiple depression-related features. Overall, working memory had independent direct influences on both ADHD and depression.

Other notable network features

Although not a central focus of our hypotheses, several other aspects of the network should be highlighted in order to guide hypothesis formation for future studies.

Outgoing strength for other temperament features

In the Y2–Y3 network temperamental fear and HIP both also had high outgoing strength due, in part, to edges connecting them to each other (bidirectional relationship between higher HIP and lower fear).

Working memory–arousal relationships

Working memory and arousal had strong transactional influences on each other with outgoing edges in both the Y1–Y2 and Y2–Y3 networks from working memory to arousal, as well as from arousal to working memory (higher working memory predicted higher arousal).

Outgoing strength for depression features

Several depression-related features also had high outgoing strength. The high centrality for these features was generally due to edges connecting depression features to each other.

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

Similarity across Y1–Y2 and Y2–Y3 networks

Edges across the two networks demonstrated a moderate but significant correlation ($r = .52$, $p < .001$). The four centrality indices were closely correlated across the two networks ($r = .69$, $p < .001$). Furthermore, about 72% of the edge weights across the two networks shared the same direction. For edges that were nonzero in either network, the percentage decreased slightly to 65%. Together these metrics suggest that there is some change in the network structure over time, but that the two networks are similar overall.

Networks with teacher-reported ADHD symptoms

Networks using teacher-reported ADHD symptoms were generally similar to those using parent-reported ADHD symptoms with a few notable exceptions described below. Supplementary Figure S1 in the depicts the overall network and Supplementary Table S3 provides the full partial correlation matrix.

Closeness centrality

Similar to results using parent-report, ADHD inattention and temperamental irritability had high closeness centrality in both the Y1–Y2 and Y2–Y3 networks. However, ODD defiance ranked much higher in closeness centrality than in the parent network. It had the highest closeness centrality in Y1–Y2 and was second only to temperamental irritability in Y2–Y3. See Supplementary Figure S2 for rank ordered closeness centrality.

Outgoing strength

Networks using teacher-reported ADHD symptoms suggested bidirectional (rather than unidirectional) relationships between ADHD and ODD in the Y1–Y2 and Y2–Y3 networks. Higher ADHD symptoms predicted worsening ODD symptoms, similar to parent networks; however, higher ODD symptoms also predicted worsening ADHD.

All other major findings were confirmed in the teacher networks. Teacher ADHD symptom networks indicated bidirectional relationships between temperamental irritability and ADHD symptoms, consistent with networks using parent-report. Relationships between temperamental irritability and depression in both the Y1–Y2 and Y2–Y3 networks also paralleled those using parent-reported ADHD symptoms. Finally, findings that working memory independently predicted both ADHD symptoms and depression were also confirmed in the networks using teacher-reported ADHD symptoms. Supplementary Figure S1 shows the networks using teacher-reported ADHD symptoms.

Discussion

Network approaches are increasingly used in adult psychopathology research to understand unique direct and indirect relationships between symptom domains, yet studies in developmental psychopathology remain surprisingly rare (Contreras et al., 2019; Robinaugh et al., 2020). Here, we build on prior DSM-symptom-based network studies by incorporating trait-based emotion ratings and performance-based measures of cognition into a multilevel, multiconstruct longitudinal network, employing a CLPN model at this level of detail for the first time.

In the resulting highly connected network, most features had edges connecting them to many other features in the network. Trait-based emotion ratings and measures of cognition were as interconnected within the psychopathology network as the symptoms themselves, consistent with an RDoC framework that emphasizes the need to understand psychopathology by looking beyond traditional core symptom domains. Of note, features from multiple reporters and at multiple levels of analysis played equally important roles in network structure. Results confirmed that ADHD-related inattention and hyperactivity–impulsivity, temperamental irritability, and working memory each exert important influence on multiple domains of psychopathology over time and can be conceptualized as conveying independent, transdiagnostic risk.

Findings from the longitudinal network supported our three primary hypotheses. First, ADHD symptom domains and temperamental irritability were among the most closely connected features in both networks. Being closely connected potentially allows these features to efficiently influence development of other features due to the relatively short paths connecting them (although, as Bringmann & Eronen, 2018 discuss, the availability of many short paths does not guarantee those are the primarily paths via which influence will actually occur). The implications from an RDoC perspective seem clear – these closely connected features have the most potential to simultaneously influence multiple other domains as transdiagnostic drivers of risk. Closeness metrics can depend heavily on the specific features included in the model. Thus, while other network models may yield alternative patterns, the breadth of domains included in the network here increases confidence in interpreting these as important transdiagnostic risk features.

Working memory also emerged as an important transdiagnostic risk feature but with some caveats. Closeness centrality was high in the Y1–Y2 network, but its closeness centrality rank dropped in the Y2–Y3 network. Several things may explain the pattern. Closeness centrality metrics were most stable in the Y1–Y2 network, and the drop in rank order closeness centrality may be a psychometric artifact of overall parameter instability. Yet it is intriguing that this pattern, if replicated, is consistent with working memory having more influence on other features earlier in development but losing some potency to influence other features over time. This pattern would be consistent with other literature suggesting the same thing: working memory impairments play large role early in development but normalize for some children over time (Karalunas et al., 2017; Ramos, Hamdan, & Machado, 2020; Sowerby, Seal, & Tripp, 2011). Although speculative, results suggest a developmentally sensitive window in which any effects of working memory interventions may be most effective. Early differences in the developmental trajectory of working memory may be an important factor accounting for differential patterns of ADHD symptom remission.

Closeness centrality provides an overall view of the direct and indirect connections of a feature within the network. Outgoing strength, in contrast, quantifies specific direct pathways between features, and we relied on it here to test directional hypotheses about developmental influences among features. Consistent with our hypotheses, ADHD symptoms exerted direct causal influence on developing depression. Further, paths were generally unidirectional. While some caution in interpreting edge weights is needed, in the current network ADHD exerted large influence on depression, explaining more than 12% of variance in the Y1–Y2 network when children were between 9 and 10 years old, whereas the few existing paths from depression to ADHD symptoms explained less than 1% of the variance. Findings are consistent with other recent work suggesting that genetic liability for ADHD directly

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

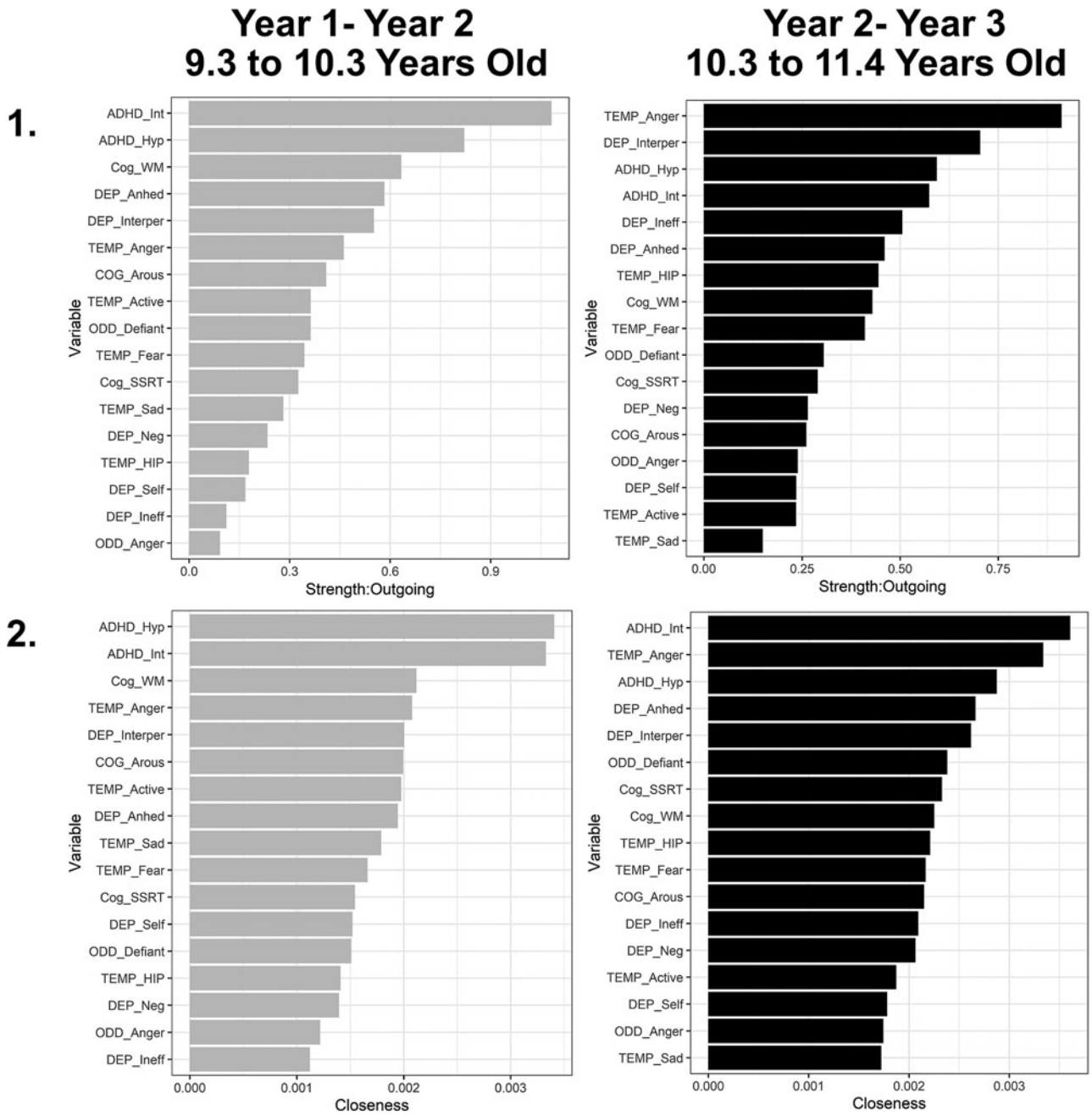

Figure 5. Shows outgoing strength (panel 1) and closeness (panel 2) centrality for each network feature in the Y1–Y2 (grey) and Y2–Y3 (black) networks.

conveys risk for categorical major depression (Riglin et al., 2020) and that ADHD predicts developing emotional problems but the reverse is not true (Stern et al., 2020). Here, we confirm that the unidirectional pathways hold even after accounting for a myriad of other emotional and cognitive features, a major step in clarifying mechanisms via which risk from categorical ADHD is conferred (Meinzer & Chronis-Tuscano, 2017).

Results also clarify unique patterns than can inform specific risk mechanisms. In particular, ADHD inattention specifically predicted developing feelings of ineffectiveness, pointing to a specific pathway via which inattention contributes to depression (McQuade, Hoza, Murray-Close, Waschbusch, & Owens, 2011) and suggesting fostering feelings of success and mastery in areas where inattention often interferes may serve a protective role, even in children who are not yet experiencing depressive symptoms. Hyperactivity–impulsivity, in contrast, uniquely contributes to depression via increasing interpersonal problems and negative self-esteem, pointing to early interventions for social problems as a key tool in preventing depression in hyperactive–impulsive children. In either case, the implication of these direct, unidirectional pathways is that early treatment of core ADHD symptoms can help to prevent later depression.

Working memory also had direct paths to multiple aspects of depression. Recent meta-analytic review also suggests that working memory impairments contribute to co-occurrence of depression and ADHD, but the review highlights the paucity of

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

prospective work using dimensional measures to characterize the cognitive mechanisms of ADHD–depression co-occurrence (Mayer et al., 2021). Prior studies have provided contradictory evidence about whether working memory impairments precede or follow onset of depression (Roy, Oldehinkel, & Hartman, 2017), as well as about whether these impairments are implicated in depression after accounting for ADHD comorbidity (Larochette, Harrison, Rosenblum, & Bowie, 2011). Results here point to a direct causal role of working memory impairments in the development of depression during middle childhood and early adolescence. In contrast to ADHD symptom domains, which had at least partially dissociable effects, working memory had outgoing edges to all depression features in the Y1–Y2 network where it played the largest role, suggesting it conveys broad, general influence on multiple domains of developing depression. Results are consistent with theory suggesting that working memory impairments make it difficult for children to exert voluntary control over thoughts (Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017; Sportel, Nauta, de Hullu, de Jong, & Hartman, 2011), thus reducing children's abilities to direct attention away from negative thoughts and contributing to increases in negative ruminative thought patterns associated with depression (Beloe & Derakshan, 2020; Kertz, Belden, Tillman, & Luby, 2016; Koster et al., 2017).

Consistent with conceptualization of temperamental irritability as a transdiagnostic risk feature, temperamental irritability had direct paths to both ADHD and depression but relationships to each domain varied. Irritability predicted depression-related interpersonal problems and negative mood. On one hand, this is unsurprising given the large literature on childhood irritability as a predictor of later mood problems (Fernandez de la Cruz et al., 2015; Leibenluft, Blair, Charney, & Pine, 2003; Leibenluft, Cohen, Gorrindo, Brook, & Pine, 2006; Stringaris, 2011). However, this study confirms a unique association between temperamental irritability and depression using a cross-lag network approach to account for a myriad of other cognitive and temperamental features, including other features related to temperamental negative affect such as sadness and fear. Of note, while relationships were bidirectional in the Y1–Y2 network, they became unidirectional as children got older. A pattern that held when considering the relationships between temperamental irritability and temperamental sadness as well. At least two pathways may account for these associations. First, irritability was related specifically to the interpersonal problems feature of depression. Irritability in middle childhood may interfere with developing the social relationships that take on a crucial role in later childhood and adolescence (Evans et al., 2017), contributing to loneliness and isolation, two key drivers of depression risk (Loades et al., 2020; Matthews et al., 2016). Second, shift to unidirectional relationship from irritability to negative mood and temperamental sadness may reflect a type of heterotypic continuity – mood dysregulation that is expressed as irritability earlier in development may increasingly manifest in terms of negative mood in later development.

In contrast to the unidirectional relationship between irritability and depression, relationships between irritability and the ADHD symptom domains were bidirectional. These bidirectional influences suggest tightly linked co-development and expression over time. They support recent suggestions that temperamental irritability should be conceptualized as a core part of ADHD symptom expression for some children (Karalunas et al., 2019; Nigg et al., 2020a, 2020b). The co-development and expression of ADHD symptoms and anger regulation difficulties may be related to their shared reliance on overlapping neural resources related to top-down regulation of attention (Karalunas, Weigard, & Alperin, 2020; Ochsner & Gross, 2008). Given the shared neural and psychological resources, weak top-down regulation may variously express itself as inattention, poor behavioral control (hyperactivity–impulsivity), or emotion dysregulation depending on the social or other environmental context. Further, for some children, the need to exert attentional control (e.g., school, homework, multitasking situations, or handling complex social interactions) may serve to exacerbate problems with emotional control, contributing to commonly observed contextual variation in symptom expression. Further, differential management of mood dysregulation in early childhood may partially explain heterogeneous course of ADHD symptoms. While existing behavioral treatments appear to have relatively small direct effects on core ADHD symptoms of inattention and hyperactivity–impulsivity (Sonuga-Barke et al., 2014), the current findings suggest that behavioral treatments to improve emotion regulation in children with ADHD may actually help modify trajectories of core ADHD symptom expression as well.

Edges connecting irritability to both ADHD domains and depression were all of similar magnitude. There is ongoing debate regarding whether irritability should be conceptualized in terms of distinct tonic negative mood and phasic temper outburst components that may have unique associations with psychopathology (Cardinale et al., 2021; Hirsch, Davis, Cao, & Roy, 2021). Future studies, particularly those using momentary assessment to differentiate these components, will be critical to further clarifying which facets of the construct are most influential on different forms of psychopathology. Similarly, the current study used widely spaced assessment points that captured developmental pathways over the course of years. Momentary assessment studies will be important for understanding dynamic causal influences on shorter timescales.

Our primary analyses used parent-reported ADHD symptoms, and networks using teacher-reported ADHD symptoms confirmed our major findings, including the bidirectional relationships between temperamental irritability and ADHD and temperamental irritability and depression features. Teacher networks also confirmed the role of working memory in worsening ADHD symptoms and depression. Teacher-reported networks also confirmed relationships between ADHD and ODD but these effects were bidirectional (as opposed to unidirectional effects in the networks using parent-reported ADHD symptoms. The overall level of convergence between networks using parent- and teacher-reported ADHD symptoms is reassuring, but additional studies using a broader set of teacher report measures may offer additional insight. In addition, studies using observational measures of irritability or ADHD symptoms may yield additional information.

Finally, the current analyses yielded wide CIs around estimated edge weights. CIs did not include zero, suggesting that we can confidently interpret the presence or absence of edges as indicating the presence or absence of relationships in our data. However, the wide confidence intervals mean preclude strong inferences about whether one edge is stronger than another (e.g., even values that superficially appear quite different may actually reflect similar strength relationships at the population level). Wide CIs are common in psychopathology networks but additional studies with larger samples and methodological advances to improve network estimation will be important for understanding the relative importance of various pathways.

https://doi.org/10.1017/S0954579421000900 Published online by Cambridge University Press

Conclusion

Despite substantial research efforts, heterogeneous clinical course in ADHD remains difficult to predict and the mechanisms accounting for secondary co-occurrence of ADHD and additional clinical problems remain poorly understood. Resolving these is crucial to improve prediction and prevention of such outcomes. Yet doing so requires accounting for transactional influences of a large number of features across development. Here, we applied a longitudinal network model to a multimodal, multilevel dataset to test RDoC-inspired hypotheses about transdiagnostic risk features. Results confirmed specific hypotheses about ADHD symptom domains, temperamental irritability, and working memory as critical transdiagnostic risk factors for psychopathology based on their direct associations with other features across time. ADHD symptoms and working memory each had direct, independent associations with depression. Further, we demonstrate tightly linked co-development of ADHD symptoms and temperamental irritability, consistent with the possibility that anger dysregulation is a core feature that is co-expressed as part of the ADHD phenotype for some children.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954579421000900

Acknowledgment. We would like to sincerely thank the children and families who have dedicated countless hour over many years to participating in this research.

Funding Statement. This project was supported by R37 MH059105 (PI: Nigg). Karalunas' time was additionally supported by R01 MH120109 (PI: Karalunas). Michelle Martel and Patrick Goh were supported by R01MH119119-01A1 (PI: Martel).

Conflicts of Interest. None.

References

Achenbach, T. M. (1966). The classification of children's psychiatric symptoms: A factor-analytic study. *Psychological Monographs: General and Applied*, *80*, 1. doi:10.1037/h0093906

Achenbach, T. M. (2020). Bottom-up and top-down paradigms for psychopathology: A half-century odyssey. *Annual Review of Clinical Psychology*, *16*, 1–24. doi:10.1146/annurev-clinpsy-071119-115831

APA. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5*. Washington, D.C.: American Psychiatric Association. doi:10.1176/appi.books.9780890425596.

Aston-Jones, G., & Cohen, J. D. (2005a). An integrative theory of locus coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annual Review of Neuroscience*, *28*, 403–450. doi:10.1146/annurev.neuro.28.061604.135709

Aston-Jones, G., & Cohen, J. D. (2005b). Adaptive gain and the role of the locus coeruleus–norepinephrine system in optimal performance. *Journal of Comparative Neurology*, *493*, 99–110. doi:10.1002/cne.20723

Banaschewski, T., Jennen-Steinmetz, C., Brandeis, D., Buitelaar, J. K., Kuntsi, J., Poustka, L., … Albrecht, B. (2012). Neuropsychological correlates of emotional lability in children with ADHD. *Journal of Child Psychology and Psychiatry*, *53*, 1139–1148. doi:10.1111/j.1469-7610.2012.02596.x

Bates, J. E., Goodnight, J. A., & Fite, J. E. (2008). Temperament and emotion. In M. Lewis, J. M. Haviland-Jones & L. F. Barrett (Eds.), *Handbook of emotion* (3rd ed., pp. 485–496). New York, NY: The Guilford Press.

Beauchaine, T. P., & Hinshaw, S. P. (2020). RDoC and psychopathology among youth: Misplaced assumptions and an agenda for future research. *Journal of Clinical Child & Adolescent Psychology*, *49*, 322–340. doi:10.1080/15374416.2020.1750022

Beauchaine, T. P., Hinshaw, S. P., & Pang, K. L. (2010). Comorbidity of attention-deficit/hyperactivity disorder and early-onset conduct disorder: Biological, environmental, and developmental mechanisms. *Clinical Psychology: Science and Practice*, *17*, 327–336. doi:10.1111/j.1468-2850.2010.01224.x

Beauchaine, T. P., & Tackett, J. L. (2020). Irritability as a transdiagnostic vulnerability trait: Current issues and future directions. *Behavior Therapy*, *51*, 350–364. doi:10.1016/j.beth.2019.10.009

Beloe, P., & Derakshan, N. (2020). Adaptive working memory training can reduce anxiety and depression vulnerability in adolescents. *Developmental Science*, *23*, e12831. doi:10.1111/desc.12831

Bergwerff, C. E., Luman, M., Weeda, W. D., & Oosterlaan, J. (2017). Neurocognitive profiles in children with ADHD and their predictive value for functional outcomes. *Journal of Attention Disorders*, *23*(13), 1567–1577. doi:10.1177/1087054716688533

Bernstein, E. E., Kleiman, E. M., van Bork, R., Moriarity, D. P., Mac Giollabhui, N., McNally, R. J., … Alloy, L. B. (2019). Unique and predictive relationships between components of cognitive vulnerability and symptoms of depression. *Depress Anxiety*, *36*, 950–959. doi:10.1002/da.22935

Biederman, J., Mick, E., & Faraone, S. V. (2000). Age-dependent decline of symptoms of attention deficit hyperactivity disorder: Impact of remission definition and symptom type. *American Journal of Psychiatry*, *157*, 816–818. doi:10.1176/appi.ajp.157.5.816

Biederman, J., Petty, C. R., Clarke, A., Lomedico, A., & Faraone, S. V. (2011). Predictors of persistent ADHD: An 11-year follow-up study. *Journal of Psychiatric Research*, *45*, 150–155. doi:10.1016%2Fj.jpsychires.2010.06.009

Bloemen, A., Oldehinkel, A., Laceulle, O., Ormel, J., Rommelse, N., & Hartman, C. (2018). The association between executive functioning and psychopathology: General or specific? *Psychological Medicine*, *48*, 1787–1794. doi:10.1017/S0033291717003269

Borsboom, D., & Cramer, A. O. (2013). Network analysis: An integrative approach to the structure of psychopathology. *Annual Review of Clinical Psychology*, *9*, 91–121. doi:10.1146/annurev-clinpsy-050212-185608

Boschloo, L., Schoevers, R. A., van Borkulo, C. D., Borsboom, D., & Oldehinkel, A. J. (2016). The network structure of psychopathology in a community sample of preadolescents. *Journal of Abnormal Psychology*, *125*, 599. doi: 10.1037/abn0000150

Bringmann, L. F., & Eronen, M. I. (2018). Don't blame the model: Reconsidering the network approach to psychopathology. *Psychological Review*, *125*, 606. doi:10.1037/rev0000108

Burke, J. D., Boylan, K., Rowe, R., Duku, E., Stepp, S. D., Hipwell, A. E., & Waldman, I. D. (2014). Identifying the irritability dimension of ODD: Application of a modified bifactor model across five large community samples of children. *Journal of Abnormal Psychology*, *123*, 841. doi:10.1037/a0037898

Bussing, R., Mason, D. M., Bell, L., Porter, P., & Garvan, C. (2010). Adolescent outcomes of childhood attention-deficit/hyperactivity disorder in a diverse community sample. *Journal of the American Academy of Child & Adolescent Psychiatry*, *49*, 595–605. doi:10.1016/j.jaac.2010.03.006

Cardinale, E. M., Freitag, G. F., Brotman, M. A., Pine, D. S., Leibenluft, E., & Kircanski, K. (2021). Phasic versus tonic irritability: Differential associations with attention-deficit/hyperactivity disorder symptoms. *Journal of the American Academy of Child & Adolescent Psychiatry*, doi:10.1016/j.jaac.2020.11.022

Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S. J., Harrington, H., Israel, S., … Poulton, R. (2014). The p factor: One general psychopathology factor in the structure of psychiatric disorders? *Clinical Psychological Science*, *2*, 119–137. doi:10.1177/2167702613497473

Clark, L. A. (2005). Temperament as a unifying basis for personality and psychopathology. *Journal of Abnormal Psychology*, *114*, 505. doi:10.1037/0021-843X.114.4.505

Conners, C. K. (2003). *Conners' rating scales: Revised technical manual*. New York, NY: Multi-Health Systems.

Contreras, A., Nieto, I., Valiente, C., Espinosa, R., & Vazquez, C. (2019). The study of psychopathology from the network analysis perspective: A systematic review. *Psychotherapy and Psychosomatics*, *88*, 71–83. doi:10.1159/000497425

Cuthbert, B. N., & Insel, T. R. (2010). Toward new approaches to psychotic disorders: The NIMH research domain criteria project. *Schizophrenia Bulletin*, *36*, 1061–1062. doi:10.1093/schbul/sbq108

de Gee, J. W., Tsetsos, K., Schwabe, L., Urai, A. E., McCormick, D., McGinley, M. J., & Donner, T. H. (2020). Pupil-linked phasic arousal predicts a reduction of choice bias across species and decision domains. *Elife*, *9*, e54014. doi:10.7554/eLife.54014

DuPaul, G., Power, T., Anastopoulos, A., & Reid, R. (1998). *ADHD rating scale—IV: Checklists, norms, and clinical interpretation*. New York, NY: Guilford Press. doi:10.1177%2F0734282905285792.

Du Rietz, E., Cheung, C. H., McLoughlin, G., Brandeis, D., Banaschewski, T., Asherson, P., & Kuntsi, J. (2016). Self-report of ADHD shows limited agreement with objective markers of persistence and remittance. *Journal of Psychiatric Research*, *82*, 91–99. doi:10.1016/j.jpsychires.2016.07.020

Epskamp, S. (2020). Psychometric network models from time-series and panel data. *Psychometrika*, *85*(1), 206–231. doi:10.1007/s11336-020-09697-3

Epskamp, S., Borsboom, D., & Fried, E. I. (2018). Estimating psychological networks and their accuracy: A tutorial paper. *Behavior Research Methods*, *50*, 195–212. doi:10.3758/s13428-017-0862-1

Erskine, H. E., Norman, R. E., Ferrari, A. J., Chan, G. C., Copeland, W. E., Whiteford, H. A., & Scott, J. G. (2016). Long-term outcomes of attention-deficit/hyperactivity disorder and conduct disorder: A systematic review and meta-analysis. *Journal of the American Academy of Child & Adolescent Psychiatry*, *55*, 841–850. doi:10.1016/j.jaac.2016.06.016

Evans, S. C., Burke, J. D., Roberts, M. C., Fite, P. J., Lochman, J. E., Francisco, R., & Reed, G. M. (2017). Irritability in child and adolescent psychopathology: An integrative review for ICD-11. *Clinical Psychology Review*, *53*, 29–45. doi:10.1016/j.cpr.2017.01.004

Fair, D. A., Nigg, J. T., Iyer, S., Bathula, D., Mills, K. L., Dosenbach, N. U., … Bangaru, S. (2012). Distinct neural signatures detected for ADHD subtypes after controlling for micro-movements in resting state functional connectivity MRI data. *Frontiers in Systems Neuroscience*, *6*, 1–31. doi:10.3389/fnsys.2012.00080

Fernandez de la Cruz, L., Simonoff, E., McGough, J. J., Halperin, J. M., Arnold, L. E., & Stringaris, A. (2015). Treatment of children with attention-deficit/hyperactivity disorder (ADHD) and irritability: Results from the multimodal treatment study of children with ADHD (MTA). *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*, 62–70.e63. doi:10.1016/j.jaac.2014.10.006

Fosco, W. D., Kofler, M. J., Groves, N. B., Chan, E. S., & Raiker, J. S. (2020). Which 'working' components of working memory aren't working in youth with ADHD? *Journal of Abnormal Child Psychology*, *48*, 647–660. doi:10.1007/s10802-020-00621-y

Franke, B., Michelini, G., Asherson, P., Banaschewski, T., Bilbow, A., Buitelaar, J. K., … Haavik, J. (2018). Live fast, die young? A review on the developmental trajectories of ADHD across the lifespan. *European Neuropsychopharmacology*, *28*, 1059–1088. doi:10.1016/j.euroneuro.2018.08.001

Fried, E. I., van Borkulo, C. D., Cramer, A. O., Boschloo, L., Schoevers, R. A., & Borsboom, D. (2017). Mental disorders as networks of problems: A review of recent insights. *Social Psychiatry and Psychiatric Epidemiology*, *52*, 1–10.

Funkhouser, C. J., Chacko, A. A., Correa, K. A., Kaiser, A. J., & Shankman, S. A. (2020). Unique longitudinal relationships between symptoms of psychopathology in youth: A cross-lagged panel network analysis in the ABCD study. *Journal of Child Psychology and Psychiatry*, *62*(2), 184–194. doi:10.1007/s00127-016-1319-z

Gagne, J. R., & Hill Goldsmith, H. (2011). A longitudinal analysis of anger and inhibitory control in twins from 12 to 36 months of age. *Developmental Science*, *14*, 112–124. doi:10.1111/j.1467-7687.2010.00969.x

Goodkind, M., Eickhoff, S. B., Oathes, D. J., Jiang, Y., Chang, A., Jones-Hagata, L. B., … Korgaonkar, M. S. (2015). Identification of a common neurobiological substrate for mental illness. *JAMA Psychiatry*, *72*, 305–315. doi:10.1001/jamapsychiatry.2014.2206

Goodman, R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *Journal of the American Academy of Child & Adolescent Psychiatry*, *40*, 1337–1345. doi:10.1097/00004583-200111000-00015

Groenman, A. P., Janssen, T. W. P., & Oosterlaan, J. (2017). Childhood psychiatric disorders as risk factor for subsequent substance abuse: A meta-analysis. *Journal of the American Academy of Child and Adolescent Psychiatry*, *56*, 556–569. doi:10.1016/j.jaac.2017.05.004

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, *42*, 377–381. doi:10.1016/j.jbi.2008.08.010

Hawkey, E. J., Tillman, R., Luby, J. L., & Barch, D. M. (2018). Preschool executive function predicts childhood resting-state functional connectivity and attention-deficit/hyperactivity disorder and depression. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*, 927–936. doi:10.1016/j.bpsc.2018.06.011

Hirsch, E., Davis, K., Cao, Z., & Roy, A. K. (2021). Understanding phasic irritability: Anger and distress in children's temper outbursts. *Child Psychiatry & Human Development*, 1–13. doi:10.1007/s10578-021-01126-5

Hoffman, M., Steinley, D., Trull, T. J., Lane, S. P., Wood, P. K., & Sher, K. J. (2019). The influence of sample selection on the structure of psychopathology symptom networks: An example with alcohol use disorder. *Journal of Abnormal Psychology*, *128*, 473. doi:10.1037/abn0000438

Huang-Pollock, C., Shapiro, Z., Galloway-Long, H., & Weigard, A. (2017). Is poor working memory a transdiagnostic risk factor for psychopathology? *Journal of Abnormal Child Psychology*, *45*, 1477–1490. doi:10.1007/s10802-016-0219-8

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., … Wang, P. (2010). Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. *The American Journal of Psychiatry*, *167*, 748–751. doi:10.1176/appi.ajp.2010.09091379

Karalunas, S. L., Fair, D., Musser, E. D., Aykes, K., Iyer, S. P., & Nigg, J. T. (2014). Subtyping attention-deficit/hyperactivity disorder using temperament dimensions: Toward biologically based nosologic criteria. *JAMA Psychiatry*, *71*, 1015–1024. doi:10.1001/jamapsychiatry.2014.763

Karalunas, S. L., Gustafsson, H. C., Dieckmann, N., Tipsord, J., Mitchell, S. H., & Nigg, J. T. (2017). Heterogeneity in development of aspects of working memory predicts longitudinal ADHD symptom change. *Journal of Abnormal Psychology*, *126*(6), 774–792. doi:10.1037/abn0000292

Karalunas, S. L., Gustafsson, H. C., Fair, D., Musser, E. D., & Nigg, J. T. (2019). Do we need an irritable subtype of ADHD? Replication and extension of a promising temperament profile approach to ADHD subtyping. *Psychological Assessment*, *31*, 236. doi:10.1037/pas0000664

Karalunas, S. L., Hawkey, E., Gustafsson, H., Miller, M., Langhorst, M., Cordova, M., … Nigg, J. T. (2018). Overlapping and distinct cognitive impairments in attention-deficit/hyperactivity and autism spectrum disorder without intellectual disability. *Journal of Abnormal Child Psychology*, *46*, 1705–1716. doi:10.1007/s10802-017-0394-2

Karalunas, S. L., & Huang-Pollock, C. L. (2013). Integrating evidence of slow RTs and impaired executive functions using a diffusion model framework. *Journal of Abnormal Child Psychology*, *41*, 837–850. doi:10.1007/s10802-013-9715-2

Karalunas, S. L., Huang-Pollock, C. L., & Nigg, J. T. (2012). Decomposing attention-deficit/hyperactivity disorder (ADHD)-related effects in response speed and variability. *Neuropsychology*, *26*, 684–694. doi:10.1037/a0029936

Karalunas, S. L., & Nigg, J. T. (2019). Heterogeneity and subtyping in attention-deficit/hyperactivity disorder—considerations for emerging research using person-centered computational approaches. *Biological Psychiatry*, *88*(1), 103–110. doi:10.1016/j.biopsych.2019.11.002

Karalunas, S. L., Weigard, A., & Alperin, B. (2020). Emotion-cognition interactions in ADHD: Increased early attention capture and weakened attentional control in emotional contexts. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *5*(5), 520–529. doi:10.1016/j.bpsc.2019.12.021

Kendler, K. S. (2009). An historical framework for psychiatric nosology. *Psychological Medicine*, *39*, 1935–1941. doi:10.1017/S0033291709005753

Kendler, K. S., & Engstrom, E. J. (2018). Criticisms of Kraepelin's psychiatric nosology: 1896–1927. *American Journal of Psychiatry*, *175*, 316–326. doi:10.1176/appi.ajp.2017.17070730

Kertz, S. J., Belden, A. C., Tillman, R., & Luby, J. (2016). Cognitive control deficits in shifting and inhibition in preschool age children are associated with increased depression and anxiety over 7.5 years of development. *Journal of Abnormal Child Psychology*, *44*, 1185–1196. doi:10.1007/s10802-015-0101-0

Kessler, R. C., Adler, L., Barkley, R., Biederman, J., Conners, C. K., Demler, O., … Secnik, K. (2006). The prevalence and correlates of adult ADHD in the United States: Results from the national comorbidity survey replication. *American Journal of Psychiatry*, *163*, 716–723. doi:10.1176/appi.ajp.163.4.716

Kessler, R., Adler, L., Berglund, P., Green, J. G., McLaughlin, K., Fayyad, J., … Zaslavsky, A. (2014). The effects of temporally secondary co-morbid mental disorders on the associations of DSM-IV ADHD with adverse outcomes in the US national comorbidity survey replication adolescent supplement (NCS-A). *Psychological Medicine*, *44*, 1779. doi:10.1017/S0033291713002419

Kofler, M. J., Rapport, M. D., Sarver, D. E., Raiker, J. S., Orban, S. A., Friedman, L. M., … Kolomeyer, E. G. (2013). Reaction time variability in ADHD: A meta-analytic review of 319 studies. *Clinical Psychology Review*, *33*(6), 795–811. doi:10.1016/j.cpr.2013.06.001

Koster, E. H., Hoorelbeke, K., Onraedt, T., Owens, M., & Derakshan, N. (2017). Cognitive control interventions for depression: A systematic review of findings from training studies. *Clinical Psychology Review*, *53*, 79–92. doi:10.1016/j.cpr.2017.02.002

Kovacs, M. (1985). The children's depression, inventory (CDI). *Psychopharmacology Bulletin*, *21*, 995–998. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/4089116

Kovacs, M. (1992). *Children's depression inventory*. North Tonawanda, NY: Multi-Health Systems.

Lahey, B. B., Pelham, W. E., Loney, J., Lee, S. S., & Willcutt, E. (2005). Instability of the DSM-IV subtypes of ADHD from preschool through elementary school. *Archives of General Psychiatry*, *62*, 896–902. Retrieved from <Go to ISI>://000231034900011. doi:10.1001/archpsyc.62.8.896.

Lahey, B. B., Rathouz, P. J., Van Hulle, C., Urbano, R. C., Krueger, R. F., Applegate, B., … Waldman, I. D. (2008). Testing structural models of DSM-IV symptoms of common forms of child and adolescent psychopathology. *Journal of Abnormal Child Psychology*, *36*, 187–206. doi:10.1007/s10802-007-9169-5

Larochette, A.-C., Harrison, A. G., Rosenblum, Y., & Bowie, C. R. (2011). Additive neurocognitive deficits in adults with attention-deficit/hyperactivity disorder and depressive symptoms. *Archives of Clinical Neuropsychology*, *26*, 385–395. doi:10.1093/arclin/acr033

Larsson, H., Dilshad, R., Lichtenstein, P., & Barker, E. D. (2011). Developmental trajectories of DSM-IV symptoms of attention-deficit/hyperactivity disorder: Genetic effects, family risk and associated psychopathology. *Journal of Child Psychology and Psychiatry*, *52*, 954–963. doi:10.1111/j.1469-7610.2011.02379.x

Lee, S. S., Humphreys, K. L., Flory, K., Liu, R., & Glass, K. (2011). Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: A meta-analytic review. *Clinical Psychology Review*, *31*, 328–341. doi:10.1016/j.cpr.2011.01.006

Leibenluft, E., Blair, R. J. R., Charney, D. S., & Pine, D. S. (2003). Irritability in pediatric mania and other childhood psychopathology. *Annals of the New York Academy of Sciences*, *1008*, 201–218. doi:10.1196/annals.1301.022

Leibenluft, E., Cohen, P., Gorrindo, T., Brook, J. S., & Pine, D. S. (2006). Chronic versus episodic irritability in youth: A community-based, longitudinal study of clinical and diagnostic associations. *Journal of Child & Adolescent Psychopharmacology*, *16*, 456–466. doi:10.1089/cap.2006.16.456

Loades, M. E., Chatburn, E., Higson-Sweeney, N., Reynolds, S., Shafran, R., Brigden, A., … Crawley, E. (2020). Rapid systematic review: The impact of social isolation and loneliness on the mental health of children and adolescents in the context of COVID-19. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(11), 1218–1239. doi:10.1016/j.jaac.2020.05.009

Macdonald, A. N., Goines, K. B., Novacek, D. M., & Walker, E. F. (2016). Prefrontal mechanisms of comorbidity from a transdiagnostic and ontogenic perspective. *Development and Psychopathology*, *28*, 1147–1175. doi:10.1017/S0954579416000742

Madole, J. W., Rhemtulla, M., Grotzinger, A. D., Tucker-Drob, E. M., & Harden, K. P. (2019). Testing cold and Hot cognitive control as moderators of a network of comorbid psychopathology symptoms in adolescence. *Clinical Psychological Science*, *7*, 701–718. doi:10.1177/2167702619842466

Martel, M. M. (2016). Dispositional trait types of ADHD in young children. *Journal of Attention Disorders*, *20*, 43–52. doi:10.1177/1087054712466915

Martel, M. M., Goth-Owens, T., Martinez-Torteya, C., & Nigg, J. T. (2010). A person-centered personality approach to heterogeneity in attention-deficit/hyperactivity disorder (ADHD). *Journal of Abnormal Psychology*, *119*, 186–196. doi:10.1037/1040-3590.4.4.512.1993-11959-00110.1037/1040-3590.4.4.512. doi:10.1037/a0017511.

Martel, M. M., Pan, P. M., Hoffmann, M. S., Gadelha, A., do Rosário, M. C., Mari, J. J., … Bressan, R. A. (2017). A general psychopathology factor (P factor) in children: Structural model analysis and external validation through familial risk and child global executive function. *Journal of Abnormal Psychology*, *126*, 137. doi:10.1037/abn0000205

Matthews, T., Danese, A., Wertz, J., Odgers, C. L., Ambler, A., Moffitt, T. E., & Arseneault, L. (2016). Social isolation, loneliness and depression in young adulthood: A behavioural genetic analysis. *Social Psychiatry and Psychiatric Epidemiology*, *51*, 339–348. doi:10.1007/s00127-016-1178-7

Mayer, J. S., Bernhard, A., Fann, N., Boxhoorn, S., Hartman, C. A., Reif, A., & Freitag, C. M. (2021). Cognitive mechanisms underlying depressive disorders in ADHD: A systematic review. *Neuroscience & Biobehavioral Reviews*, *121*, 307–345. doi:10.1016/j.neubiorev.2020.12.018

McElroy, E., Shevlin, M., Murphy, J., & McBride, O. (2018). Co-occurring internalizing and externalizing psychopathology in childhood and adolescence: A network approach. *European Child & Adolescent Psychiatry*, *27*, 1449–1457. doi:10.1007/s00787-018-1128-x

McNally, R. J. (2016). Can network analysis transform psychopathology? *Behaviour Research and Therapy*, *86*, 95–104. doi:10.1016/j.brat.2016.06.006

McNally, R. J. (2020). Network analysis of psychopathology: Controversies and challenges. *Annual Review of Clinical Psychology*, *17*, 31–53. doi:10.1146/annurev-clinpsy-081219-092850

McQuade, J. D., Hoza, B., Murray-Close, D., Waschbusch, D. A., & Owens, J. S. (2011). Changes in self-perceptions in children with ADHD: A longitudinal study of depressive symptoms and attributional style. *Behavior Therapy*, *42*, 170–182. doi:10.1016/j.beth.2010.05.003

McTeague, L. M., Goodkind, M. S., & Etkin, A. (2016). Transdiagnostic impairment of cognitive control in mental illness. *Journal of Psychiatric Research*, *83*, 37–46. doi:10.1016/j.jpsychires.2016.08.001

Meinzer, M. C., & Chronis-Tuscano, A. (2017). ADHD and the development of depression: Commentary on the prevalence, proposed mechanisms, and promising interventions. *Current Developmental Disorders Reports*, *4*, 1–4. doi:10.1007/s40474-017-0106-1

Mittal, V. A., & Wakschlag, L. S. (2017). Research domain criteria (RDoC) grows up: Strengthening neurodevelopmental investigation within the RDoC framework. *Journal of Affective Disorders*, *216*, 30. doi:10.1016/j.jad.2016.12.011

Muris, P., Meesters, C., & Blijlevens, P. (2007). Self-reported reactive and regulative temperament in early adolescence: Relations to internalizing and externalizing problem behavior and "Big three" personality factors. *Journal of Adolescence*, *30*, 1035–1049. doi:10.1016/j.adolescence.2007.03.003

Murphy, P. R., Vandekerckhove, J., & Nieuwenhuis, S. (2014). Pupil-linked arousal determines variability in perceptual decision making. *PLoS Computational Biology*, *10*, e1003854. doi:10.1371/journal.pcbi.1003854

Nigg, J. T., Gustafsson, H. C., Karalunas, S. L., Ryabinin, P., McWeeney, S. K., Faraone, S. V., … Wilmot, B. (2018). Working memory and vigilance as multivariate endophenotypes related to common genetic risk for attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *57*, 175–182. doi:10.1016/j.jaac.2017.12.013

Nigg, J. T., Jester, J. M., Stavro, G. M., Ip, K. I., Puttler, L. I., & Zucker, R. A. (2017). Specificity of executive functioning and processing speed problems in common psychopathology. *Neuropsychology*, *31*, 448. doi:10.1037/neu0000343

Nigg, J. T., Karalunas, S. L., Feczko, E., & Fair, D. A. (2020a). Toward a revised nosology for ADHD heterogeneity. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *5*(8), 726–737. doi:10.1016/j.bpsc.2020.02.005

Nigg, J. T., Karalunas, S. L., Gustafsson, H. C., Bhatt, P., Ryabinin, P., Mooney, M. A., … Wilmot, B. (2020b). Evaluating chronic emotional dysregulation and irritability in relation to ADHD and depression genetic risk in children with ADHD. *Journal of Child Psychology and Psychiatry*, *61*, 205–214. doi:10.1111/jcpp.13132

Nigg, J. T., Sibley, M. H., Thapar, A., & Karalunas, S. L. (2020c). Development of ADHD: Etiology, heterogeneity, and early life course. *Annual Review of Developmental Psychology*, *2*, 559–583. doi:10.1146/annurev-devpsych-060320-093413

Ochsner, K. N., & Gross, J. J. (2008). Cognitive emotion regulation insights from social cognitive and affective neuroscience. *Current Directions in Psychological Science*, *17*, 153–158. doi:10.1111/j.1467-8721.2008.00566.x,

Olino, T. M., Bufferd, S. J., Dougherty, L. R., Dyson, M. W., Carlson, G. A., & Klein, D. N. (2018). The development of latent dimensions of psychopathology across early childhood: Stability of dimensions and moderators of change. *Journal of Abnormal Child Psychology*, *46*, 1373–1383. doi:10.1007/s10802-018-0398-6

Patrick, C. J., & Hajcak, G. (2016). RDoc: Translating promise into progress. *Psychophysiology*, *53*, 415–424. doi:10.1111/psyp.12612

Preszler, J., & Burns, G. L. (2019). Network analysis of ADHD and ODD symptoms: Novel insights or redundant findings with the latent variable model? *Journal of Abnormal Child Psychology*, *47*, 1599–1610. doi:10.1007/s10802-019-00549-y

Preszler, J., Burns, G. L., Becker, S. P., & Servera, M. (2020). Multisource longitudinal network and latent Variable model analyses of ADHD symptoms in children. *Journal of Clinical Child & Adolescent Psychology*, *53*, 1–8. doi:10.1080/15374416.2020.1756297

Puig-Antich, J., & Ryan, N. (1986). *Kiddie schedule for affective disorders and schizophrenia*. Pittsburgh, PA: Western Psychiatric Institute.

Ramos, A. A., Hamdan, A. C., & Machado, L. (2020). A meta-analysis on verbal working memory in children and adolescents with ADHD. *The Clinical Neuropsychologist*, *34*, 873–898. doi:10.1080/13854046.2019.1604998

Ratcliff, R., & McKoon, G. (2008). The diffusion decision model: Theory and data for two-choice decision tasks. *Neural Computation*, *20*, 873–922. doi:10.1037/h0027366

Rhemtulla, M., van Bork, R., & Cramer, A. (2020). Cross-lagged network models. Retrieved from https://osf.io/r24q6/.

Riglin, L., Leppert, B., Dardani, C., Thapar, A. K., Rice, F., O'Donovan, M. C., … Thapar, A. (2020). ADHD and depression: Investigating a causal explanation. *Psychological Medicine*, 1–8. doi: 10.1017/S0033291720000665

Robinaugh, D. J., Hoekstra, R. H., Toner, E. R., & Borsboom, D. (2020). The network approach to psychopathology: A review of the literature 2008–2018 and an agenda for future research. *Psychological Medicine*, *50*, 353–366. doi:10.1017/S0033291719003404

Robinaugh, D. J., Millner, A. J., & Mcnally, R. J. (2016). Identifying highly influential nodes in the complicated grief network. *Journal of Abnormal Psychology*, *125*(6), 747.

Rothbart, M. K. (2007). Temperament, development, and personality. *Current Directions in Psychological Science*, *16*, 207–212. doi.org/10.1111/j.1467-8721.2007.00505.x

Rothbart, M. K. (2011). *Becoming who we are: Temperament and personality in development*. New York, NY: Guidford Press.

Rothbart, M. K., & Ahadi, S. A. (1994). Temperament and the development of personality. *Journal of Abnormal Psychology*, *103*, 55. doi:10.1037//0021-843x.103.1.55

Rothbart, M. K., Sheese, B. E., & Posner, M. I. (2014). Temperament and emotion regulation. In J. J. Gross (Ed.), *Handbook of emotion regulation* (2nd ed., pp. 305–320), New Your, NY, USA: Guilford Press.

Rouquette, A., Pingault, J.-B., Fried, E. I., Orri, M., Falissard, B., Kossakowski, J. J., … Borsboom, D. (2018). Emotional and behavioral symptom network structure in elementary school girls and association with anxiety disorders and depression in adolescence and early adulthood: A network analysis. *JAMA Psychiatry*, *75*, 1173–1181. doi:10.1001/jamapsychiatry.2018.2119

Roy, A., Oldehinkel, A. J., & Hartman, C. A. (2017). Cognitive functioning in adolescents with self-reported ADHD and depression: Results from a population-based study. *Journal of Abnormal Child Psychology*, *45*, 69–81. doi:10.1007/s10802-016-0160-x

Rutter, T. M., & Arnett, A. B. (2020). Temperament traits mark liability for coexisting psychiatric symptoms in children with elevated ADHD symptoms. *Journal of Attention Disorders*, 1–10. doi:10.1177/1087054720943282

Sattler, J., & Dumont, R. (2004). *Assessment of children: WISC-IV and WPPSI-III supplement*. San Diego: Jerome Sattler Publisher, Inc.

Savage, J., Verhulst, B., Copeland, W., Althoff, R. R., Lichtenstein, P., & Roberson-Nay, R. (2015). A genetically informed study of the longitudinal relation between irritability and anxious/depressed symptoms. *Journal of the American Academy of Child & Adolescent Psychiatry*, *54*, 377–384. doi:10.1016/j.jaac.2015.02.010

Sibley, M. H., Pelham, W. E., Molina, B. S., Gnagy, E. M., Waschbusch, D. A., Garefino, A. C., … Karch, K. M. (2012). Diagnosing ADHD in adolescence. *Journal of Consulting and Clinical Psychology*, *80*, 139. doi:10.1037/a0026577

Silk, T. J., Malpas, C. B., Beare, R., Efron, D., Anderson, V., Hazell, P., … Sciberras, E. (2019). A network analysis approach to ADHD symptoms: More than the sum of its parts. *PLoS One*, *14*, e0211053. doi:10.1371/journal.pone.0211053

Simonds, J., & Rothbart, M. K. (2004). *The Temperament in Middle Childhood Questionnaire (TMCQ): A computerized self-report measure of temperament for ages 7-10*. Paper Presented at the Occasional Temperament Conference, Athens, GA.

Smith, G. T., Atkinson, E. A., Davis, H. A., Riley, E. N., & Oltmanns, J. R. (2020). The general factor of psychopathology. *Annual Review of Clinical Psychology*, *16*, 75–98. doi:10.1146/annurev-clinpsy-071119-115848

Smith, T. E., & Martel, M. M. (2019). Trait-Based profiles of ADHD in adolescents and young adults. *Journal of Clinical Child & Adolescent Psychology*, *48*, 440–454. doi:10.1080/15374416.2018.1491004

Sonuga-Barke, E. J., Brandeis, D., Cortese, S., Daley, D., Ferrin, M., Holtmann, M., … Döpfner, M. (2014). Nonpharmacological interventions for ADHD: Systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *American Journal of Psychiatry*, *170*(3), 275–289. doi:10.1176/appi.ajp.2012.12070991

Sowerby, P., Seal, S., & Tripp, G. (2011). Working memory deficits in ADHD: The contribution of age, learning/language difficulties, and task parameters. *Journal of Attention Disorders*, *15*, 461–472. doi:10.1177/1087054710370674

Sportel, B. E., Nauta, M. H., de Hullu, E., de Jong, P. J., & Hartman, C. A. (2011). Behavioral inhibition and attentional control in adolescents: Robust relationships with anxiety and depression. *Journal of Child and Family Studies*, *20*, 149–156. doi:10.1007/s10826-010-9435-y

Stern, A., Agnew-Blais, J. C., Danese, A., Fisher, H. L., Matthews, T., Polanczyk, G. V., … Arseneault, L. (2020). Associations between ADHD and emotional problems from childhood to young adulthood: A longitudinal genetically sensitive study. *Journal of Child Psychology and Psychiatry*, *61*, 1234–1242. doi:10.1111/jcpp.13217

Stringaris, A. (2011). Irritability in children and adolescents: A challenge for DSM-5. *European Child & Adolescent Psychiatry*, *20*, 61–66. doi:10.1007/s00787-010-0150-4

Stringaris, A., & Goodman, R. (2009). Three dimensions of oppositionality in youth. *Journal of Child Psychology and Psychiatry*, *50*, 216–223. doi:10.1111/j.1469-7610.2008.01989.x

Sturm, A., McCracken, J. T., & Cai, L. (2019). Evaluating the hierarchical structure of ADHD symptoms and invariance across age and gender. *Assessment*, *26*, 508–523. doi:10.1177/1073191117714559

Thomas, J. G., & Sharp, P. B. (2019). Mechanistic science: A new approach to comprehensive psychopathology research that relates psychological and biological phenomena. *Clinical Psychological Science*, *7*, 196–215. doi:10.1177%2F2167702618810223

Van Lier, P. A., Der Ende, J. v., Koot, H. M., & Verhulst, F. C. (2007). Which better predicts conduct problems? The relationship of trajectories of conduct problems with ODD and ADHD symptoms from childhood into adolescence. *Journal of Child Psychology and Psychiatry*, *48*, 601–608. doi:10.1111/j.1469-7610.2006.01724.x

Vidal-Ribas, P. (2021). The distinction between phasic and tonic irritability: Moving from concept to proof. *Journal of the American Academy of Child & Adolescent Psychiatry*. doi:10.1016/j.jaac.2021.02.002.

Vidal-Ribas, P., Brotman, M. A., Valdivieso, I., Leibenluft, E., & Stringaris, A. (2016). The status of irritability in psychiatry: A conceptual and quantitative review. *Journal of the American Academy of Child & Adolescent Psychiatry*, *55*(7), 556–570. doi:10.1016/j.jaac.2016.04.014

Wakefield, J. C. (2016). Diagnostic issues and controversies in DSM-5: Return of the false positives problem. *Annual Review of Clinical Psychology*, *12*, 105–132. doi:10.1146/annurev-clinpsy-032814-112800

Waljee, A. K., Mukherjee, A., Singal, A. G., Zhang, Y., Warren, J., Balis, U., … Higgins, P. D. (2013). Comparison of imputation methods for missing laboratory data in medicine. *BMJ Open*, *3*, 1–7. doi:10.1136/bmjopen-2013-002847

Wechsler, D. (2002). *Wechsler individual achievement test, 2nd Ed (WIAT-II) examiner's manual*. San Antonio: Harcourt Brace.

White, L. K., Moore, T. M., Calkins, M. E., Wolf, D. H., Satterthwaite, T. D., Leibenluft, E., … Gur, R. E. (2017). An evaluation of the specificity of executive function impairment in developmental psychopathology. *Journal of*

the American Academy of Child & Adolescent Psychiatry, *56*, 975–982. e973. doi:10.1016/j.jaac.2017.08.016

Whittle, S., Allen, N. B., Lubman, D. I., & Yücel, M. (2006). The neurobiological basis of temperament: Towards a better understanding of psychopathology. *Neuroscience & Biobehavioral Reviews*, *30*, 511–525. doi:10.1016/j.neubiorev.2005.09.003

Whittle, S., Yücel, M., Fornito, A., Barrett, A., Wood, S. J., Lubman, D. I., … Allen, N. B. (2008). Neuroanatomical correlates of temperament in early adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*, 682–693. doi:10.1097/chi.0b013e31816bffca

Wickens, T. D. (2002). *Elementary signal detection theory*. New York, NY USA: Oxford University Press.

Willcutt, E. G., Doyle, A., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). Validity of the executive function theory of attention-deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry*, *57*, 1336–1346. doi:10.1016/j.biopsych.2005.02.006

Willoughby, M. T. (2003). Developmental course of ADHD symptomatology during the transition from childhood to adolescence: A review with recommendations. *Journal of Child Psychology and Psychiatry*, *44*, 88–106. doi:10.1111/1469-7610.t01-1-00104