The Monash Autism-ADHD Genetics and Neurodevelopment (MAGNET) Project Design and Methodologies: A dimensional approach to understanding neurobiological and genetic aetiology.

Rachael Knott (rachael.knott@monash.edu)  
Monash University, School of Psychological Sciences  
https://orcid.org/0000-0003-0903-2650

Beth P Johnson  
Monash University School of Psychological Sciences  
https://orcid.org/0000-0002-6336-0092

Jeggan Tiego  
Monash University School of Psychological Sciences

Olivia Mellahn  
Monash University School of Psychological Sciences

Amy Finlay  
Monash University School of Psychological Sciences

Kathryn Kallady  
Monash University School of Psychological Sciences

Maria Kouspous  
Monash University School of Psychological Sciences

Vishnu Priya Mohankuma Sindhu  
Monash University School of Psychological Sciences

Ziarih Hawi  
Monash University School of Psychological Sciences

Aurina Armatkeviciute  
Monash University School of Psychological Sciences

Tracey Chau  
Monash University School of Psychological Sciences

Dalia Maron  
Monash University School of Psychological Sciences

Emily-Clare Mercieca  
Monash University School of Psychological Sciences

Kirsten Furley  
Monash University School of Psychological Sciences

Katrina Harris  
Monash University Department of Paediatrics

Katrina Williams  
Monash University Department of Paediatrics

Alexandra Ure  
Monash University Department of Paediatrics

Alex Fornito  
Monash University School of Psychological Sciences

Kylie Gray
University of Warwick

**David Coghill**  
Murdoch Childrens Research Institute

**Ann Nicholson**  
Monash University Faculty of Information Technology

**Dinh Phuong**  
Monash University Faculty of Information Technology

**Eva Loth**  
King's College London

**Luke Mason**  
Birkbeck University of London Department of Psychological Sciences Centre for Brain and Cognitive Development

**Declan Murphy**  
King's College London

**Jan Buitelaar**  
Radboud Universiteit Donders Institute for Brain Cognition and Behaviour

**Mark A. Bellgrove**  
Monash University School of Psychological Sciences

---

**Methodology**

**Keywords:** ASD, ADHD, cognition, genetics, neuroimaging, eye-tracking, HiTOP, RDoC

**DOI:** [https://doi.org/10.21203/rs.3.rs-207275/v1](https://doi.org/10.21203/rs.3.rs-207275/v1)

**License:** ☛ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)
Abstract

Background

ASD and ADHD are prevalent neurodevelopmental disorders that frequently co-occur and have strong evidence for a degree of shared genetic aetiology. Behavioural and neurocognitive heterogeneity in ASD and ADHD has hampered attempts to map the underlying genetics and neurobiology, predict intervention response, and improve diagnostic accuracy. Moving away from categorical conceptualisations of psychopathology to a dimensional approach is anticipated to facilitate discovery of data-driven clusters and enhance our understanding of the neurobiological and genetic aetiology of these conditions. The Monash Autism-ADHD Genetics and Neurodevelopment (MAGNET) Project is one of the first large-scale, family-based studies to take a truly transdiagnostic approach to ASD and ADHD. Using a comprehensive phenotyping protocol capturing dimensional traits central to ASD and ADHD, the MAGNET Project aims to identify data-driven clusters across ADHD-ASD spectra using deep phenotyping of symptoms and behaviours; investigate the degree of familiality for different dimensional ASD-ADHD phenotypes and clusters; and map the neurocognitive, brain imaging, and genetic correlates of these data-driven symptom-based clusters.

Methods

The MAGNET Project will recruit 1,200 families with children who are either typically developing, or who display elevated ASD, ADHD, or ASD-ADHD traits, in addition to affected and unaffected biological siblings of probands, and parents. All children will be comprehensively phenotyped for behavioural symptoms, comorbidities, neurocognitive and neuroimaging traits and genetics.

Conclusion

The MAGNET Project will be the first large-scale family study to take a transdiagnostic approach to ASD-ADHD, utilising deep phenotyping across behavioural, neurocognitive, brain imaging and genetic measures.

Background

Overview

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are neurodevelopmental disorders affecting 1 – 2% and 5% of the population, respectively (Lord et al., 2020; Polanczyk, Willcutt, Salum, Kieling, & Rohde, 2014). ASD is defined by deficits in social communication, and restricted and repetitive patterns of behaviour and interests and altered sensory processing, whereas ADHD is defined by hyperactivity, impulsivity and inattention (Diagnostic and Statistical Manual - Fifth Edition [DSM-5]; American Psychiatric Association, 2013). In ASD, 30 – 80% of cases exhibit ADHD symptomatology (Mayes, Calhoun, Mayes, & Molitoris, 2012; Reiersen & Todd, 2008), and 20 – 50% of ADHD cases display ASD symptoms (Grzadzinski, Dick, Lord, & Bishop, 2016; Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010). The introduction of the DSM-5 has allowed, for the first time, the concurrent diagnosis of ASD and ADHD, and the two disorders are now recognized to co-occur in up to 50% of cases (Grzadzinski et al., 2016; Stevens, Peng, & Barnard-Brak, 2016). This comorbidity can be associated with a more severe ADHD phenotype and higher treatment needs overall (Cooper, Martin, Langley, Hamshire, & Thapar, 2014; Zablotsky, Bramlett, & Blumberg, 2017).

Although ASD and ADHD are diagnosed according to a symptomatic and behavioural presentation and developmental history, both conditions have a strong genetic aetiology and are highly heritable with estimates of up to 85% for ASD (Yip et al., 2018) and 70-90% for ADHD (Farone et al., 2005; Levy, Hay, McStephen, Wood, & Waldman, 1997). Evidence of familiality comes from findings that first degree relatives of affected individuals often show subclinical behavioural or neurocognitive
difficulties characteristic of ASD and ADHD (Hoekstra, Bartels, Verweij, & Boomsma, 2007; Oerlemans et al., 2015; Rommelse et al., 2008; Schachar et al., 2005; Slaats-Willemsen, Swaab-Barneveld, De Sonneville, & Buitelaar, 2005). Furthermore, siblings of children with ASD have a greater likelihood of having ADHD than the general population (Ghirardi et al., 2018, 2019), and siblings of children with ADHD exhibit greater ASD symptoms than healthy controls (Mulligan et al., 2009) suggesting shared familiality. It is becoming clear that multiple genes are implicated in ASD and ADHD and these are associated with multiple biological systems. The genetic links may also transcend diagnostic categories, with twin studies providing evidence for shared genetic liability for ASD and ADHD (Ghirardi et al., 2018, 2019) and strong evidence for a degree of shared genetic aetiology (Rommelse et al., 2010).

Copy number variations (CNVs; Durand et al., 2007; Wang, Xu, Bey, Lee, & Jiang, 2014), de novo mutations (Iossifov et al., 2012; O’Roak et al., 1989; Roak et al., 2011; Sanders et al., 2012), and common genetic variation from Genome-Wide Association Studies (Gaugler et al., 2014; Grove et al., 2019) are all implicated in the genetic aetiology of ASD. Similarly, CNVs (Faraone & Larsson, 2019), rare variants (Hawi et al., 2016), and GWAS single nucleotide polymorphisms (SNPs; Demontis et al., 2019) are implicated in the genetics of ADHD. Nevertheless, despite known genetic and phenotypic overlap between ASD and ADHD, these disorders continue to be studied within their discrete diagnostic categories without consideration for their heterogeneity (Fischbach & Lord, 2010; Grove et al., 2019), and often with minimal consideration of the impact of comorbidities.

**The Research Domain Criteria (RDoC) and Hierarchical Taxonomy of Psychopathology (HiTOP): Complementary Frameworks for Research in ASD and ADHD**

As the search for biological causes and accurate ways to identify psychiatric disorders gains traction, there is a move away from categorical conceptualisations of disorders towards a more dimensional understanding of psychopathology (Coghill & Sonuga-Barke, 2012). The National Institute of Mental Health's (NIMH) Research Domain Criteria (RDoC) project (Insel, 2014; Insel et al., 2010) and the Hierarchical Taxonomy of Psychopathology (HiTOP) consortium (Kotov et al., 2017) represent complementary approaches to addressing the limitations of traditional categorical nosologies by using dimensional models of psychiatric and neurodevelopmental disorders evaluated at multiple levels of measurement.

The principal focus of RDoC is the analysis of dimensional phenomena at multiple levels of analysis across several core functional domains. These include behaviour, cognition, neural circuits, and genes in areas such as social processes and cognitive systems. These elements are organised within the RDoC matrix, which is primarily intended as a heuristic framework to encourage and facilitate psychiatric research that is unconstrained by traditional diagnostic categories.

The primary focus of HiTOP is the articulation of the structure of the symptoms of psychopathology, which are conceptualised as hierarchically organised dimensions (Kotov et al., 2017; Krueger et al., 2018). These dimensions can be studied at varying levels of generality and specificity to uncover shared and unique genetic, neurobiological, and clinical correlates (Conway et al., 2019; Latzman et al., 2020; Waszczuk et al., 2020). The RDoC and HiTOP approaches are thus complementary: the hierarchically organised phenotypic dimensions furnished by HiTOP provide the structural framework for exploring the functional domains and elements of the RDoC matrix (Krueger & Deyoung, 2016).

**Alignment of ASD and ADHD Neurocognitive Endophenotypes with the RDoC Matrix**

A number of neurocognitive traits have been identified as areas of difficulty for children with ASD and ADHD. Some neurocognitive domains are associated with similar levels of impairment across ASD and ADHD, while others appear to differentiate between them. Although atypical neurocognitive profiles are frequently observed at a group level, not all
individuals within a disorder show divergence across all behavioural and neurocognitive domains. This heterogeneity has hindered clinical translation of group-level findings to individuals (Brunsdon & Happé, 2014; D. R. Coghill, Seth, & Matthews, 2014; Craig et al., 2016; Dajani, Llabre, Nebel, Mostofsky, & Uddin, 2016; Demetriou, DeMayo, & Guastella, 2019; Faraone et al., 2015; Schachar et al., 2005; Uddin, 2020; Waddington et al., 2018a). Within ASD and ADHD, deficits are seen on tasks of sustained attention and arousal (Barkley, 1997; Bellgrove, Hawi, Kirley, Gill, & Robertson, 2005; Chien et al., 2016; Craig et al., 2016; Coghill, Seth, & Matthews, 2014; Dajani, Llabre, Nebel, Mostofsky, & Uddin, 2016; Demetriou, DeMayo, & Guastella, 2019; Faraone et al., 2015; Schachar et al., 2005; Uddin, 2020; Waddington et al., 2018a). Within ASD and ADHD, deficits are seen on tasks of sustained attention and arousal (Barkley, 1997; Bellgrove, Hawi, Kirley, Gill, & Robertson, 2005; Chien et al., 2016; Craig et al., 2016; Coghill, Seth, & Matthews, 2014; Dajani, Llabre, Nebel, Mostofsky, & Uddin, 2016; Demetriou, DeMayo, & Guastella, 2019; Faraone et al., 2015; Schachar et al., 2005; Uddin, 2020; Waddington et al., 2018a).

Social processes such as emotion recognition and/or theory of mind (e.g., Barneveld, De Sonneville, Van Rijn, Van Engeland, & Swaab, 2013; Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004; Quay, 1997; van der Plas, Dupuis, Arnold, Crosbie, & Schachar, 2016; Wodka et al., 2007; Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014), social processes such as emotion recognition and/or theory of mind (e.g., Barneveld, De Sonneville, Van Rijn, Van Engeland, & Swaab, 2013; Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004; Quay, 1997; van der Plas, Dupuis, Arnold, Crosbie, & Schachar, 2016; Wodka et al., 2007; Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014), and cognitive control, for example in inhibition (e.g., Barneveld, De Sonneville, Van Rijn, Van Engeland, & Swaab, 2013; Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004; Quay, 1997; van der Plas, Dupuis, Arnold, Crosbie, & Schachar, 2016; Wodka et al., 2007; Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014), social processes such as emotion recognition and/or theory of mind (e.g., Barneveld, De Sonneville, Van Rijn, Van Engeland, & Swaab, 2013; Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004; Quay, 1997; van der Plas, Dupuis, Arnold, Crosbie, & Schachar, 2016; Wodka et al., 2007; Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014), and reward sensitivity and decision-making (Johansen, Aase, Meyer, & Sagvolden, 2002; Mowinckel, Pedersen, Eilertsen, & Biele, 2015; Ziegler, Pedersen, Mowinckel, & Biele, 2016). Sensorimotor abnormalities are common in ASD. In particular, oculomotor deficits are robustly associated with ASD (Gargaro, Rinehart, Bradshaw, Tonge, & Sheppard, 2011; Johnson, Lum, Rinehart, & Fielding, 2016; Mosconi & Sweeney, 2015), with emerging evidence for oculomotor impairments in ADHD (Falck-Ytter et al., 2020). These areas of neurocognitive divergence broadly align with five RDoC matrix domains: positive valence systems, cognitive systems, arousal/regulatory systems, social processes and sensorimotor systems (Morris & Cuthbert, 2012; National Institute of Mental Health, 2018).

**Relationship between ASD and ADHD within HiTOP model**

Although dimensional models of psychopathology originated in the developmental literature (Achenbach & Edelbrock, 1978; Hudziak, Achenbach, Althoff, & Pine, 2007), neurodevelopmental disorders are yet to be fully integrated into the HiTOP model (Krueger et al., 2018). The HiTOP framework conceptualises psychopathology as a multi-dimensional hierarchy, with an overarching factor for general psychopathology, or ‘p’ factor, represented at the top of the hierarchy and reflecting a common liability for mental disorder (Caspi et al., 2014; Conway & Simms, 2020). Below this ‘p’ factor are super spectra; internalising, externalising, and psychosis; representing shared vulnerabilities to more specific ranges of problems. Internalising symptoms encompass depression, anxiety and somatic, eating and sexual difficulties, and subsumes the narrower and distinct subspectra of fear and distress. The externalising domain subsumes substance abuse and antisocial behaviours and is further differentiated into the disinhibited externalising (e.g. impulse-control problems) and antagonistic externalising (e.g. antisocial personality traits) subspectra. The psychosis super-spectra capture phenotypic variance related to psychotic disorders, but can be further differentiated into thought disorder (i.e. positive symptoms, experiences, and traits, such as reality distortion) and detachment (negative symptoms, experience, and traits, such as social withdrawal and emotional detachment). To date, the full HiTOP model is more clearly articulated in adult populations (Kotov et al., 2017; Krueger et al., 2018). However, the general ‘p’ factor and three major super-spectra (internalising, externalising, and psychosis) have been consistently replicated in children (e.g. McElroy, Belsky, Carragher, Fearon, & Patalay, 2018; Michelini et al., 2019) and adolescents (e.g. Carragher et al., 2015; Castellanos-Ryan et al., 2016; Martel et al., 2017).

ADHD symptoms have consistently been linked to the externalising spectrum in dimensional models of developmental psychopathology (Martel et al., 2017), with the exception of the ADHD inattentive subtype. However, debate continues regarding the exact relationship between ASD and other neurodevelopmental conditions with more common forms of internalising and externalising psychopathology, and whether they should be integrated within the same nosological framework (Ronald, 2019). The Child Behavior Checklist is one of the earliest developed and most widely-used measures of developmental psychopathology from a dimensional perspective, but does not have a scale that adequately evaluates the symptomatology of ASD (Achenbach, 2009). Few alternative measurement instruments include a comprehensive assessment of all dimensions of developmental psychopathology. Thus, very little progress has been made in understanding the relationship between ASD and other forms of developmental psychopathology, particularly ADHD, within the context of a hierarchical dimensional model.
To date, there have been no large-scale studies that have integrated the RDoC and HiTOP frameworks for exploring the phenotypic and genetic overlap between ASD and ADHD. Leveraging the RDoC and HiTOP approaches has the potential to pave the way for a unified nosology, which is biologically informed and has clinical application (Kotov et al., 2017; Latzman et al., 2020; Michellini, Palumbo, DeYoung, Latzman, & Kotov, 2020; Patrick & Hajcak, 2016). Symptom rating, behavioural measures and neurocognitive tasks selected to measure psychopathology, and more specifically core ASD-ADHD traits, will allow for characterisation of ASD-ADHD within an integrated RDoC-HiTOP framework. It is anticipated that this move away from categorical diagnostic groups characterised by clinical heterogeneity, towards data-driven dimensional approaches will facilitate more powerful and precise mapping of neurobiological correlates (Sanchez-Roige & Palmer, 2020; Sullivan et al., 2018; Waszczuk et al., 2020).

**Precision Phenotyping to Facilitate Genetic Discovery**

Current studies attempting to uncover the neurobiological correlates of ASD and ADHD typically take one of two approaches. The first approach aims to recruit large sample sizes to facilitate high powered genetic analyses, with the trade-off being that only surface level phenotyping of behaviour is typically captured (Sanchez-Roige & Palmer, 2020). The second approach recruits smaller samples with deeper phenotyping using multiple modalities and informants, at the cost of reduced sample sizes, lower statistical power and greater financial expense per participant (Sanchez-Roige & Palmer, 2020). Large biobanking projects for ASD (e.g. SFARI, [Abrahams et al., 2013], Australian Autism CRC biobank, [Alvares et al., 2018], and Norwegian Autism Birth Cohort [Stoltenberg et al., 2011]) and ADHD (Anney et al., 2008; Demontis et al., 2019) have achieved large sample sizes but only capture clinical symptom level data which provides minimal insight into the structure of developmental psychopathology and associated neurobiology. Other projects with more comprehensive phenotyping protocols including clinical, neurocognitive and imaging measures such as the EU-AIMS (LEAP) study (Loth et al., 2017), Biological Origins of Autism (BOA) study (Van Steijn et al., 2012), and ENIGMA-ADHD/ASD (Boedhoe et al., 2020; Hoogman et al., 2015, 2019, 2020). However, these projects typically confine recruitment to DSM-5 categories for either ASD or ADHD, either excluding on the basis of comorbidity or not accounting for the effects.

The NIMH-funded Bipolar Schizophrenia Network on Intermediate Phenotypes (B-SNIP) project applied a dimensional framework to schizophrenia and bipolar disorder. Like ASD and ADHD, schizophrenia and bipolar are highly heterogeneous disorders with significant phenotypic and genetic overlap. Using transdiagnostic dimensional measures of symptomatology and neurocognition associated with psychosis, B-SNIP derived biologically distinct subtypes through data reduction and cluster analysis techniques (Clementz et al., 2016). Each subtype had a distinct neurocognitive profile, and the prediction of independent clinically relevant outcomes within each psychosis subtype was superior to DSM-defined categories. Further, within each subtype, unaffected first-degree relatives showed similar, yet less compromised, patterns of neurocognitive performance. These similar patterns of performance between probands and unaffected relatives suggest familiality of profiles and thus the potential for shared genetic underpinnings.

A hierarchical approach to psychopathology and neurodevelopment, whereby phenotypic variation is dimensionally measured in both cases and key comparison groups, and at multiple levels of measurement, provides more specific phenotypic targets for genetic discovery (Waszczuk et al., 2020). This circumvents the current difficulties that broad heterogeneous diagnostic categories pose for mapping the underlying genetic architecture of psychiatric illness (Sanchez-Roige & Palmer, 2020; Waszczuk et al., 2020). Looking outside of the confines of DSM-defined diagnostic categories for genetic associations using a hierarchical framework will allow for identification of both general and specific levels of genetic risk. Indeed, GWAS studies suggest pleiotropy is prevalent in psychopathology, with multiple genes and common genetic variation implicated across a number of disorders (Sullivan et al., 2018; Waszczuk et al., 2020). Further, dimensional approaches confer substantially higher statistical power to detect trait-associated genetic variation (van der Sluis, Posthuma, Nivard, Verhage, & Dolan, 2013; van der Sluis, Verhage, Posthuma, & Dolan, 2010). Case-control designs have the potential to weaken the genetic signal, with classification of subthreshold cases as controls increasing the breadth of phenotypic and...
genetic variability within groups. In contrast, analysis of continuous phenotypes yields superior power in GWAS studies when compared to case-control designs (van der Sluis et al., 2013; Yang, Wray, & Visscher, 2010).

The Monash Autism-ADHD Genetics and Neurodevelopment (MAGNET) Project

To our knowledge there is no current study taking a truly transdiagnostic approach to understand the symptomatic, neurobiological (neurocognitive and neuroimaging) and genetic overlap between ASD and ADHD. A transdiagnostic sampling strategy that combines a family study design with deep dimensional phenotyping is needed across the ASD-ADHD spectra. By drawing on both RDoC and HiTOP frameworks, the MAGNET Project will contribute to our understanding of how neurodevelopmental disorders fit into a data-driven hierarchical taxonomy. Further, by understanding how these dimensional phenotypes present in families of children with ASD and ADHD, and whether siblings share similar behavioural signatures provide crucial evidence for familiality of different ASD-ADHD phenotypes. The MAGNET Project therefore aims to: 1) identify data-driven symptom clusters across ADHD-ASD spectra using deep phenotyping of symptoms and behaviours; 2) investigate the degree of familiality for these data-driven symptom clusters; 3) map the neurocognitive and brain imaging correlates of these data-driven symptom clusters; and 4) explore their genetic correlates.

Methods

Study Design

The MAGNET Project will enrol 1,200 families with children aged between 4 and 18 years of age. Children who are typically developing, as well as those with elevated ASD, ADHD, or ASD+ADHD symptoms will be recruited to ensure both ends of the ASD-ADHD spectra are appropriately sampled. In addition, unaffected and affected siblings of probands will be recruited. A dimensional enhancement approach to sampling will be taken, as it augments clinical samples with non-clinical participants and those exhibiting subthreshold symptoms (Cuthbert, 2014; Krueger & Bezdjian, 2009). This sampling strategy combines the strengths and offsets the weaknesses of categorical and dimensional approaches to psychopathology research by increasing statistical power whilst maintaining clinical validity and enabling direct comparisons with existing diagnostic classifications systems (Cuthbert, 2014; Helzer, Kraemer, & Krueger, 2006). The MAGNET Protocol comprehensively phenotypes all children and siblings, irrespective of case-control status, for behavioural and neurocognitive constructs that are central to ASD and ADHD symptomatology and align with RDoC and HiTOP frameworks (e.g. internalising and externalising symptoms, attention and cognitive control, arousal, reward, working memory, perception, social processes, and sensorimotor processes). The battery uniquely captures dimensional traits across ASD-ADHD spectra using a range of symptom, parent-report, neurocognitive, and direct behavioural observation measures to capture the target domains from multiple perspectives. This approach will provide a rich source of data unconfounded by informant bias and method bias, with the opportunity to model the correspondence and complex interactions of information obtained from multiple informants (Achenbach, 2006; De Los Reyes, Salas, Menzer, & Daruwalla, 2013; De Los Reyes, Thomas, Goodman, & Kundey, 2013; Patrick et al., 2013; Perkins, Latzman, & Patrick, 2020; Podsakoff, Mackenzie, & Podsakoff, 2012).

Targeted sampling through hospitals, schools, private practice clinicians, and social media across Victoria, Australia will allow for a broad and representative distribution of socioeconomic status (SES) and symptom presentation. Currently the MAGNET Project is in an open recruitment phase. The MAGNET Project will actively recruit females and children with mild-severe intellectual disability, as these children are typically under-represented, or excluded from, studies of ASD and ADHD. The study has been piloted on control and clinical children aged 4 to 17 years of age (see Table 1 for preliminary demographic and clinical data) to assist in deciding appropriate age and cognitive ranges for tasks and minimum dataset requirements. See Figure 1 for an overview of the MAGNET Project study protocol (see supplementary material 1 for the MAGNET Project Protocol).
Table 1.

Preliminary demographic and clinical data for the MAGNET Project for N=216 participants across Controls, Probands and Siblings.

| Total | Controls | Probands | Sibling Unaffected | Sibling Affected | Total |
|-------|----------|----------|--------------------|-----------------|------|
| ASD   | 33       | 95       | -                  | -               | 216  |
| ADHD  | -        | 25       | -                  | 8               | 34   |
| ASD/ADHD | -     | 27       | -                  | 4               | 32   |
| Sus. ASD/ADHD | - | -       | -                  | 13              | 27   |
| Sex   | Male     | 15       | 69                 | 18              | 119  |
| Female| 18       | 26       | 38                 | 15              | 97   |

Notes. ASD = Autism Spectrum Disorder. ADHD = Attention-Deficit/Hyperactivity Disorder. Sus. = suspected. Age = average age in months.

**Participant eligibility**

Children with a diagnosis of ASD and/or ADHD provide the clinical report from their clinician with evidence of diagnosis. Children who are under investigation, or queried for, ASD and/or ADHD are required to have a clinician (paediatrician, psychologist, and/or general practitioner) currently managing their care. Siblings of probands must share two biological parents with the proband. The healthy control children are required to have no neurodevelopmental diagnosis, and no first-degree relative with a diagnosis of ASD and/or ADHD.

Probands and siblings with comorbidities such as anxiety, depression, oppositional defiant disorder (ODD), and conduct disorder (CD) are not excluded. As a large proportion of children with ASD and ADHD experience comorbid disorders, exclusion of these disorders may engender a sample that is not representative of the target population. Where possible, one or both biological parents complete a battery of questionnaires examining ASD and ADHD symptomatology, mental health, and quality of life. Exclusion criteria for all children include known genetic (e.g. Fragile X, Angelman's Syndrome) or environmental (e.g. traumatic brain injury, foetal alcohol syndrome) causes. A peri/prenatal environment questionnaire retrospectively captures maternal alcohol and drug use, medication, illness/infection, and complications during the pregnancy and delivery. Retrospective information on the child's development, including developmental milestones and regression is obtained via parent-report. As the questionnaire battery is extensive, at least one parent/caregiver is required to speak English. Parents complete approximately 3 hours of online questionnaires, and one (control families) or two (clinical families) 3-hour research visits at Monash University to complete the testing protocol.

All children undergo case review by a registered psychologist and paediatrician, and speech pathologist if available, to determine a 'best clinical estimate' of that child's current diagnostic status. A best clinical estimate will be given for ASD, ADHD, comorbid ASD/ADHD, intellectual disability (ID), CD, and ODD (see supplementary material 2). The best clinical estimate will not be used as exclusion criteria for the study. Children who do not meet thresholds for ASD and/or ADHD will still provide useful information about the dimensionality of ASD and ADHD symptoms. Children with an estimated full-scale intelligence quotient (FSIQ) in the range for ID (IQ ≤ 70) as measured using standardised psychometric assessment (see Table 2) are administered a minimum dataset protocol (see supplementary material 3), but will attempt additional tasks from the battery wherever possible.

**Ethnicity.** Single-nucleotide polymorphisms (SNPs) may vary between ethnic populations and potentially cause false positive results in genetic association studies. To avoid the potential impact of population stratification only children with four grandparents of European ancestry are invited to complete the genetic component of the protocol.
Siblings. Only full biological siblings will be eligible to take part in the study. Within simplex families, that is, families where only one child has an ASD and/or ADHD diagnosis, the child with the ASD/ADHD diagnosis is nominated as the proband. In multiplex families, families where more than one child has an ASD and/or ADHD diagnosis, the eldest child is denoted as the proband and younger children are designated as affected or unaffected siblings. Unaffected siblings of ASD/ADHD probands have no diagnosis of ASD/ADHD, are not under investigation for ASD/ADHD, and are not assigned a neurodevelopmental disorder diagnostic category during their best clinical estimate review.

Medication.

The child's current and previous medication history, medication prescriber (e.g. paediatrician, general practitioner), and reasons for any medication changes, will be recorded.

Children who are taking medication remain on their medication during Visit 2 when their relevant Wechsler and Autism Diagnostic Observation Schedule – Second Edition (ADOS-2) assessments are completed (see supplementary material 4 for clinical assessment protocol). However children taking stimulant or non-stimulant medication for ADHD including methylphenidate, lisdexamfetamine, or dexamfetamine are required to withdraw from their medication 48 – 72 hours prior to completing the neurocognitive test battery during Visit 1 (Chamberlain et al., 2011; Mostofsky, Lasker, Cutting, Denckla, & Zee, 2001). Participants taking guanfacine or antipsychotics (e.g. risperideone, aripiprazole) do not withdraw for any component of the protocol as abrupt withdrawal from these medications may be associated with adverse side effects (Howland, 2010; Strange, 2008; Zamboulis & Reid, 1981). Children taking melatonin are not required to withdraw prior to participating.

Phenotyping overview

Each of the measures or tasks included were selected as gold standard measures that are widely used, have biological plausibility, and show robust effect sizes when differentiating controls from either ASD or ADHD (See Table 2 for the MAGNET Project symptom and environmental phenotyping measures, and Table 3 for neurocognitive phenotyping measures).

The components of the MAGNET protocol intended to measure phenotypic dimensions relevant to ASD were chosen in consultation and collaboration with the European Autism Interventions - A Multicentre Study for Developing New Medications – Longitudinal European Autism Project (EU-AIMS [LEAP]) study team (Isaksson et al., 2018; Loth et al., 2017). The EU-AIMS (LEAP) study is a European multi-centre study that aims to identify risk factors contributing to differences in brain development, social difficulties and other core ASD symptoms. Through aligning parts of the MAGNET and EU-AIMS (LEAP) protocols, the MAGNET project will also act as a replication site for the EU-AIMS (LEAP) study. The addition of measures for dimensional phenotyping of ADHD symptoms and relevant neurocognitive traits are unique to the MAGNET project and make ours the first large-scale family-based project to take a truly transdiagnostic approach to understanding ASD and ADHD (see supplementary material 1 for MAGNET protocol summary).

Characterisation of ASD, ADHD and comorbid symptoms

Dimensional ASD symptomatology is measured through parent-report measures capturing social communication (Autism Quotient - Child [AQ-C], Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008; Child Communication Checklist - Second Edition [CCC-2], Bishop, 2003; Social Responsive Scale - Second Edition [SRS-2], Constantino, 2011), social competence (Child Behaviour Checklist [CBCL], Achenbach & Edelbrock, 1983), restricted, repetitive, and stereotyped behaviours (Constantino, 2011; The Childhood Routines Inventory - Revised [CRI-R], Evans, Uljarević, Lusk, Loth, & Frazier, 2017), and autism symptomatology overall (Auyeung et al., 2008; Constantino, 2011). Dimensional traits central to ADHD are captured through parent-report questionnaires, and an in-house observation checklist for ADHD behaviours completed during ADOS-2 coding. Parent rated measures of attention and inattention (Strengths and Weaknesses of ADHD Symptoms and Normal Behaviour
Application development and wellbeing assessment [DAWBA], Goodman, Ford, Richards, Gatward, & Meltzer, 2000), hyperactivity (Aberrant Behaviour Checklist [ABC], Aman & Singh, 1986; Strengths and Difficulties Questionnaire [SDQ], Goodman, 1997; Goodman et al., 2000), impulsivity, and overall ADHD symptomatology (Conners et al., 1998), are comprehensively assessed, alongside an additional measure of attention appropriate for children with intellectual disability (Scale of Attention in Intellectual Disability [SAID], Freeman, Gray, Taffe, & Cornish, 2015). Teachers are invited to complete the SRS-2, SDQ, and Conners’ Teacher Rating Scale – Revised (Conners, 1997), although completion rates are typically lower than for parent report. Height, weight, head circumference, and joint mobility and hypomobility (Beighton & Horan, 1969) are also recorded for every child.

**Comorbidities.** Comorbidities commonly observed in ASD and ADHD are captured in all children, including anxiety (Child Behaviour Checklist [CBCL], Achenbach & Rescorla, 2001; Spence Children’s Anxiety Scale [SCAS], Spence, 1998) and depression (Achenbach & Rescorla, 2001; Goodman et al., 2000; Childhood Depression Inventory - Second Edition [CDI-2], Kovacs & Beck, 1977; Smucker, Craighead, Craighead, & Green, 1986). Conduct problems and oppositional defiant problems are also indexed (Achenbach & Rescorla, 2001; Conners et al., 1998; Goodman et al., 2000). Level of current cognitive function is determined using age appropriate Wechsler intelligence scales (Wechsler, 2011, 2012a, 2012b, 2016). See supplementary material 4 for clinical assessment protocol.

**Adaptive behaviours and quality of life**

Adaptive behaviour (Vineland Adaptive Behaviour Scale - Third Edition [VABS-3]; Sparrow, Cicchetti, & Saulnier, 2016) and quality of life (Child Health and Illness Profile - Child Edition [CHIP-CE], Riley et al., 2004) are measured in all children through parent-report questionnaires.

**Language assessment.**

Language profiles in ASD are heterogeneous, ranging from non-verbal (Gerenser, 2009) to superior linguistic abilities (Kim et al., 2014). Although language impairments are not a hallmark diagnostic criteria for ADHD, both linguistic and pragmatic deficits are commonly part of the symptom presentation (Bellani, Moretti, Perlini, & Brambilla, 2011). Recent empirical records on the co-occurrence of language impairments in ASD and ADHD have identified impairments in structural and pragmatic aspects of language in both the groups (Baixauli-Fortea, Miranda Casas, Berenguer-Forner, Colomer-Diago, & Roselló-Miranda, 2019; Kuijper, Hartman, Bogaards-Hazenberg, & Hendriks, 2017; Norbury, Gemmell, & Paul, 2014; Sciberras et al., 2014). Despite the presence of language difficulties in ASD and ADHD, and indeed, in a number of other neurodevelopmental disorders and psychopathology, language constructs are not currently included in RDoC or HiTOP frameworks. Thus, the inclusion of language assessments in the MAGNET Project protocol will provide a novel and unique contribution to these nosologies.

A standardised screening measure for language difficulties (Clinical Evaluation of Language Fundamentals - Fifth Edition [CELF-5]: Screening Test; Wiig, Secord, & Semel, 2013) is administered to all enrolled children over 5 years of age. Children with a diagnosis of ASD and/or ADHD or those who are under investigation for these disorders, and control children who fall below criterion on the screening measure for language difficulties, are administered the Australian adaptation of the Clinical Evaluation of Language Fundamentals - Fifth Edition (CELF-5; Age group 5 to 21 years; Coret & McCrimmon, 2015; Wiig, Semel, & Secord, 2017) or Clinical Evaluation of Language Fundamentals – Preschool Edition (CELF-P2; Age group 3 to 6 years 11 months; Semel, Wiig, & Secord, 2004). This clinician-administered assessment provides a comprehensive global measure of language abilities, and characterises structural and pragmatic language in children.

The Preschool Language Scale – Fifth Edition (PLS-5; Zimmerman, Steiner, & Pond, 2011) is administered to younger minimally verbal children. The PLS-5 incorporates information from clinical observation, direct measurement and parent report to assess domains of attention, play, gesture, vocal development, social communication, semantics, language structure, integrative language skills and emergent literacy skills in children from birth to 7 years 11 months. A parent
administered, Children's Communication Checklist 2 (Bishop, 2003) measures both structural (language form / content) and pragmatic traits of communication impairment in children. The CCC-2 includes an overall measure of communication skills and a Social Interaction Deviance Composite (SIDC) which indexes the strength of relationships between the social domains of communication and structural components of language, thereby aiming to attain and identify traits associated with pragmatic language difficulties. With poorer overall language performance and SIDC linked to ASD traits (Bishop, 2003), these measures provide valuable information when differentiating comorbid presentations of language impairment in neurodevelopmental disorders. The SRS-2 also provides a parent-reported index of social communication. Recordings from the ADOS-2 provide high-resolution natural speech and language samples. See supplementary material 4 for clinical assessment protocol.

**Measures of Neurocognition**

We assess the domains of sustained attention, inhibition, cognitive control, arousal, reward, working memory, perception, social processes, and sensorimotor processes with the view to utilising neurocognitive data to discover neurobiological correlates of novel ASD-ADHD data-driven clusters. The tasks chosen are widely used, have biological plausibility and show robust effects sizes when differentiating clinical cases from controls. See Table 2 for the MAGNET Project neurocognitive phenotyping measures. Supplementary material 5 summarises the MAGNET Project's neurocognitive assessment protocol.

**Neurocognitive tasks.**

The neurocognitive tasks will be completed on a desktop computer and touchscreen laptops. Amsterdam Neuropsychological Tasks (ANT), Psytools, PsychoPy and STOP-IT software programmes were used for task administration (De Sonneville, 1999; Delosis, 2018; Peirce, 2007; Verbruggen, Logan, & Stevens, 2008).

**Response inhibition, sustained attention and cognitive control.** Response inhibition refers to the ability to withhold or cancel a motor response (Chambers, Garavan, & Bellgrove, 2009). Sustained attention, or vigilance, can be defined as the ability to maintain engagement in a task over a prolonged period of time (Fortenbaugh, Degutis, & Esterman, 2018). This component of attention is thought to be mediated by top down, or endogenous processes, and is controlled by internal goals (Morandini et al., 2020). These cognitive functions are measured using a Go/No-Go and Stop Signal Task which are standard measures of top-down/endogenous sustained attention and response inhibition. Response inhibition is indexed through stop-signal reaction time (SSRT) and the percentage of failed attempts to inhibit a response on tasks. Longer stop signal reaction times and commission errors indicate poor inhibition and more omission errors and are indicative of poorer sustained attention (Verbruggen & Logan, 2008). Response inhibition and sustained attention deficits are central to the conceptualisation of ADHD (Barkley, 1997; M. A. Bellgrove, Hawi, Gill, & Robertson, 2006; Quay, 1997; Wodka et al., 2007; Wright et al., 2014), with some support for deficits in ASD (Barneveld et al., 2013; Chien et al., 2015; Johnston, Madden, Bramham, & Russell, 2011; Schmitt et al., 2019; van der Plas et al., 2016). Further, these deficits are heritable, with unaffected siblings of ADHD probands demonstrating response inhibition and sustained attention difficulties (Chien et al., 2017; Friedman et al., 2016; Schachar et al., 2005; Slaats-Willemse et al., 2005). Similarly, reduced inhibitory control has been demonstrated to be familial in ASD families (Schmitt et al., 2019).

**Arousal.** Arousal can be understood as an individual's state of reactivity, and although arousal is intimately linked with constructs like attention, the neural correlates of these processes are largely distinct (Coull, 1998). Arousal will be examined by deriving measures of intra-individual variability in response times across tasks of sustained attention and response inhibition, as suboptimal arousal is thought to underpin intra-individual variability in ADHD (M. A. Bellgrove et al., 2006; M. a Bellgrove et al., 2005; Castellanos et al., 2005; Sergeant, 2000). Increased response time variability is a hallmark feature of neurocognitive performance in ADHD (Bellgrove et al., 2005; Johnson, Kelly, et al., 2008a; Johnson et al., 2008, 2007; Shallice et al., 2002) and is familial (Kuntsi et al., 2010; Nigg, Blaskey, Stawicki, & Sachek, 2004). Variability in response time is thought to be a marker for dysfunction in the frontal areas of the brain (M. a Bellgrove, Hester, & Garavan, 2004; MacDonald, Nyberg, & Bäckman, 2006), which is consistent with theories of hypo-arousal and fronto-striatal dysfunction in
ADHD (Cupertino et al., 2020; Satterfield, Cantwell, & Satterfield, 1974). Although children with ASD show similar response time variability to typically developing children (Johnson et al., 2007), variability in response time appears to index ADHD symptomatology across diagnostic boundaries as children with comorbid ASD and ADHD show similar variability to those with ADHD (Tye et al., 2016). Thus, response time variability as a proxy measure for arousal shows promise for effectively stratifying children with ASD, ADHD and ASD-ADHD.

**Reward sensitivity.** Reward sensitivity refers to the tendency to respond more strongly to incentives, or rewards, and is a process implicated in decision making. ADHD is associated with divergent decision making, differing sensitivity to reward, and elevated risk-taking behaviour (Dekkers, Popma, Agelink van Rentergem, Bexkens, & Huizenga, 2016; Johansen et al., 2002; Luman, Tripp, & Scheres, 2010; Ziegler et al., 2016). Effect sizes for decision making difficulties are comparable to the attention difficulties seen in ADHD (Mowinckel et al., 2015). Altered reward processing in ADHD is well-studied, and posited as central to the disorder (Taurines et al., 2012). Children with ADHD show poorer decision making as they have difficulty adjusting their responses in the face of changing levels of risk (D. R. Coghill et al., 2014; Groen, Gaastra, Lewis-Evans, & Tucha, 2013; Sørensen et al., 2017). Biological plausibility is evidenced with correlative neuroimaging in ADHD of under activation in brain regions associated with decision making (i.e. ventral and dorsolateral prefrontal cortex, and insula; Broche-Pérez, Herrera Jiménez, & Omar-Martínez, 2016; Ernst et al., 2003) and hyporesponsiveness in neural circuitry involved with reward anticipation (i.e. ventral striatal circuitry; Scheres, Milham, Knutson, & Castellanos, 2007). Dopamine is one of the neurotransmitters implicated in decision making and reward, and indeed, dopamine deficiency is a leading hypothesis in ADHD (Ziegler et al., 2016). Together, a task engaging decision making, reward sensitivity, and risk-taking behaviour is a well-positioned ADHD trait for discovery of clusters.

In ASD, there is evidence for aberrant reward processing, but to a lesser extent than that observed in ADHD (Kohls et al., 2011; Taurines et al., 2012). Children with ASD showed increased activation in the anterior cingulate cortex during reward achievement compared to controls (Schmitz et al., 2008). This region is thought to be involved with self-monitoring of performance in line with reward feedback (Bloom & Hynd, 2005; Rogers et al., 2004) and risk assessment (Bush, Luu, & Posner, 2000). However, there is some evidence to suggest ASD and control groups perform similarly on goal-directed decision making tasks in the context of explicit reward (Faja, Murias, Beauchaine, & Dawson, 2013) and have similar sensitivity to monetary reward (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2011; Stavropoulos & Carver, 2014), with no difference in neural activation while processing reward (Larson, South, Krauskopf, Clawson, & Crowley, 2011). The less definitive evidence in ASD may indicate that only a subgroup of these children may in fact have altered reward processing and decision making.

To assess decision making, reward sensitivity, and risk-taking, the New Cambridge Gambling Task (Cambridge Cognition, 2018a) will be used. It allows for delineation of risk-taking behaviours from impulsivity, and explicitly states the probability for each trial. Unlike other gambling tasks (e.g. Iowa Gambling Task), explicit statement of probability reduces the working memory load, thus reducing confounds of additional working memory deficits.

**Probabilistic reversal learning.** Broadly, cognitive flexibility is a component of executive function that encompasses adaptability at a behavioural level and is studied from a variety of perspectives such as set shifting, task-switching, and reversal learning (Cools, 2015). More specifically, contingency-related cognitive flexibility is the adaptation of behaviour after negative feedback, typically measured using probabilistic reversal learning paradigms. In typical development, contingency-related cognitive flexibility specifically is associated with the orbitofrontal cortex, parietal cortex, and subcortical connections (Fineberg et al., 2014). Impairments in contingency-related cognitive flexibility are seen in ASD (Corbett et al., 2009; D’Cruz et al., 2013) and ADHD probands (Itami & Uno, 2002; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), with impairments also observed in unaffected first degree relatives of ASD probands (Schmitt et al., 2019). In ASD, cognitive inflexibility has been associated with restricted, repetitive, and stereotyped behaviours (D’Cruz et al., 2013; Lopez, Lincoln, Ozonoff, & Lai, 2005; Miller, Ragozzino, Cook, Sweeney, & Mosconi, 2015). Neuroimaging findings demonstrate aberrant activation of networks during cognitive flexibility tasks in children with ASD (Uddin, 2020) and fronto-striatal function, which is implicated in cognitive flexibility, is thought to be impaired in ADHD (Casey et al., 1997; Durston et al., 2003). In the MAGNET Project
contingency-related cognitive flexibility will be measured using a probabilistic reversal learning paradigm with positive and negative feedback (Loth et al., 2017; van Ouden et al., 2013). The number of trials required to shift to a new response choice, perseverative errors, and regressive errors index cognitive inflexibility.

2. The MAGNET Project Symptom Phenotyping Measures.
| Tasks                                      | Attention | Working Memory | Speech & Language | Social Processes | Cognitive Control | Reward | Sensorimotor | Perception |
|-------------------------------------------|-----------|----------------|-------------------|------------------|------------------|--------|--------------|------------|
| WISC-V/WPPSI-IV/WAIS-IV/WAIS-II           | X         | X              | X                 |                  | X                | X      | X            | X          |
| Dimensional measures of ASD traits        |           |                |                   |                  |                  |        |              |            |
| ADOS-2 + 3DI                              | X         | X              | X                 |                  |                  |        |              |            |
| Childhood & Adult Routines Inventory     |           |                |                   |                  |                  |        |              |            |
| Autism Quotient                           | X         |                | X                 | X                |                  | X      | X            | X          |
| Social Responsiveness Scale               |           | X              | X                 |                  |                  |        |              |            |
| Dimensional measures of ADHD traits       |           |                |                   |                  |                  |        |              |            |
| Conners' Parent Rating Scale - Revised   | X         | X              | X                 | X                | X                | X      |              | X          |
| SWAN                                      | X         |                |                   |                  |                  |        |              | X          |
| Scale of Attention in Intellectual Disability | X         | X              |                   |                  |                  |        |              | X          |
| Comorbid Symptoms                         |           |                |                   |                  |                  |        |              |            |
| Aberrant Behaviour Checklist              |           |                |                   |                  |                  |        |              |            |
| Child Behaviour Checklist                 |           |                |                   |                  |                  |        |              |            |
| DAWBA                                      | X         |                | X                 | X                | X                | X      | X            | X          |
| Children's Communication Checklist 2      |           |                |                   |                  |                  |        |              |            |
| CELF-5                                    | X         | X              | X                 | X                | X                | X      | X            | X          |
| CELF-P2                                   | X         | X              | X                 |                  |                  |        |              | X          |
| PLS-5                                     | X         |                | X                 |                  |                  |        |              | X          |
| PEP-3                                     | X         | X              | X                 | X                |                  |        |              | X          |
| Strengths and Difficulties Questionnaire  | X         |                |                   |                  |                  |        |              | X          |
| Spence                                    |           |                |                   |                  |                  |        |              |            |
| Childhood Anxiety Scale                   |           |                |                   |                  |                  |        |              |            |
| Childhood Depression Inventory            |           |                |                   |                  |                  |        |              |            |
| Beck                                      |           |                |                   |                  |                  |        |              |            |
| Beck Anxiety Inventory                    |           |                |                   |                  |                  |        |              |            |
| Domain general rating scales              |           |                |                   |                  |                  |        |              |            |
| Child Health and Illness Profile          | X         | X              |                   |                  |                  |        |              | X          |
| WHO Quality of Life Questionnaire         |           |                |                   |                  |                  |        |              | X          |
| Vineland Adaptive Behaviour Scale         | X         | X              | X                 | X                |                  |        |              | X          |

*Note. WISC-V = Wechsler Intelligence Scale for Children - Fifth Edition. WPPSI-IV = Wechsler Preschool and Primary Scale of Intelligence - Fourth Edition. WAIS-IV = Wechsler Adult Intelligence Scale - Fourth Edition. SWAN = Strengths and Weaknesses of ADHD symptoms and Normal Behaviour. DAWBA = Development and Well-Being Assessment. CELF-5 = Clinical Evaluation of Language Fundamentals - Fifth edition. CELF-P2 = Clinical Evaluation of Language Fundamentals - Preschool-2. PLS-5 = Preschool Language Scales - Fifth Edition. PEP-3 = Psychoeducation Profile - Third Edition. WHO = World Health Organisation.*
Table 3. The MAGNET Project Neurocognitive Phenotyping Measures.

| Neurocognitive Tasks | Attention | Working Memory | Speech & Language | Social Processes | Cognitive Control | Reward | Sensorimotor | Perception |
|---------------------|-----------|----------------|-------------------|-----------------|------------------|--------|--------------|------------|
| Go/No-Go            |           | X              |                   | X               |                   |        |              |            |
| Stop Signal         |           | X              |                   | X               | X                |        |              |            |
| Task                |           |                |                   |                 |                  |        |              |            |
| Reflexive saccade   |           |                |                   | X               | X                |        |              |            |
| Antisaccades        |           |                |                   | X               | X                |        |              |            |
| Sinusoidal pursuit  | X         |                |                   | X               | X                |        |              |            |
| Step-ramp pursuit   |           |                |                   | X               | X                |        |              |            |
| Spatial             |           | X              |                   | X               | X                |        |              |            |
| Working Memory      |           |                |                   |                 |                  |        |              |            |
| Probabilistic       | X         |                |                   |                 | X                |        |              |            |
| Reversal Learning   |           |                |                   |                 |                 |        |              |            |
| Cambridge Gambling  | X         |                |                   | X               | X                |        |              |            |
| Task Facial         | X         | X              |                   |                 |                 |        |              |            |
| Recognition Task    |           |                |                   |                 |                 |        |              |            |
| Karolinska Directed |           |                |                   |                 |                 |        | X            |            |
| Emotional Faces     |           |                |                   |                 |                 |        |              |            |
| Reading the Mind in | X         | X              |                   |                 |                 |        |              |            |
| the Eyes            |           |                |                   |                 |                 |        |              |            |
| Continuous          |           |                |                   |                 |                 |        | X            |            |
| False Belief task   |           |                |                   |                 |                 |        |              |            |

Note. WISC-V = Wechsler Intelligence Scale for Children - Fifth Edition.

Working memory. Internationally, the definitions of working memory are contentious, with working memory and short-term memory sometimes still used interchangeably. Some conceptualise working memory as the process of holding information in the mind for a short period of time, which can also be thought of as short-term memory (Gleitman, Fridlund, & Reisberg, 1999). Others understand working memory, also referred to as executive memory, as the ability to maintain and manipulate information, where this manipulation may have low or high executive demands (Baddeley, 1986; Daneman & Carpenter, 1980). Tasks are then modality specific, using verbal or visual stimuli. The MAGNET Project's conceptualisation of working memory aligns with executive memory that has high and low executive demands. Verbal and visual working memory difficulties are seen in both ASD and ADHD (Dowson et al., 2004; Kercood, Grskovic, Banda, & Begeske, 2014; Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Schoechlin & Engel, 2005; Schuh & Eigsti, 2012; Seng et al., 2020), with deficits becoming more pronounced as the cognitive load increases (Rhodes et al., 2004, 2005; Seng et al., 2020; Steele, Minshew, Luna, & Sweeney, 2007; Vogan, Francis, Morgan, Smith, & Taylor, 2018). These difficulties on working memory tasks with higher cognitive load correspond with atypical neural processing in children with ASD (Rahko et al., 2016; Vogan et al., 2018), providing biological plausibility for working memory performance as a neurocognitive marker of ASD. Further, unaffected siblings of children with ASD and ADHD showed more impaired verbal and visuospatial working memory performance than typically developing controls (Rhodes et al., 2004, 2005; Seng et al., 2020). The verbal and visuospatial working memory divergence seen in unaffected siblings of children with ASD and ADHD positions working memory as a good candidate endophenotype (Flint & Munafò, 2007; Miller & Rockstroh, 2013). Verbal (Wechsler, 2008, 2016; Wig et al., 2013, 2017) and visuospatial (Cambridge Cognition, 2018b, 2018c) working memory tasks which increase in cognitive load across trials allows us to index working memory capacity across the broad range of cognitive abilities captured in the study.

Social Processes.

Emotion recognition. Emotion recognition is the ability to correctly identify another person's emotion based on their facial expression and is crucial for effective social communication. Emotion recognition difficulties in children with ASD are a consistent and robustly replicated finding (Harms et al., 2010; Ujarevic & Hamilton, 2013). Atypical processing of emotions is also thought to be familial, with unaffected relatives of individuals with ASD also showing less severe, but still significant emotion recognition difficulties (das Neves et al., 2011; Oerlemans et al., 2014). Although emotion recognition is not as extensively researched in ADHD, there is some evidence for emotion recognition divergence in these children (Aspan et al., 2014; Bora & Pantelis, 2016; Demopoulos, Hopkins, & Davis, 2013; Waddington et al., 2018b). Emotion recognition in the MAGNET project is conceptualised, and measured, as the ability to recognise both simple and complex emotional states (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Goeleven, De Raedt, Leyman, & Verschuere, 2008).

Theory of Mind. Theory of Mind (ToM) is the ability to understand and attribute mental states to oneself and to others and understand that others can have different mental states to yourself. Profound difficulties with understanding others’ thoughts and intentions in day-to-day life are common in ASD (Peterson et al., 2009). These difficulties with ToM have been
linked to genetic anomalies associated with ASD (Rodrigues, Saslow, Garcia, John, & Keltner, 2009). False-belief tasks are widely used for assessing ToM and individuals with ASD typically show egocentric biases when completing these tasks compared to their typically developing peers (Begeer, Bernstein, van Wijhe, Scheeren, & Koot, 2012). These difficulties are less definitive in high functioning individuals with ASD however, with some able to successfully complete continuous false-belief tasks (Scheeren, de Rosnay, Koot, & Begeer, 2013). The ability of such a task to separate different individuals with ASD positions it well to stratify these individuals. Conversely, the findings within ADHD are currently heterogeneous. More research is necessary to understand whether these deficits are present in only a subset of these children (Pineda-Alhucema, Aristizabal, Escudero-Cabarcas, Acosta-López, & Vélez, 2018).

### Oculomotor measures

Saccade and pursuit eye movement abnormalities have the potential to reliably distinguish ASD and ADHD children from controls (Johnson et al., 2016). Oculomotor abnormalities can arise as the result of abnormalities in a range of well-mapped neural circuitry throughout the brain, spanning motion sensitive visual area V5, parietal and frontal areas supporting visual attention and sensorimotor transformation, basal ganglia, brainstem and cerebellar circuitry (Johnson et al., 2016). Oculomotor control is ideal to measure in children, as it is quick, and affords sensitive, high-resolution recording, and requires minimal-to-no language comprehension for children to perform. Sensorimotor measures from ocular motor tasks include accuracy, motor dynamics (e.g. velocity profiles), initial eye acceleration in response to the onset of a visual target or target movement and integration of visual feedback in motor responses. The anti-saccade task, completed in children eight years and over, also provides a measure of how attentional processes and inhibition interface with oculomotor control (Everling & Fischer, 1998; Hutton & Ettinger, 2006; Klein & Foerster, 2001; Munoz & Everling, 2004). Other studies in schizophrenia and bipolar disorder have found unique relationships between genes associated with nervous system development and function and with sensorimotor processing and pursuit maintenance (Lencer et al., 2017). See supplementary material 6 for oculomotor testing protocol.

### Brain structure and function

Large-scale neuroimaging studies have identified robust structural differences associated with ASD and ADHD, demonstrating both common and disorder-specific brain alterations. In both ASD and ADHD, cases showed reduced subcortical volumes (Hoogman et al., 2017; Van Rooij et al., 2018) and cortical thinning in temporal regions (Hoogman et al., 2019; Van Rooij et al., 2018). Reduced surface areas were specific to ADHD (Hoogman et al., 2019), whereas ASD showed increased cortical thickness in frontal regions (Van Rooij et al., 2018). Evidence regarding differences in diffusion weighted imaging (DWI) and resting state fMRI (rs-fMRI) are based on smaller studies demonstrating wide-spread alterations in fractional anisotropy (Di, Azeez, Li, Haque, & Biswal, 2018; van Ewijk, Heslenfeld, Zwierts, Buitelaar, & Oosterlaan, 2012) and less consistent changes in rsfMRI (Lau, Leung, & Lau, 2019; Zhou et al., 2019).

Structural and functional brain imaging (resting state fMRI) will be collected to determine if neurobiological differences exist as a function of symptom-based data-driven clusters. All scans will be performed using Siemens Skyra 3T scanner following previously established protocols (Oldham et al., 2020; Sabariedin et al., 2019). Data processing pipelines will include extensive correction for in-scanner motion (Oldham et al., 2020; Parkes, Fülscher, Yücel, & Fornito, 2018) which is the most prevalent MRI artefact in paediatric populations.

### Genetics

Saliva is collected from all probands, affected and unaffected biological siblings, biological parents of probands, and healthy controls for DNA extraction (see supplementary material 7 for DNA collection and extraction protocol). DNA will be subjected to array-based genotyping (e.g. Illumina Global Screen Array for GWAS) and/or whole genome sequencing, as funding allows. Because our study sample size has limited power to reliably detect novel associations with DNA variants, we will capitalise on existing publicly available data and consortia science in the following ways. First, we will derive Polygenic Risk Scores (PGRS; Choi & O’Reilly, 2019; Euesden, Lewis, & O’Reilly, 2015) for ASD and ADHD using international datasets as the base dataset (Demontis et al., 2019; Grove et al., 2019) and our entire sample of probands as the target dataset. We will estimate the relationships between polygenic risk scores for ADHD and/or ASD and each of our symptom-based data-driven clusters. Second, our family-based design is optimal for whole genome sequencing and will allow us to determine whether patterns of inherited versus de novo mutations differentially cluster across the data-driven clusters. Again, we acknowledge the limited power of our sample for whole genome sequencing, and will join collaborative efforts (e.g. PGC, iPSYCH, Autism Speaks MSSNG Project; EU-Aims; Province of Ontario Neurodevelopmental Network [POND]).

### Parent phenotyping

Both biological parent’s complete self-report dimensional measures of ASD (Autism Quotient - Adults [AQ-A, Broadbent, Galic, & Stokes, 2013; SRS-2, Constantino, 2011; Adult Routines Inventory [ARI], Evans et al., 2017] and ADHD symptomatology (SWAN, Arnett et al., 2013; Conners’ Adult ADHD Rating Scale, Conners, Erhardt, & Sparrow, 1999; SDQ, Goodman, 1997). Parent’s complete self-report measures of depression (Beck Depression Inventory [BDI], Beck, Ward, Mendelson, & Erbaugh, 1961), anxiety (Beck Anxiety Inventory [BAI], Beck, Epstein, Brown, & Steer, 1988), and a quality of
life measures (World Health Organisation Quality of Life Measure [WHOQOL-BREF], WHOQOL Group, 1996) as parents of children with ASD and ADHD can experience poorer mental health and quality of life outcomes compared to parents with typically developing children (Green et al., 2015; Kvist, Nielsen, & Simonsen, 2013; Walton, 2019).

Database access

All raw data is stored on a central database with access only granted to current members of the research team who have personalised login details. Oculomotor and neuroimaging data are downloaded to local devices from the central database for cleaning, pre-processing, and analysis. Currently, access to the MAGNET Project's data is only granted for members of the MAGNET research team and our collaborators from the EU-AIMS (LEAP) study (Loth et al., 2017). Genotyping information will be made available to international research consortia, such as the PGC, where participant consent for sharing has been given. Upon completion of the project, the MAGNET Project data set will be changed to open access. Consent for sharing neuroimaging data will be in line with recommendations from the Open Brain Consent working group (Open Brain Consent, 2020).

Planned statistical analysis

A combination of supervised psychometric analyses and unsupervised clustering approaches will be used to converge on data-driven homogeneous ASD-ADHD clusters embedded within biologically-relevant dimensions based on previously derived factor score estimates (Borsboom, Rhemtulla, Cramer, Maas, & Scheffer, 2016; Feczko et al., 2019). By using multiple measures of target constructs to create latent variable phenotypes, we can maximise our study’s statistical power and strengthen the representation of our key constructs (van der Sluis et al., 2010). Obtaining information from multiple informants controls for informant bias, whilst discrepancies between informant reports provides additional sources of information relevant to developmental psychopathology that can be the subject of further analysis (De Los Reyes, Salas, et al., 2013; De Los Reyes, Thomas, et al., 2013). Moreover, the MAGNET Project's representative sample and measures are important prerequisites for robust clustering methods to avoid model overfitting and poor reproducibility (Bzdok, Altman, & Krzywinski, 2018; Rashid & Calhoun, 2020).

Dimension reduction strategies, such as exploratory factor analysis and exploratory structural equation modelling (Asparouhov & Muthén, 2009; Costello & Osborne, 2005; Marsh, Morin, Parker, & Kaur, 2014), or multidimensional item response theory (Reckase, 2009), will be used on each participant’s raw scores to first identify their factor or scale score estimates representing their standing on these latent dimensions. Unbiased feature selection and optimising latent model fit in this step, prior to later clustering analyses, can reduce the interference of variance from extraneous noise. It is also acknowledged that there may be clustering and nesting within the data based on sampling (e.g. participants from the same family) and testing (e.g. testing sessions, assessors) procedures (Clarke, 2008; McNeish, 2014). Subsequent analyses will account for these effects, though the choice of correction method will depend on the characteristics of our final dataset.

Factor mixture modelling is one possible supervised clustering method that we will employ for our subtyping analyses. Factor mixture modelling can uncover homogeneous clusters within continuous and categorical data embedded within dimensional models of psychopathology by utilising probabilistic modelling techniques (Borsboom et al., 2016; Lubke & Muthén, 2005; Miettunen, Nordström, Kaakinen, & Ahmed, 2016). The flexibility of factor mixture modelling permits the testing and comparison of multiple models with varying numbers of a priori specified clusters. Alternatively, where unsupervised machine learning techniques may be better suited for addressing specific research questions, community detection is one possible approach. This method combines graph theoretic analyses to detect homogeneous communities/clusters (i.e. highly connected sets of nodes). By ensuring that the algorithm achieves a connected graph, our analyses will parsimoniously account for all participants. These approaches empirically unify the theoretical grounding of MAGNET’s research questions with the power of cutting-edge data-driven analysis techniques. Moreover, both techniques are diagnosis-naive, thus allowing MAGNET to fully embrace the transdiagnostic features of our biobehavioural subtypes. Normative modelling can also be incorporated to better understand heterogeneity, wherein inter-individual differences are mapped in reference to a normative sample, to help map typical development, as well as understanding true deviations from the norm (Marquand, Rezek, Buitelaar, & Beckmann, 2016). Finally, although MAGNET aims towards data-driven clusters using symptom and behavioural data, the potential utility of incorporating neurocognitive or genetic components in defining clusters will not be overlooked (Clementz et al., 2016; Fair, Bathula, Nikolas, & Nigg, 2012).

Discussion

The MAGNET Project has completed initial piloting of the study protocol and entered into an open recruitment phase. It is the first large-scale study using a family design to take a truly transdiagnostic approach to ASD and ADHD that aligns with the principles of the RDoC matrix and HiTOP model of psychopathology.

Challenges in Study Design, Recruitment, and Data Quality
**Study design.**

A significant amount of time is required in the conceptualisation of an assessment battery that is appropriate for the large range of cognitive abilities and ages, while adequately capturing dimensional ASD and ADHD traits. As a number of the measures included in the protocol were not initially intended for use across broad age ranges or levels of cognitive ability, it is important to allow for extra time during piloting to determine the minimum age and cognitive level for tasks with novel applications. Although such an approach required more time initially, it will translate into a high-quality dataset upon project completion.

One of the measures used to confirm an ASD diagnosis, the ADOS-2, was chosen as it is internationally recognised as part of gold standard assessment. Uniquely, all children who participate in the MAGNET Project complete an ADOS-2. The ADOS-2 research training dictates coding of observed behaviours with no clinical interpretation to ensure research-reliable coding. Differentiating the social difficulties of children with ADHD on the ADOS-2 can be challenging, which has also been previously noted by Grzdzinski and colleagues (Grzdzinski et al., 2016). ADOS data from children with ASD and ADHD also has the potential to improve clinical phenotyping across the ASD-ADHD spectra. Analysis of individual ADOS items may elucidate which items are more sensitive to ASD and which items are driven by ADHD presentations. Clinical cases are reviewed using all measures, including the ADOS-2 and the DAWBA, by the team’s paediatrician and psychologist to determine a best clinical estimate (see supplementary material 2). The best clinical estimate process has been imperative in confirming diagnostic status.

**Recruitment.**

The inclusion of children with ID will facilitate a sample that is largely representative of our target population, specifically within ASD. However, recruitment uptake for families of children with ID has been slow. These families often have children with high treatment needs which can be time consuming, in turn reducing the likelihood of these parents enrolling in a time-intensive research protocol. An alternative targeted recruitment strategy for these families will be needed moving forward, including direct communication with specialist school settings to engage teaching staff in the recruitment process for their learning community. Partnering with community grant funds and the Australian National Disability Insurance Scheme (NDIS) are further strategies the MAGNET team intends to utilise for recruitment of these children.

As ASD and ADHD are highly heritable, with evidence for shared genetic liability in families, this inherently limits the number of possible unaffected siblings. A large number of families with children with ASD and/or ADHD will therefore be required to achieve sufficient numbers of unaffected siblings for high powered statistical analysis.

**Data quality.**

A number of the large-scale biobanking projects and multi-site studies can experience significant missingness in their data. Protecting against missing data has been a key priority in the MAGNET Project protocol development. Initial piloting highlighted that ensuring parents completed all online questionnaires before attending the in-person research visits reduced missing data, and increased attendance rates to research visits. Comprehensive data collection at the initial point of contact with families will also allow us to determine if attrition and resulting missingness is attributed to characteristics of the family or child, thus allowing us to model the missingness and avoid bias in our results. With the oversight from the project’s supervising psychologist, families are provided with a results summary after participating, including outcomes from cognitive assessments, language assessments (where applicable), ASD and ADHD symptom scales, and ADOS-2 ratings. To increase retention rates between the first and second research visit for each family, the neurocognitive tasks are completed in the first research visit and the cognitive assessment and ADOS-2 are completed in the second. Importantly, other measures used in the best clinical estimate review, such as the DAWBA, are completed prior to participants first research visit. Saliva collection from all members of the family pedigree has also been challenging, especially from fathers. Currently we have noted that
mothers will primarily bring children to their research visits. Good follow-up and regular contact with the family is imperative in ensuring the least amount of missing genetic data. Minimal manual handling of data with automatic backups of all clinical, neurocognitive, and oculomotor data reduces the risk of missing data through technical or human error. Sophisticated analysis strategies to manage missingness will be utilised by the MAGNET Project that accommodates some missing data under assumptions of Missing Completely At Random, or Missing At Random, such as multiple imputation, auxiliary variables, and expectations-maximisation algorithm (Enders, 2010; Graham, 2009).

The diversity of clinical specialists on the MAGNET Project team, including psychologists, cognitive neuroscientists, paediatricians, psychiatrists, and speech pathologists, is relatively unique. When research teams are large, this increases potential variability in administration of assessments, and thus variability in data quality. The MAGNET Project team undergo regular and ongoing staff training and clinical supervision from the project’s supervising psychologist. As a result, all members are consistently building skills to maximise participant engagement and data-capture across all tasks and assessments.

Limitations

It is possible that the MAGNET Project’s sampling strategy will not achieve a true community sample upon completion. However, a variety of recruitment avenues and methods will be utilised to achieve a sample with breadth in symptomatology and phenotype. The project will provide insight into ASD and ADHD’s place within a hierarchical taxonomy of psychopathology and neurodevelopment. Although the study primarily targets traits central to these disorders, the full breadth of neurodevelopmental difficulties and common comorbidities (e.g. anxiety) are not captured with the same degree of granularity. The MAGNET Project will therefore provide one piece of the much larger puzzle in the quest for understanding neurodevelopment in a hierarchical framework. The broad range of cognitive abilities captured by the project, which allows a more representative sample, also means a proportion of children with more severe ID may not be able to complete all neurocognitive and/or imaging protocols. Nevertheless, our minimum dataset protocol is designed to provide minimal missing data across key tasks.

Conclusion

Clinical heterogeneity and unitary conceptualisations of ASD and ADHD have hampered attempts to understand the structure of developmental psychopathology and associated neuropsychology, neurobiology and genetics. Current attempts to uncover the genetic aetiology of ASD/ADHD are limited with respect to one or more of the following: 1) recruitment is restricted to diagnostic categories that ignore the dimensional organisation of psychopathology symptoms, comorbidity, and within-group heterogeneity (Krueger et al., 2018); 2) minimal phenotyping in large samples; or 3) deep phenotyping in smaller samples (Sanchez-Roige & Palmer, 2020). Using deep phenotyping, dimension reduction techniques, factor mixture modelling, and machine learning techniques, the MAGNET Project aims to identify unique, homogeneous ASD-ADHD clusters of individuals with similar behavioural, neurocognitive, neuroimaging and, potentially, genetic profiles. The MAGNET Project will be one of the first studies to combine a dimensional conceptualisation of developmental psychopathology, in combination with deep phenotyping in a large sample to investigate the behavioural, neurocognitive, neuroimaging and genetic markers in ASD and ADHD. This study is well-positioned to uncover novel, homogeneous data-driven clusters with potential implications for ASD and ADHD diagnosis and treatment.

Declarations

Ethics approval and consent to participate.

This study was approved by the Monash University Human Research Ethics Committee (CF16/1537 - 2016000806), Department of Education and Training Victoria Human Research Ethics Committee (2017_003570), and Monash Health
Human Research Ethics Committee (RES-19-0000-372A). It will comply with the conditions of these ethics committee approvals, and the NHMRC National Statement on ethical Conduct in Human Research (2018).

**Consent for publication.**

Consent for publication was obtained from all participants prior to the study.

**Availability of data and materials.**

Currently MAGNET Project data is stored on a central database with access currently granted to members of the research team and our collaborators from the EU-AIMS (LEAP) study (Loth et al., 2017). Upon study completion database access will be opened to the scientific community.

**Competing interests.**

No conflicts of interest to report.

**Funding.**

The MAGNET Project is supported by a grant from the Federal Department of Health of Australia under Medical Research Future Fund (MRFF) Emerging Priorities and Consumer-Driven Research initiative. B.P.J is supported by the Peter Doherty Early Career Fellowship (APP1112348) from the National Health and Medical Research Council (NHMRC) of Australia and the Medical Research Future Fund (EPCD000002) from the Department of Health Australia. M.A.B is supported by a Senior Research Fellowship (Level B) from the NHMRC of Australia.

**Authors contributions.**

R.K, B.J, J.T, O.M, A.F, K.K, M.K, V.P.M, Z.H, K.F, K.H, K.W, A.U, A.F, K.G, D.C, A.N, D.P, E.L, L.M, D.M, J.B and M.A.B contributed to study design, developed data acquisition and/or analysis protocols. R.K, B.J, O.M, A.F, K.K, M.K, V.P.M, D.M, E-C.M, and K.F collected data. RK wrote the first and final draft. B.J, J.T, O.M, K.K, V.P.M, A.A, T.C, K.H, K.W, and M.A.B contributed to writing the manuscript. All authors read and approved the final manuscript.

**Acknowledgements.**

A huge thank you to all the families who have participated so far.

**References**

1. Abrahams BS, Arking DE, Campbell DB, Mefford HC, Morrow EM, Weiss LA, ... Packer A. SFARI Gene 2.0: A community-driven knowledgebase for the Autism Spectrum Disorders (ASDs). Molecular Autism. 2013;4(1):2–4. https://doi.org/10.1186/2040-2392-4-36.

2. Achenbach TM. As others see us: Clinical and research implications of cross-informant correlations for psychopathology. Curr Dir Psychol Sci. 2006;15(2):94–8. https://doi.org/10.1111/j.0963-7214.2006.00414.x.

3. Achenbach TM. The Achenbach System of Empirically Based Assessment (ASEBA): Development, Findings, Theory, and Applications. Burlington: University of Vermont Research Center for Children, Youth and Families; 2009.
4. Achenbach TM, Edelbrock CS. The classification of child psychopathology: A review and analysis of empirical efforts. Psychol Bull. 1978;85:1275–301. https://doi.org/10.1037/0033-2909.85.6.1275.

5. Achenbach TM, Edelbrock CS. Manual for the Child Behaviour Checklist and Revised Child Behaviour Profile. Burlington: Vermont; 1983. (D. of P. University of Vermont, Ed.).

6. Achenbach TM, Rescorla LA. Manual for the ASEBA school-age forms & profiles: An integrated system of mult-informant assessment. Burlington: Vermont: University of Vermont, Research Center for Children, Youth & Families; 2001.

7. Alvares GA, Dawson PA, Dissanayake C, Eapen V, Gratten J, Grove R, ... Whitehouse AJO. Study protocol for the Australian autism biobank: an international resource to advance autism discovery research. BMC Pediatrics. 2018;18(1):284. https://doi.org/10.1186/s12887-018-1255-z.

8. Aman MG, Singh NN. Aberrant Behavior Checklist. East Aurora: Slosson; 1986.

9. Anney RJL, Hawi Z, Sheehan K, Mulligan A, Pinto C, Brookes KJ, ... Gill M. Parent of origin effects in attention/deficit hyperactivity disorder (ADHD): Analysis of data from the international multicenter ADHD genetics (IMAGE) program. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics. 2008;147(8):1495–500. https://doi.org/10.1002/ajmg.b.30659.

10. Arnett AB, Pennington BF, Friend A, Willcutt EG, Byrne B, Samuelsson S, Olson RK. The SWAN captures variance at the negative and positive ends of the ADHD symptom dimension. Journal of Attention Disorders. 2013;17(2):152–62. https://doi.org/10.1177/1087054711427399.

11. Aspa N, Bozsik C, Gadoros J, Nagy P, Inantsy-Pap J, Vida P, Halasz J. (2014). Emotion recognition pattern in adolescent boys with Attention-Deficit/Hyperactivity Disorder. BioMed Research International, 2014, 761340. https://doi.org/10.1155/2014/761340.

12. Asparouhov T, Muthén B. (2009). Exploratory structural equation modeling. In Structural Equation Modeling (Vol. 16). https://doi.org/10.1080/10705510903008204.

13. Association AP, American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington: American Psychiatric Publishing; 2013.

14. Auyeung B, Baron-Cohen S, Wheelwright S, Allison C. The Autism Spectrum Quotient: Children's version (AQ-Child). J Autism Dev Disord. 2008;38(7):1230–40. https://doi.org/10.1007/s10803-007-0504-z.

15. Baddeley A. Working memory. Oxford: Oxford University Press; 1986.

16. Baixauli-Forteà I, Miranda Casas A, Berenguer-Forner C, Colomer-Diago C, Roselló-Miranda B. Pragmatic competence of children with Autism Spectrum Disorder. Impact of theory of mind, verbal working memory, ADHD symptoms, and structural language. Applied Neuropsychology: Child. 2019;8(2):101–12. https://doi.org/10.1080/21622965.2017.1392861.

17. Barkley RA. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. 121(c), 65–94.

18. Barneveld PS, De Sonneville L, Van Rijn S, Van Engeland H, Swaab H. Impaired response inhibition in autism spectrum disorders, a marker of vulnerability to schizophrenia spectrum disorders? J Int Neuropsychol Soc. 2013;19(6):646–55. https://doi.org/10.1017/S1355617713000167.

19. Baron-Cohen S, Jolliffe T, Mortimore C, Robertson M. Another advanced test of theory of mind: Evidence from very high functioning adults with autism or asperger syndrome. J Child Psychol Psychiatry. 1997;38(7):813–22. https://doi.org/10.1111/j.1469-7610.1997.tb01599.x.

20. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol. 1988;56:893–7.

21. Beck AT, Ward CH, Mendelson MM, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4:561–71.

22. Begeer S, Bernstein DM, van Wijhe J, Scheeren AM, Koot HM. A continuous false belief task reveals egocentric biases in children and adolescents with Autism Spectrum Disorders. Autism. 2012;16(4):357–66.
23. Beighton P, Horan F. Orthopaedic aspects of the Ehlers-Danlos syndrome. The Journal of Bone Joint Surgery British Volume. 1969;51(3):444. https://doi.org/10.1302/0301-620X.51B3.444.

24. Bellani M, Moretti A, Perlini C, Brambilla P. Language disturbances in ADHD. Epidemiology Psychiatric Sciences. 2011;20(4):311–5. https://doi.org/10.1017/S2045796011000527.

25. Bellgrove MA, Hawi Z, Gill M, Robertson IH. The cognitive genetics of attention deficit hyperactivity disorder (ADHD): Sustained attention as a candidate phenotype. Cortex. 2006;42(6):838–45. https://doi.org/10.1016/S0010-9452(08)70426-X.

26. Bellgrove M, Hawi Z, Kirley A, Gill M, Robertson IH. Dissecting the attention deficit hyperactivity disorder (ADHD) phenotype: sustained attention, response variability and spatial attentional asymmetries in relation to dopamine transporter (DAT1) genotype. Neuropsychologia. 2005;43(13):1847–57. https://doi.org/10.1016/j.neuropsychologia.2005.03.011.

27. Bellgrove M, Hester R, Garavan H. The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. Neuropsychologia. 2004;42(14):1910–6. https://doi.org/10.1016/j.neuropsychologia.2004.05.007.

28. Bidwell LC, Willcutt EG, DeFries JC, Pennington BF. Testing for neuropsychological endophenotypes in siblings discordant for Attention-Deficit/Hyperactivity Disorder. Biol Psychiat. 2007;62(9):991–8. https://doi.org/10.1016/j.biopsych.2007.04.003.

29. Bishop D. Child Communication Checklist - Second Edition. Sydney: Pearson Clinical: Second; 2003.

30. Bloom JS, Hynd GW. The role of the corpus callosum in interhemispheric transfer of information: Excitation or inhibition? Neuropsychol Rev. 2005;15(2):59–71. https://doi.org/10.1007/s11065-005-6252-y.

31. Boedhoe PSW, van Rooij D, Hoogman M, Twisk JWR, Schmaal L, Abe Y, … van den Heuvel OA. Subcortical brain volume, regional cortical thickness, and cortical surface area across disorders: Findings from the ENIGMA ADHD, ASD, and OCD working groups. Am J Psychiatry. 2020;177(9):834–43. https://doi.org/10.1176/appi.ajp.2020.19030331.

32. Bora E, Pantelis C. Meta-analysis of social cognition in attention-deficit/hyperactivity disorder (ADHD): Comparison with healthy controls and autistic spectrum disorder. Psychol Med. 2016;46(4):699–716. https://doi.org/10.1017/S0033291715002573.

33. Borsboom D, Rhemtulla M, Cramer AOJ, Maas HLJ, Van Der, Scheffer M. (2016). Kinds versus continua: A review of psychometric approaches to uncover the structure of psychiatric constructs. (2016), 1567–1579. https://doi.org/10.1017/S0033291715001944.

34. Broche-Pérez Y, Jiménez H, L. F., & Omar-Martínez E. Neural substrates of decision-making. Neurología (English Edition). 2016;31(5):319–25. https://doi.org/10.1016/j.nrleng.2015.03.009.

35. Brunsdon VEA, Happé F. Exploring the "fractionation" of autism at the cognitive level. Autism. 2014;18(1):17–30. https://doi.org/10.1177/1362361314534545.

36. Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. Trends in Cognitive Sciences. 2000;4(6):215–22. https://doi.org/10.1016/S1364-6613(00)01483-2.

37. Bzdok D, Altman N, Krzywinski M. Statistics versus machine learning. Nat Methods. 2018;15(4):233–4. https://doi.org/10.1038/nmeth.4642.

38. Cambridge Cognition. (2018a). Cambridge Gambling Task (CGT).

39. Cambridge Cognition. (2018b). Cambridge Neuropsychological Test Automated Battery [CANTAB]. Cognitive Assessment Software.

40. Cambridge Cognition. (2018c). Spatial Working Memory (SWM).

41. Carragher N, Teesson M, Sunderland M, Newton NC, Krueger RF, Conrod PJ, … Slade T. The structure of adolescent psychopathology: A symptom-level analysis. Psychol Med. 2015;46(5):981–94.
42. Casey BJ, Castellanos FX, Giedd JN, Marsh WL, Hamburger SD, Schubert AB, … Rapoport JL. Implication of right frontostriatal circuitry in response inhibition and Attention-Deficit/Hyperactivity Disorder. J Am Acad Child Adolesc Psychiatry. 1997;36(3):374–83. https://doi.org/10.1097/00004583-199703000-00016.

43. Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, … Moffitt TE. The p factor: One general psychopathy factor in the structure of psychiatric disorders? Clinical Psychological Science. 2014;2(2):119–37. https://doi.org/10.1177/2167702613497473.

44. Castellanos-Ryan N, Briere FN, O'Leary-Barrett M, Banaschewski T, Bokde A, Bromberg U. … The IMAGEN Consortium. (2016). The structure of psychopathology in adolescence and its common personality and cognitive correlates. J Abnorm Psychol, 125(8), 1039–52. https://doi.org/10.1037/abn0000193.

45. Castellanos FX, Sonuga-Barke EJS, Scheres A, Di Martino A, Hyde C, Walters JR. Varieties of attention-deficit/hyperactivity disorder-related intra-individual variability. Biol Psychiat. 2005;57(11):1416–23. https://doi.org/10.1016/j.biopsych.2004.12.005.

46. Chamberlain SR, Robbins TW, Winder-Rhodes S, Miller U, Sahakian BJ, Blackwell AD, Barnett JH. Translational approaches to frontostriatal dysfunction in Attention-Deficit/Hyperactivity Disorder using a computerized neuropsychological battery. Biol Psychi. 2011;69(12):1192–203. https://doi.org/10.1016/j.biopsych.2010.08.019.

47. Chambers CD, Garavan H, Bellgrove MA. Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. Neurosci Biobehav Rev. 2009;33(5):631–46. https://doi.org/10.1016/j.neubiorev.2008.08.016.

48. Chien YL, Chou MC, Chiu YN, Chou WJ, Wu YY, Tsai WC, Gau SSF. (2017). ADHD-related symptoms and attention profiles in the unaffected siblings of probands with autism spectrum disorder: Focus on the subtypes of autism and Asperger's disorder. Molecular Autism, 8(1). https://doi.org/10.1186/s13229-017-0153-9.

49. Chien YL, Gau SS-F, Shang C-Y, Chiu Y-N, Tsai W-C, Wu Y-Y. (2015). Visual memory and sustained attention impairment in youths with autism spectrum disorders. Psychol Med, 45(11), 2263–73. https://doi.org/10.1017/S0033291714003201.

50. Choi SW, O'Reilly PF. PRSice-2: Polygenic Risk Score software for biobank-scale data. GigaScience. 2019;8(7):1–6. https://doi.org/10.1093/gigascience/giz082.

51. Clarke P. When can group level clustering be ignored? Multilevel models versus single-level models with sparse data. J Epidemiol Community Health. 2008;62(8):752–8. https://doi.org/10.1136/jech.2007.060798.

52. Clementz BA, Sweeney JA, Hamm JP, Ileva EL, Ethridge LE, Pearson GD, … Tammimia CA. Identification of distinct psychosis biotypes using brain-based biomarkers. Am J Psychiatry. 2016;173(4):373–84. https://doi.org/10.1176/appi.ajp.2015.14091200.

53. Coghill DR, Seth S, Matthews K. A comprehensive assessment of memory, delay aversion, timing, inhibition, decision making and variability in attention deficit hyperactivity disorder: Advancing beyond the three-pathway models. Psychol Med. 2014. https://doi.org/10.1017/S0033291713002547.

54. Coghill D, Sonuga-Barke EJS. Annual research review: Categories versus dimensions in the classification and conceptualisation of child and adolescent mental disorders - Implications of recent empirical study. J Child Psychol Psychiatry. 2012;53(5):469–89. https://doi.org/10.1111/j.1469-7610.2011.02511.x.

55. Conners CK. Conners' Rating Scales - Revised: User's Manual. Incorporated: Multi-Health Systems; 1997.

56. Conners CK, Erhardt D, Sparrow E. Conners Adult ADHD Rating Scales (CAARS). Toronto: Pearson; 1999.

57. Conners CK, Sitarenios G, Parker JDA, Epstein JN. The revised Conners’ Parent Rating Scale (CPRS-R): Factor structure, reliability, and criterion validity. J Abnorm Child Psychol. 1998;26(4):257–68. https://doi.org/10.1023/A:1022602400621.

58. Constantino JN. Social Responsiveness Scale, Second Edition (SRS-2). Torrence: Western Psychological Services; 2011.

59. Conway C, Forbes MK, Forbush KT, Fried EI, Hallquist MN, Kotov R, … Eaton NR. A Hierarchical Taxonomy of Psychopathology can transform mental health research. Perspectives on Psychological Science. 2019;14(3):419–36. https://doi.org/10.1177/1745691618810696.
60. Conway C, Simms LJ. Maximizing the applied value of structural models of psychopathology: Introduction to a special issue of Personality and Mental Health. Personality Mental Health. 2020;14(1):3–8. https://doi.org/10.1002/pmh.1474.

61. Cools R. (2015). Neuropsychopharmacology of cognitive flexibility. In Brain Mapping: An Encyclopedic Reference (Vol. 3). https://doi.org/10.1016/B978-0-12-397025-1.00253-0.

62. Cooper M, Martin J, Langley K, Hamshere M, Thapar A. Autitic traits in children with ADHD index clinical and cognitive problems. Eur Child Adolesc Psychiatry. 2014;23:23–34. https://doi.org/10.1007/s00787-013-0398-6.

63. Corbett BA, Constantine LJ, Hendren R, Rocke D, Ozonoff S. Examining executive functioning in children with autism spectrum disorder, attention deficit hyperactivity disorder and typical development. Psychiatry Res. 2009;166(2–3):210–22. https://doi.org/10.1016/j.psychres.2008.02.005.

64. Coret MC, McCrimmon AW. (2015). Test Review: Wiig, Semel EH, & Secord WA. (2013). Clinical Evaluation of Language Fundamentals–Fifth Edition (CELF-5). Journal of Psychoeducational Assessment, 33(5), 495–500. https://doi.org/10.1177/0734282914557616.

65. Costello AB, Osborne JW. (2005). Best practices in exploratory factor analysis: Four recommendations for getting the most from your analysis. Practical Assessment, Research and Evaluation, 10(7).

66. Coull JT. Neural correlates of attention and arousal: Insights from electrophysiology, functional neuroimaging and psychopharmacology. Prog Neurobiol. 1998;55(98):343–61. https://doi.org/10.10016/S0301-0082(98)00011-2.

67. Craig F, Margari F, Legrottaglie AR, Palumbi R, de Giambattista C, Margari L. A review of executive function deficits in Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder. Neuropsychiatric Disease Treatment. 2016;12:1191–202. https://doi.org/10.2147/NDT.S104620.

68. Cupertino RB, Soheili-Nezhad S, Grevet EH, Bandeira CE, Picon FA, Tavares ME, de A, … Sprooten, E. Reduced fronto-striatal volume in Attention-Decit/Hyperactivity Disorder in two cohorts across the lifespan. Neurolmage: Clinical. 2020;28(June):102403. https://doi.org/10.1016/j.nicl.2020.102403.

69. Cuthbert BN. The RDoC framework: Facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. World Psychiatry. 2014;13(1):28–35. https://doi.org/10.1002/wps.20087.

70. C’D’Cruz AM, Ragozzino ME, Mosconi MW, Shrestha S, Cook EH, Sweeney JA. Reduced behavioral flexibility in Autism Spectrum Disorders. Neuropsychology. 2013;27(2):152–60. https://doi.org/10.1037/a0031721.

71. Dajani DR, Llabre MM, NEbel MB, Mostofsky SH, Uddin LQ. Heterogeneity of executive functions among comorbid neurodevelopmental disorders. Sci Rep. 2016;6:1–10. https://doi.org/10.1038/srep36566.

72. Daneman M, Carpenter PA. (1980). Individual differences in working memory and reading. Journal of Verbal Learning and Verbal Behaviour, 19(4), 450–466. https://doi.org/0022-5371/80/040450-17$02.00/0.

73. das Neves MDCL, Tremeau F, Nicolato R, Lauar H, Aurelio M, Romano-Silva MA, Correa H. Facial emotion recognition deficits in relatives of children with autism are not associated with 5HTTLPR. Revista Brasileira de Psiquiatria. 2011;33(3):261–7.

74. De Los Reyes A, Salas S, Menzer MM, Daruwala SE. Criterion validity of interpreting scores from multi-informant statistical interactions as measures of informant discrepancies in psychological assessments of children and adolescents. Psychol Assess. 2013;25(2):509–19. https://doi.org/10.1037/a0032081.

75. De Los Reyes A, Thomas SA, Goodman KL, Kundey SMA. Principles underlying the use of multiple informants’ reports. Annu Rev Clin Psychol. 2013;9(1):123–49. https://doi.org/10.1146/annurev-clinpsych-050212-185617.

76. De Sonneville LMJ. Amsterdam Neuropsychological Tasks: A computer-aided assessment program. Computers In Psychology. 1999;6:187–203.

77. Dekkers TJ, Popma A, Agelink van Rentergem JA, Bexkens A, Huizenga HA. Risky decision making in Attention-Deficit/Hyperactivity Disorder: A meta-regression analysis. Clin Psychol Rev. 2016;45:1–16. https://doi.org/10.1016/j.cpr.2016.03.001.

78. Delosis. (2018). Psytools. London, UK.
79. Demetriou EA, DeMayo MM, Guastella AJ. Executive function in Autism Spectrum Disorder: History, theoretical models, empirical findings, and potential as an endophenotype. Front Psychiatry. 2019;10(November):1–17. https://doi.org/10.3389/fpsyt.2019.00753.

80. Demontis D, Walters RK, Martin J, Mattheisen M, Als TD, Agerbo E, ... Neale BM. Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. Nat Genet. 2019;51(1):63–75. https://doi.org/10.1038/s41588-018-0269-7.

81. Demopoulos C, Hopkins J, Davis A. A comparison of social cognitive profiles in children with Autism Spectrum Disorders and Attention-Deficit/Hyperactivity Disorder: A matter of quantitative but not qualitative difference? J Autism Dev Disord. 2013;43(5):1157–70. https://doi.org/10.1007/s10803-012-1657-y.

82. Demurie E, Roeyers H, Baeyens D, Sonuga-Barke E. Common alterations in sensitivity to type but not amount of reward in ADHD and Autism Spectrum Disorders. J Child Psychol Psychiatry. 2011;52(11):1164–73. https://doi.org/10.1111/j.1469-7610.2010.02374.x.

83. Di X, Azeez A, Li X, Haque E, Biswal BB. (2018). Disrupted focal white matter integrity in Autism Spectrum Disorder: A voxel-based meta-analysis of diffusion tensor imaging studies. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 82(November 2017), 242–248. https://doi.org/10.1016/j.pnpbp.2017.11.007.

84. Dowson JH, McLean A, Bazanis E, Toone B, Young S, Robbins TW, Sahakian BJ. Impaired spatial working memory in adults with attention-deficit/ hyperactivity disorder: Comparisons with performance in adults with borderline personality disorder and in control subjects. Acta Psychiatr Scand. 2004;110(1):45–54. https://doi.org/10.1111/j.1600-0447.2004.00292.x.

85. Durand CM, Betancur C, Boeckers TM, Bockmann J, Chaste P, Fauchereau F, ... Bourgeron T. Mutations in the gene encoding the synaptic scaffolding protein SHANK3 are associated with autism spectrum disorders. Nat Genet. 2007;39(1):25–7. https://doi.org/10.1038/ng1933.

86. Durston S, Tottenham NT, Thomas KM, Davidson MC, Eigsti IM, Yang Y, ... Casey BJ. Differential patterns of striatal activation in young children with and without ADHD. Biol Psychiat. 2003;53(10):871–8. https://doi.org/10.1016/S0006-3223(02)01904-2.

87. Enders CK. Applied missing data analysis. New York: The Guilford Press; 2010.

88. Ernst M, Kimes AS, London ED, Matochik JA, Eldreth D, Tata S, ... Bolla K. Neural substrates of decision making in adults with attention deficit hyperactivity disorder. Am J Psychiatry. 2003;160(6):1061–70. https://doi.org/10.1176/appi.ajp.160.6.1061.

89. Euesden J, Lewis CM, O’Reilly PF. PRSice: Polygenic Risk Score software. Bioinformatics. 2015;31(9):1466–8. https://doi.org/10.1093/bioinformatics/btu848.

90. Evans DW, Uljarević M, Lusk LG, Loth E, Frazier T. Development of two dimensional measures of restricted and repetitive behavior in parents and children. Journal of the American Academy of Child Adolescent Psychiatry. 2017;56(1):51–8. https://doi.org/10.1016/j.jaac.2016.10.014.

91. Everling S, Fischer B. (1998). The antisaccade: a review of basic research and clinical studies. Neuropsychologia, 36(9), 774–788. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9740362.

92. Fair DA, Bathula D, Nikolas MA, Nigg JT. Distinct neuropsychological subgroups in typically developing youth inform heterogeneity in children with ADHD. Proc Natl Acad Sci USA. 2012;109(17):6769–74. https://doi.org/10.1073/pnas.1115365109.

93. Faja S, Murias M, Beauchaine TP, Dawson G. Reward-based decision making and electrodermal responding by young children with Autism Spectrum Disorders during a gambling task. Autism Res. 2013;6(6):494–505. https://doi.org/10.1002/aur.1307.

94. Falck-Ytter T, Pettersson E, Bölte S, D’Onofrio B, Lichtenstein P, Kennedy DP. Difficulties maintaining prolonged fixation and attention-deficit/hyperactivity symptoms share genetic influences in childhood. Psychiatry Res. 2020;293(August):4–6. https://doi.org/10.1016/j.psychres.2020.113384.
95. Faraone SV, Asherson P, Banaschewski T, Biederman J, Buitelaar JK, Ramos-Quiroga JA, ... Franke B. (2015). Attention-deficit/hyperactivity disorder. *Nature Reviews Disease Primers*, 1. https://doi.org/10.1038/nrdp.2015.20.

96. Faraone SV, Larsson H. Genetics of Attention Deficit Hyperactivity Disorder. *Mol Psychiatry*. 2019;24(4):562–75. https://doi.org/10.1038/s41380-018-0070-0.

97. Faraone SV, Perlis RH, Doyle AE, Smoller JW, Goralnick JJ, Holmgren MA, Sklar P. Molecular genetics of Attention-Deficit/Hyperactivity Disorder. *Biol Psychiat*. 2005;57(1):1313–23. https://doi.org/10.1016/j.biopsych.2004.11.024.

98. Feczko E, Miranda-Dominguez O, Marr M, Graham AM, Nigg JT, Fair DA. The heterogeneity problem: Approaches to identify psychiatric subtypes. *Trends in Cognitive Sciences*. 2019;23(7):584–601. https://doi.org/10.1016/j.tics.2019.03.009.

99. Fineberg NA, Chamberlain SR, Goudriaan AE, Stein DJ, Vanderschuren LJMJ, Gillan CM, ... Potenza MN. New developments in human neurocognition: Clinical, genetic, and brain imaging correlates of impulsivity and compulsivity. *CNS Spectr*. 2014;19(1):69–89. https://doi.org/10.1017/S1092852913000801.

100. Fischbach GD, Lord C. The Simons Simplex Collection: A resource for identification of autism genetic risk factors. *Neuron*. 2010;68(2):192–5. https://doi.org/10.1016/j.neuron.2010.10.006.

101. Flint J, Munafò MR. The endophenotype concept in psychiatric genetics. *Psychol Med*. 2007;37(2):163–80. https://doi.org/10.1017/S0033291706008750.

102. Fortenbaugh FC, Degutis J, Esterman M. Recent theoretical, neural, and clinical advances in sustained attention research. *Ann N Y Acad Sci*. 2018;1396(1):70–91. https://doi.org/10.1111/nyas.13318.Recent.

103. Freeman NC, Gray KM, Taffe JR, Cornish KM. Development of a new attention rating scale for children with intellectual disability: The scale of attention in intellectual disability (SAID). *American Journal on Intellectual Developmental Disabilities*. 2015;120(2):91–109. https://doi.org/10.1352/1944-7558-120.2.91.

104. Friedman NP, Miyake A, Altamirano LJ, Corley RP, Young SE, Rhea SA, Hewitt JK. Stability and change in executive function abilities from late adolescence to early adulthood: A longitudinal twin study. *Dev Psychol*. 2016;52(2):326–40. https://doi.org/10.1037/dev0000075.

105. Gargaro B, Rinehart NJ, Bradshaw JL, Tonge BJ, Sheppard DM. Autism and ADHD: How far have we come in the comorbidity debate? *Neurosci Biobehav Rev*. 2010;35(5):1081–8. https://doi.org/10.1016/j.neubiorev.2010.11.002.

106. Gaugler T, Klei L, Sanders SJ, Bodea CA, Goldberg AP, Lee AB, ... Buxbaum JD. Most genetic risk for autism resides with common variation. *Nat Genet*. 2014;46(8):881–5. https://doi.org/10.1038/ng.3039.

107. Gerenser J. Language disorders in children with autism. In: *Handbook of Child Language Disorders*. New York: Psychology Press; 2009. pp. 67–89.

108. Geurts HM, Verte S, Oosterlaan J, Roeyers H, Sergeant JA. How specific are executive functioning deficits in attention deficit hyperactivity disorder and autism? *J Child Psychol Psychiatry*. 2004;45(4):836–54.

109. Ghirardi L, Brikell I, Kuja-Halkola R, Freitag CM, Franke B, Asherson P, ... Larsson H. The familial co-aggregation of ASD and ADHD: A register-based cohort study. *Mol Psychiatry*. 2018;23(2):257–62. https://doi.org/10.1038/mp.2017.17.

110. Ghirardi L, Pettersson E, Taylor MJ, Freitag CM, Franke B, Asherson P, ... Kuja-Halkola R. Genetic and environmental contribution to the overlap between ADHD and ASD trait dimensions in young adults: A twin study. *Psychol Med*. 2019;49(10):1713–21. https://doi.org/10.1017/S003329171800243X.

111. Gleitman H, Fridlund A, Reisberg D. Memory. In: *Psychology*. New York: W.W. Norton; 1999. pp. 260–99.

112. Goeleven E, De Raedt R, Leyman L, Verschuere B. The Karolinska directed emotional faces: A validation study. *Cogn Emot*. 2008. https://doi.org/10.1080/02699930701626582.

113. Goldberg MC, Mostofsky SH, Cutting LE, Mahone EM, Astor BC, Denckla MB, Landa RJ. Subtle Executive Impairment in Children with Autism and Children with ADHD. *J Autism Dev Disord*. 2005;35(3):279–93. https://doi.org/10.1007/s10803-005-3291-4.
114. Goodman R. The Strengths and Difficulties Questionnaire: A research note. J Child Psychol Psychiatry. 1997;38(5):581–6.

115. Goodman R, Ford T, Richards H, Gatward R, Meltzer H. (2000). The Development and Well-Being Assessment: Description and initial validation of an integrated assessment of child and adolescent psychopathology. The Journal of Child Psychology and Psychiatry and Allied Disciplines, 41(5), 645–655. https://doi.org/DOI: undefined.

116. Graham JW. Missing data analysis: Making it work in the real world. Annu Rev Psychol. 2009;60:549–76. https://doi.org/10.1146/annurev.psych.58.110405.085530.

117. Green JL, Rinehart N, Anderson V, Nicholson JM, Jongeling B, Sciberras E. Autism spectrum disorder symptoms in children with ADHD: A community-based study. Res Dev Disabil. 2015;47:175–84. https://doi.org/10.1016/j.ridd.2015.09.016.

118. Groen Y, Gaastra GF, Lewis-Evans B, Tucha O. Risky behavior in gambling tasks in individuals with ADHD – A systematic literature review. PLoS ONE. 2013;8(9):e74909. https://doi.org/10.1371/journal.pone.0074909.

119. Grove J, Ripke S, Als TD, Mattheisen M, Walters RK, Won H, ... Børglum AD. Identification of common genetic risk variants for autism spectrum disorder. Nat Genet. 2019. https://doi.org/10.1038/s41588-019-0344-8.

120. Grzadzinski R, Dick C, Lord C, Bishop S. Parent-reported and clinician-observed autism spectrum disorder (ASD) symptoms in children with attention deficit/hyperactivity disorder (ADHD): Implications for practice under DSM-5. Molecular Autism. 2016;7:7. https://doi.org/10.1186/s13229-016-0072-1.

121. Harms MB, Martin A, Wallace GL. Facial emotion recognition in Autism Spectrum Disorders: A review of behavioral and neuroimaging studies. Neuropsychol Rev. 2010;20(3):290–322. https://doi.org/10.1007/s11065-010-9138-6.

122. Hawi Z, Cummins TDR, Tong J, Arcos-Burgos M, Zhao Q, Matthews N, ... Bellgrove MA. Rare DNA variants in the brain-derived neurotrophic factor gene increase risk for attention-deficit hyperactivity disorder: a next-generation sequencing study. Mol Psychiatry. 2016. https://doi.org/10.1038/mp.2016.117.

123. Helzer JE, Kraemer HC, Krueger RF. The feasibility and need for dimensional psychiatric diagnoses. Psychol Med. 2006;36(12):1671–80. https://doi.org/10.1017/S027936950600821X.

124. Hoekstra R, Bartels M, Verweij CJH, Boomsma DI. Heritability of autistic traits in the general population. Archives of Pediatrics Adolescent Medicine. 2007;161(4):372–7. https://doi.org/10.1001/archpedi.161.4.372.

125. Hoogman M, Bralten J, Hibar DP, Mennes M, Zwiers MP, Schweren LSJ, ... Franke B. Subcortical brain volume differences in participants with Attention Deficit Hyperactivity Disorder in children and adults: A cross-sectional mega-analysis. The Lancet Psychiatry. 2017;4(4):310–9. https://doi.org/10.1016/S2215-0366(17)30049-4.

126. Hoogman M, Bralten J, Mennes M, Zwiers M, Van Hulzen K, Schweren L, ... Franke B. Subcortical volumes across the life span in ADHD: An ENIGMA collaboration. Eur Neuropsychopharmacol. 2015;25:189–9.

127. Hoogman M, Muetzel R, Guimaraes JP, Shumskaya E, Mennes M, Zwiers MP, ... Franke B. Brain Imaging of the Cortex in ADHD: A Coordinated Analysis of Large-Scale Clinical and Population-Based Samples. Am J Psychiatry. 2019;176(7):531–42. https://doi.org/10.1176/appi.ajp.2019.18091033.

128. Hoogman M, van Rooij D, Klein M, Boedhoe P, Illsoska I, Li T, ... Franke B. (2020). Consortium neuroscience of Attention Deficit/Hyperactivity Disorder and Autism Spectrum Disorder: The ENIGMA adventure. Hum Brain Mapp, 1–19. https://doi.org/10.1002/hbm.25029.

129. Howland RH. Potential adverse effects of discontinuing psychotropic drugs part 3: Antipsychotic, dopaminergic, and mood-stabilizing drugs. Journal Of Psychosocial Nursing Mental Health Services. 2010;48(11):11–4. https://doi.org/10.3928/02793695-20100708-01.

130. Hudziak JJ, Achenbach TM, Althoff RR, Pine DS. A dimensional approach to developmental psychopathology. International Journal of Methods in Psychiatric Research. 2007;16(S1):16–23. https://doi.org/10.1002/mpr.217.

131. Hutton SB, Ettinger U. The antisaccade task as a research tool in psychopathology: A critical review. Psychophysiology. 2006;43(3):302–13. https://doi.org/10.1111/j.1469-8986.2006.00403.x.
132. Insel T. The NIMH Research Domain Criteria (RDoC) Project: Precision medicine for psychiatry. Am J Psychiatry. 2014;171(4):395–7. https://doi.org/10.1176/appi.ajp.2014.14020138.

133. Insel T, Cuthbert B, Garvey M, Heinssen R, Pine D, Quinn K, … Wang P. (2010). Research Domain Criteria (RDoC): Toward a new classification framework for research on mental disorders. American Journal of Psychiatry Online, (July), 748–51. https://doi.org/10.1176/appi.ajp.2010.09091379.

134. Iossifov I, Ronemus M, Levy DL, Wang Z, Hakker I, Rosenbaum J, … Wigler M. De novo gene disruptions in children on the Autistic Spectrum. Neuron. 2012;74(2):285–99. https://doi.org/10.1016/j.neuron.2012.04.009.

135. Isaksson J, Tammimies K, Neufeld J, Cauvet É, Lundin K, Buitelaar JK, … Zwiers MP. (2018). EU-AIMS Longitudinal European Autism Project (LEAP): The autism twin cohort. Molecular Autism, 9(1). https://doi.org/10.1186/s13229-018-0212-x.

136. Itami S, Uno H. Orbitofrontal cortex dysfunction in Attention-Decit Hyperactivity Disorder revealed by reversal and extinction tasks. NeuroReport. 2002;13(18):2453–7. https://doi.org/10.1097/00001756-200212200-00016.

137. Johansen EB, Aase H, Meyer A, Sagvolden T. Attention-decit/hyperactivity disorder (ADHD) behaviour explained by dysfunctioning reinforcement and extinction processes. Behav Brain Res. 2002;130(1–2):37–45. https://doi.org/10.1016/S0166-4328(01)00434-X.

138. Johnson BP, Lum JAG, Rinehart NJ, Fielding J. Ocular motor disturbances in autism spectrum disorders: Systematic review and comprehensive meta-analysis. Neuroscience Biobehavioral Reviews. 2016;69:260–79. https://doi.org/10.1016/j.neubiorev.2016.08.007.

139. Johnson KA, Kelly SP, Robertson IH, Barry E, Mulligan A, Daly M, … Bellgrove MA. Absence of the 7-repeat variant of the DRD4 VNTR is associated with drifting sustained attention in children with ADHD but not in controls. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics. 2008;147(6):927–37. https://doi.org/10.1002/ajmg.b.30718.

140. Johnson KA, Robertson IH, Barry E, Mulligan A, Dáibhis A, Daly M, … Bellgrove MA. Impaired conflict resolution and alerting in children with ADHD: Evidence from the Attention Network Task (ANT). Journal of Child Psychology Psychiatry Allied Disciplines. 2008;49(12):1339–47. https://doi.org/10.1111/j.1469-7610.2008.01936.x.

141. Johnson KA, Robertson IH, Kelly SP, Silk TJ, Barry E, Dáibhis A, … Bellgrove MA. Dissociation in performance of children with ADHD and high-functioning autism on a task of sustained attention. Neuropsychologia. 2007;45(10):2234–45. https://doi.org/10.1016/j.neuropsychologia.2007.02.019.

142. Johnston K, Madden AK, Bramham J, Russell AJ. Response inhibition in adults with Autism Spectrum Disorder compared to Attention Deficit/Hyperactivity Disorder. J Autism Dev Disord. 2011;41(7):903–12. https://doi.org/10.1007/s10803-010-1113-9.

143. Kercood S, Grskovic JA, Banda D, Begeske J. Working memory and autism: A review of literature. Research in Autism Spectrum Disorders. 2014;8(10):1316–32. https://doi.org/10.1016/j.rasd.2014.06.011.

144. Kim YS, Fombonne E, Koh YJ, Kim SJ, Cheon KA, Leventhal BL. A comparison of DSM-IV pervasive developmental disorder and DSM-5 autism spectrum disorder prevalence in an epidemiologic sample. J Am Acad Child Adolesc Psychiatry. 2014;53(5):500–8. https://doi.org/10.1016/j.jaac.2013.12.021.

145. Klein C, Foerster F. (2001). Development of prosaccade and antisaccade task performance in participants aged 6 to 26 years. *Psychophysiology*, 38(2), 179–189. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11347863.

146. Kohls G, Peltzer J, Schulte-Rüther M, Kamp-Becker I, Remschmidt H, Herpertz-Dahlmann B, Konrad K. Atypical brain responses to reward cues in autism as revealed by event-related potentials. J Autism Dev Disord. 2011;41(11):1523–33. https://doi.org/10.1007/s10803-011-1177-1.

147. Kotov R, Waszczuk MA, Krueger RF, Forbes MK, Watson D, Clark LA, … Zimmerman M. The hierarchical taxonomy of psychopathology (HiTOP): A dimensional alternative to traditional nosologies. J Abnorm Psychol. 2017;126(4):454–77. https://doi.org/10.1037/abn0000258.

148. Kovacs M, Beck AT. (1977). An empirical-clinical approach toward a definition of childhood depression. *Depression in Childhood: Diagnosis, Treatment, and Conceptual Models*, 1–25.
149. Krueger RF, Bezdjian S. Enhancing research and treatment of mental disorders with dimensional concepts: Toward DSM-V and ICD-11. World Psychiatry. 2009;8(1):3–6. https://doi.org/10.1002/j.2051-5545.2009.tb00197.x.

150. Krueger RF, Deyoung CG. The RDoC initiative and the structure of psychopathology. Psychophysiology. 2016;53(3):351–4. https://doi.org/10.1111/psyp.12551.

151. Krueger RF, Kotov R, Watson D, Forbes MK, Eaton NR, Ruggero CJ, ... Zimmermann J. Progress in achieving quantitative classification of psychopathology. World Psychiatry. 2018;17(3):282–93. https://doi.org/10.1002/wps.20566.

152. Kuijper SJM, Hartman CA, Bogaerds-Hazenber STM, Hendriks P. Narrative production in children with autism spectrum disorder (ASD) and children with attention-deficit/hyperactivity disorder (ADHD): Similarities and differences. J Abnorm Psychol. 2017;126(1):63–75. https://doi.org/10.1037/abn0000231.

153. Kuntsi J, Wood AC, Johnson KA, Andreou P, Arias-Vasquez A, Buitelaar JK, ... Asherson P. Separation of cognitive impairments in Attention-Deficit/Hyperactivity Disorder into 2 familial factors. Arch Gen Psychiatry. 2010;67(11):1159–67.

154. Kvist AP, Nielsen HS, Simonsen M. The importance of children's ADHD for parents' relationship stability and labor supply. Soc Sci Med. 2013;88:30–8. https://doi.org/10.1016/j.socscimed.2013.04.001.

155. Larson MJ, South M, Krauskopf E, Clawson A, Crowley MJ. Feedback and reward processing in high-functioning autism. Psychiatry Res. 2011;187(1–2):198–203. https://doi.org/10.1016/j.psychres.2010.11.006.

156. Latzman RD, DeYoung CG, Afzali MH, Allen TA, Althoff RR, DeYoung CG, ... Zald DH. Using empirically-derived dimensional phenotypes to accelerate clinical neuroscience: The Hierarchical Taxonomy of Psychopathology (HiTOP) framework. Neuropsychopharmacology. 2020;45(7):1083–5. https://doi.org/10.1038/s41386-020-0639-6.

157. Lau WKW, Leung MK, Lau BWM. Resting-state abnormalities in Autism Spectrum Disorders: A meta-analysis. Sci Rep. 2019;9(1):1–8. https://doi.org/10.1038/s41598-019-40427-7.

158. Lencer R, Mills LJ, Alliey-Rodriguez N, Shafee R, Lee AM, Reilly JL, ... Bishop JR. Genome-wide association studies of smooth pursuit and antisaccade eye movements in psychotic disorders: Findings from the B-SNIP study. Translational Psychiatry. 2017;7(10):e1249. https://doi.org/10.1038/tp.2017.210.

159. Levy F, Hay D, McStephen M, Wood C, Waldman I. Attention-deficit hyperactivity disorder: a category or a continuum? Genetic analysis of a large-scale twin study. J Am Acad Child Adolesc Psychiatry. 1997;36(6):737–44. https://doi.org/10.1097/00004583-199706000-00009.

160. Lopez BR, Lincoln A, Ozonoff S, Lai Z. Examining the relationship between executive functions and restricted, repetitive symptoms of autistic disorder. Journal of Autism Developmental Disorders. 2005;35(4):445–60.

161. Lord C, Brugha TS, Charman T, Cusack J, Dumas G, Frazier T, ... Veenstra-VanderWeele J. Autism spectrum disorder. Nature Reviews Disease Primers. 2020;6(10):1–8. https://doi.org/10.1038/s41572-020-0251-2.

162. Loth E, Charman T, Mason L, Tillmann J, Jones EJH, Wooldridge C, ... Buitelaar JK. (2017). The EU-AIMS Longitudinal European Autism Project (LEAP): Design and methodologies to identify and validate stratification biomarkers for autism spectrum disorders. Molecular Autism, 8(1 LB-Loth2017), 24. https://doi.org/10.1186/s13229-017-0146-8.

163. Lubke GH, Muthén B. Investigating population heterogeneity with factor mixture models. Psychol Methods. 2005;10(1):21–39. https://doi.org/10.1037/1082-989X.10.1.21.

164. Luman M, Tripp G, Scheres A. Identifying the neurobiology of altered reinforcement sensitivity in ADHD: A review and research agenda. Neurosci Biobehav Rev. 2010;34(5):744–54. https://doi.org/10.1016/j.neubiorev.2009.11.021.

165. MacDonald SWS, Nyberg L, Bäckman L. Intra-individual variability in behavior: Links to brain structure, neurotransmission and neuronal activity. Trends Neurosci. 2006;29(8):474–80. https://doi.org/10.1016/j.tins.2006.06.011.

166. Marquand AF, Rezek I, Buitelaar J, Beckmann CF. Understanding Heterogeneity in Clinical Cohorts Using Normative Models: Beyond Case-Control Studies. Biol Psychiat. 2016. https://doi.org/10.1016/j.biopsych.2015.12.023.

167. Marsh HW, Morin AJS, Parker PD, Kaur G. Exploratory structural equation modeling: An integration of the best features of exploratory and confirmatory factor analysis. Annu Rev Clin Psychol. 2014. https://doi.org/10.1146/annurev-clinpsy-
168. Martel MM, Pan PM, Hoffmann MS, Gadelha A, do Rosário MC, Mari JJ, ... Salum GA. (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*(1), 137–148. https://doi.org/10.1037/abn0000205.

169. Martinussen R, Hayden J, Hogg-Johnson S, Tannock R. A meta-analysis of working memory impairments in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2005;44(4):377–84. https://doi.org/10.1097/chi.0b013e3182591773.

170. Mayes SD, Calhoun SL, Mayes RD, Molitoris S. Autism and ADHD: Overlapping and discriminating symptoms. *Research in Autism Spectrum Disorders*. 2012;6(1):277–85. https://doi.org/10.1016/j.rasd.2011.05.009.

171. McElroy E, Belsky J, Carragher N, Fearon P, Patalay P. Developmental stability of general and specific factors of psychopathology from early childhood to adolescence: Dynamic mutualism or p-differentiation? *J Child Psychol Psychiatry*. 2018;59(6):667–75. https://doi.org/10.1111/jcpp.12849.

172. McNeish DM. Modeling sparsely clustered data: Design-based, model-based, and single-level methods. *Psychol Methods*. 2014;19(4):552–63. https://doi.org/10.1037/met0000024.

173. Michelini G, Barch DM, Tian Y, Watson D, Klein DN, Kotov R. Delineating and validating higher-order dimensions of psychopathology in the Adolescent Brain Cognitive Development (ABCD) study. *Translational Psychiatry*. 2019;9(1):21–5. https://doi.org/10.1038/s41398-019-0593-4.

174. Michelini G, Palumbo IM, DeYoung CG, Latzman RD, Kotov R. (2020). Linking RDoC and HiTOP: A new interface for advancing psychiatric nosology and neuroscience. *PsyArxiv*, (June). https://doi.org/10.31234/osf.io/ps7tc.

175. Miettunen J, Nordström T, Kaakinen M, Ahmed AO. Latent variable mixture modeling in psychiatric research - A review and application. *Psychol Med*. 2016. https://doi.org/10.1017/S0033291715002305.

176. Miller GA, Rockstroh B. Endophenotypes in psychopathology research: Where do we stand? *Annu Rev Clin Psychol*. 2013;9:177–213. https://doi.org/10.1146/annurev-clinpsy-050212-185540.

177. Miller HL, Ragozzino ME, Cook EH, Sweeney JA, Mosconi MW. Cognitive set shifting deficits and their relationship to repetitive behaviors in Autism Spectrum Disorder. *J Autism Dev Disord*. 2015;45(3):805–15. https://doi.org/10.1007/s10803-014-2244-1.

178. Morandini HAE, Silk TJ, Griffiths K, Rao P, Hood S, Zepf FD. Meta-analysis of the neural correlates of vigilant attention in children and adolescents. *Cortex*. 2020;132:374–85. https://doi.org/https://doi.org/10.1016/j.cortex.2020.08.008.

179. Morris SE, Cuthbert BN. Research Domain Criteria: Cognitive systems, neural circuits, and dimensions of behavior. *Dialogues in Clinical Neuroscience*. 2012;14(1):29–37.

180. Mosconi MW, Sweeney JA. Sensorimotor dysfunctions as primary features of Autism Spectrum Disorders. *Science China Life Sciences*. 2015;58(10):1016–23. https://doi.org/10.1007/s11427-015-4894-4.

181. Mostofsky SH, Lasker AG, Cutting LE, Denckla MB, Zee DS. Oculomotor abnormalities in attention deficit hyperactivity disorder: A preliminary study. *Neurology*. 2001;57(3):423–30. https://doi.org/10.1212/WNL.57.3.423.

182. Mowinckel AM, Pedersen ML, Eilertsen E, Biele G. A meta-analysis of decision-making and attention in adults with ADHD. *Journal of Attention Disorders*. 2015;19(5):355–67. https://doi.org/10.1177/1087054714558872.

183. Mulligan A, Anney RJL, O'Regan M, Chen W, Butler L, Fitzgerald M, ... Gill M. Autism symptoms in Attention-Deficit/Hyperactivity Disorder: A familial trait which correlates with Conduct, Oppositional Defiant, Language and Motor Disorders. *J Autism Dev Disord*. 2009;39(2):197–209. https://doi.org/10.1007/s10803-008-0621-3.

184. Munoz DP, Everling S. Look away: the anti-saccade task and the voluntary control of eye movement. *Nat Rev Neurosci*. 2004;5(3):218–28. https://doi.org/10.1038/nrn1345.

185. National Institute of Mental Health. (2018). *RDoC Changes to the Matrix (CMAT) Workgroup Update: Proposed Positive Valence Domain Revisions*. [Online].
186. Nigg JT, Blaskey LG, Stawicki JA, Sachek J. Evaluating the endophenotype model of ADHD neuropsychological deficit: Results for parents and siblings of children with ADHD combined and inattentive subtypes. J Abnorm Psychol. 2004;113(4):614–25. https://doi.org/10.1037/0021-843X.113.4.614.

187. Norbury CF, Gemmell T, Paul R. Pragmatics abilities in narrative production: A cross-disorder comparison. Journal of Child Language. 2014;41(3):485–510. https://doi.org/10.1017/S030500091300007X.

188. O’Roak BJ, Vives L, Girirajan S, Karakoc E, Krumm N, Coe BP, ... Eichler EE. Sporadic autism exomes reveal a highly interconnected protein network of de novo mutations. Nature. 1989;485(7397):246–50. https://doi.org/10.1038/nature10989.

189. Oerlemans AM, Droste K, Van Steijn DJ, De Sonneville LMJ, Buitelaar JK, Rommelse NNJ. Co-segregation of social cognition, executive function and local processing style in children with ASD, their siblings and normal controls. J Autism Dev Disord. 2013;43(12):2764–78. https://doi.org/10.1007/s10803-013-1807-x.

190. Oerlemans AM, Hartman CA, De Bruin YGE, Van Steijn DJ, Franke B, Buitelaar JK, Rommelse NNJ. Simplex and multiplex stratification in ASD and ADHD families: A promising approach for identifying overlapping and unique underpinnings of ASD and ADHD? J Autism Dev Disord. 2015;45(3):645–57. https://doi.org/10.1007/s10803-014-2220-9.

191. Oerlemans AM, van der Meer JM, van Steijn DJ, de Ruiter SW, de Bruijn YGE, de Sonneville LMJ, ... Rommelse NNJ. Recognition of facial emotion and affective prosody in children with ASD (+ ADHD) and their unaffected siblings. European Child Adolescent Psychiatry. 2014;23(5):257–71. https://doi.org/10.1007/s00787-013-0446-2.

192. Oldham S, Amatkevičiūtė A, Smith RE, Tiego J, Bellgrove MA, Fornito A. (2020). The efficacy of different preprocessing steps in reducing motion-related confounds in diffusion MRI connectomics. NeuroImage, 222(July), 117252. https://doi.org/10.1016/j.neuroimage.2020.117252.

193. Open Brain Consent. (2020). Make open data sharing a no-brainer for ethics committees.

194. Parkes L, Fulcher B, Yücel M, Fornito A. (2018). An evaluation of the efficacy, reliability, and sensitivity of motion correction strategies for resting-state functional MRI. NeuroImage, 171(December 2017), 415–436. https://doi.org/10.1016/j.neuroimage.2017.12.073.

195. Patrick CJ, Hajcak G. RDoC: Translating promise into progress. Psychophysiology. 2016;53(3):415–24. https://doi.org/10.1111/psyp.12612.

196. Patrick CJ, Venables NC, Yancey JR, Hicks BM, Nelson LD, Kramer MD. A construct-network approach to bridging diagnostic and physiological domains: Application to assessment of externalizing psychopathology. J Abnorm Psychol. 2013;122(3):902–16. https://doi.org/10.1037/a0032807.

197. Peirce JW. PsychoPy—psychophysics software in Python. J Neurosci Methods. 2007;162(2):8–13.

198. Perkins ER, Latzman RD, Patrick CJ. Interfacing neural constructs with the Hierarchical Taxonomy of Psychopathology: ‘Why’ and ‘how.’. Personality Mental Health. 2020;14:106–22. https://doi.org/10.1002/pmhy.1460.

199. Peterson CC, Garnett M, Kelly A, Atwood T, Pineda-Alhucema W, Aristizabal E, ... Vézéol J. Everyday social and conversation applications of theory-of-mind understanding by children with autism-spectrum disorders or typical development. European Child Adolescent Psychiatry. 2009;28(2):105–15. https://doi.org/10.1007/s11065-008-9381-9.

200. Pineda-Alhucema W, Aristizabal E, Escudero-Cabarcas J, Acosta-López JE, Vézéol J. Executive function and theory of mind in children with ADHD: A systematic review. Neuropsychol Rev. 2018;28(3):341–58. https://doi.org/10.1007/s11065-018-9381-9.

201. Podsakoff PM, MacKenzie SB, Podsakoff NP. Sources of method bias in social science research and recommendations on how to control it. Annu Rev Psychol. 2012;63(1):539–69. https://doi.org/10.1146/annurev-psych-120710-100452.

202. Polanczyk GV, Willcutt EG, Salum GA, Kieling C, Rohde LA. ADHD prevalence estimates across three decades: An updated systematic review and meta-regression analysis. Int J Epidemiol. 2014. https://doi.org/10.1093/ije/dyt261.

203. Quay HC. Inhibition and Attention Deficit Hyperactivity Disorder. J Abnorm Child Psychol. 1997;25(1):7–13. https://doi.org/10.1023/A:1025799122529.
204. Rahko JS, Vuontela VA, Carlson S, Nikkinen J, Hurtig TM, Kuusikko-Gauffin S, … Kiviniemi VJ. Attention and working memory in adolescents with Autism Spectrum Disorder: A functional MRI study. Child Psychiatry Hum Dev. 2016;47(3):503–17. https://doi.org/10.1007/s10578-015-0583-6.

205. Rashid B, Calhoun V. Towards a brain-based predictome of mental illness. Hum Brain Mapp. 2020. https://doi.org/10.1002/hbm.25013.

206. Reckase MD. Multidimensional Item Response Theory. New York: Springer; 2009.

207. Reiersen AM, Todd RD. Co-occurrence of ADHD and autism spectrum disorders: phenomenology and treatment. Expert Rev Neurother. 2008;8(4):657–69. https://doi.org/10.1586/14737175.8.4.657.

208. Rhodes SM, Coghill D, Matthews K. Methylphenidate restores visual memory, but not working memory function in Attention Deficit-Hyperkinetic Disorder. Psychopharmacology. 2004;175(3):319–30. https://doi.org/10.1007/s00213-004-1833-7.

209. Rhodes SM, Coghill D, Matthews K. Neuropsychological functioning in stimulant-naive boys with hyperkinetic disorder. Psychol Med. 2005;35(8):1109–20. https://doi.org/10.1017/S0033291705004599.

210. Riley AW, Forrest CB, Starfield B, Rebok GW, Robertson JA, Green BF. (2004). The parent report form of the CHIP – Child Edition: Reliability and validity. 42(3), 210–220. https://doi.org/10.1017/S0033291703375876.

211. Roak BJO, Deriziotis P, Lee C, Vives L, Schwartz JJ, Girirajan S, … Eichler EE. Exome sequencing in sporadic Autism Spectrum Disorders identifies severe de novo mutations. 2011;43(6):585–9. https://doi.org/10.1038/ng.835.Exome.

212. Rodrigues SM, Saslow LR, Garcia N, John OP, Keltner D. Oxytocin receptor genetic variation relates to empathy and stress reactivity in humans. Proc Natl Acad Sci USA. 2009;106(50):21437–41. https://doi.org/10.1073/pnas.0905791106.

213. Rogers RD, Rammani N, Mackay C, Wilson JL, Jezzard P, Carter CS, Smith SM. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. Biol Psychiat. 2004;55(6):594–602. https://doi.org/10.1016/j.biopsych.2003.11.012.

214. Rommelse NNJ, Altink ME, Oosterlaan J, Buschgens CJM, Buitelaar J, Sergeant Ja. Support for an independent familial segregation of executive and intelligence endophenotypes in ADHD families. Psychol Med. 2008;38(11):1595–606. https://doi.org/10.1017/S0033291708002869.

215. Rommelse NNJ, Franke B, Geurts HM, Hartman CA, Buitelaar JK. Shared heritability of attention-deficit/hyperactivity disorder and autism spectrum disorder. Eur Child Adolesc Psychiatry. 2010;19(3):281–95. https://doi.org/10.1007/s00787-010-0092-x.

216. Ronald A. Editorial: The psychopathology p factor: Will it revolutionise the science and practice of child and adolescent psychiatry? J Child Psychiatr Psychiatry. 2019;60(5):497–9. https://doi.org/10.1111/jcpp.13063.

217. Sanchez-Roige S, Palmer AA. (2020). Emerging phenotyping strategies will advance our understanding of psychiatric genetics. Nat Neurosci, 23(April). https://doi.org/10.1038/s41593-020-0609-7.

218. Sanders S, Murtha M, Gupta A, Murdoch JD, Raubeson MJ, Willsey AJ, ... State MW. De novo mutations revealed by whole exome sequencing are strongly associated with autism. Nature. 2012;485(7397):237–41. https://doi.org/10.1038/nature10945.De.

219. Satterfield JH, Cantwell DP, Satterfield BT. Pathophysiology of the hyperactive child syndrome. Arch Gen Psychiatry. 1974;31(6):839–44. https://doi.org/10.1001/archpsyc.1974.01760180079010.

220. Schachar RJ, Crosbie J, Barr CL, Ornstein TJ, Kennedy J, Malone M, … Pathare T. Inhibition of motor responses in siblings concordant and discordant for attention deficit hyperactivity disorder. Am J Psychiatry. 2005;162(6):1076–82. https://doi.org/10.1176/appi.ajp.162.6.1076.

221. Scheeren AM, de Rosnay M, Koot HM, Beeger S. Rethinking theory of mind in high-functioning autism spectrum disorder. J Child Psychiatr Psychiatry. 2013;54(6):628–35. https://doi.org/10.1111/jcpp.12007.
223. Scheres A, Milham MP, Knutson B, Castellanos FX. Ventral striatal hyporesponsiveness during reward anticipation in Attention-Deficit/Hyperactivity Disorder. Biol Psychiat. 2007;61(5):720–4. https://doi.org/10.1016/j.biopsych.2006.04.042.

224. Schmitt LM, Bojanek E, White SP, Ragozzino ME, Cook EH, Sweeney JA, Mosconi MW. Familiality of behavioral flexibility and response inhibition deficits in autism spectrum disorder (ASD). Molecular Autism. 2019;10(1):47. https://doi.org/10.1186/s13229-019-0296-y.

225. Schmitz N, Rubia K, Van Amelsvoort T, Daly E, Smith A, Murphy DGM. Neural correlates of reward in autism. Br J Psychiatry. 2008;192(1):19–24. https://doi.org/10.1192/bjp.bp.107.036921.

226. Schoechlin C, Engel RR. Neuropsychological performance in adult attention-deficit hyperactivity disorder: Meta-analysis of empirical data. Arch Clin Neuropsychol. 2005;20(6):727–44. https://doi.org/10.1016/j.acn.2005.04.005.

227. Schuh JM, Eigsti IM. Working memory, language skills, and autism symptomatology. Behavioral Sciences. 2012;2(4):207–18. https://doi.org/10.3390/bs2040207.

228. Sciberras E, Mueller KL, Efron D, Bisset M, Anderson V, Schilpzand EJ, … Nicholson JM. Language problems in children with ADHD: A community-based study. Pediatrics. 2014;133(5):793–800. https://doi.org/10.1542/peds.2013-3355.

229. Semel E, Wiig EH, Secord WA. Clinical Evaluation of Language Fundamentals Preschool-2 (CELF P2). Sydney: AU: Pearson Clinical; 2004.

230. Seng G, Tseng W, Chiu Y, Tsai W, Wu Y, Gau SS. (2020). Executive functions in youths with Autism Spectrum Disorder and their unaffected siblings. Psychol Med, 4(May). https://doi.org/https://doi.org/10.1017/S0033291720001075.

231. Sergeant J. The cognitive-energetic model: An empirical approach to Attention-Deficit Hyperactivity Disorder. Neurosci Biobehav Rev. 2000;24:7–12.

232. Shaikh AG, Zee DS, Broadbent J, Galic I, Stokes MA, Goodman R, … Barnard-Brak L. The SWAN captures variance at the negative and positive ends of the ADHD symptom dimension. J Autism Dev Disord. 2015;38(6):1974–84. https://doi.org/https://doi.org/10.1016/j.biopsych.2005.02.006.

233. Shallice T, Marzocchi GM, Coser S, Del Savio M, Meuter RF, Rumiati RI. Executive function profile of children with Attention Deficit Hyperactivity Disorder. Developmental Neuropsychology. 2002;21(1):43–71. https://doi.org/10.1207/S15326942DN2101.

234. Slaats-Willemse D, Swaab-Barneveld H, De Sonneville LEO, Buitelaar JAN. Familial clustering of executive functioning in affected sibling pair families with ADHD. Journal of the American Academy of Child Adolescent Psychiatry. 2005;44(4):385–91. https://doi.org/https://doi.org/10.1097/01.chi.0000153227.34473.c7.

235. Smucker MR, Craighead WE, Craighead LW, Green BJ. Normative and reliability data for the children's depression inventory. J Abnorm Child Psychol. 1986;14(1):25–39. https://doi.org/10.1007/BF00917219.

236. Sørensen L, Sonuga-Barke E, Eichele H, van Wageningen H, Wollschlaeger D, Plessen KJ. Suboptimal decision making by children with ADHD in the face of risk: Poor risk adjustment and delay aversion rather than general proneness to taking risks. Neuropsychology. 2017;31(2):119–28. https://doi.org/10.1037/neu0000297.

237. Sparrow SS, Cicchetti DV, Saulnier CA. Vineland Adaptive Behavior Scales, Third Edition (Vineland-3). Sydney: Pearson; 2016.

238. Spence SH. A measure of anxiety symptoms among children. Behav Res Ther. 1998;36:545–66.

239. Stavropoulos KKM, Carver LJ. Reward anticipation and processing of social versus nonsocial stimuli in children with and without Autism Spectrum Disorders. J Child Psychol Psychiatry. 2014;55(12):1398–408. https://doi.org/10.1111/jcpp.12270.

240. Steele SD, Minshew NJ, Luna B, Sweeney JA. Spatial working memory deficits in autism. J Autism Dev Disord. 2007;37(4):605–12. https://doi.org/10.1007/s10803-006-0202-2.

241. Stevens T, Peng L, Barnard-Brak L. The comorbidity of ADHD in children diagnosed with Autism Spectrum Disorder. Research in Autism Spectrum Disorders. 2016;31:11–8. https://doi.org/10.1016/j.rasd.2016.07.003.
242. Stoltenberg C, Schjølberg S, Bresnahan M, Hornig M, Hirtz D, Dahl C, ... Susser E. (2011). *The Autism Birth Cohort (ABC): A paradigm for gene-environment-timing research.* 15(7), 676–680. https://doi.org/10.1038/mp.2009.143.

243. Strange BC. Once-daily treatment of ADHD with guanfacine: Patient implications. Neuropsychiatric Disease Treatment. 2008;4(3):499–506. https://doi.org/10.2147/ndt.s1711.

244. Sullivan PF, Agrawal A, Bulik CM, Andreassen OA, Børglum AD, Breen G, ... O'Donovan MC. Psychiatric genomics: An update and an agenda. Am J Psychiatry. 2018;175(1):15–27. https://doi.org/10.1176/appi.ajp.2017.17030283.

245. Taurines R, Schwenck C, Westerwald E, Sachse M, Siniatckhin M, Freitag C. ADHD and autism: Differential diagnosis or overlapping traits? A selective review. ADHD Attention Deficit Hyperactivity Disorders. 2012;4(3):115–39. https://doi.org/10.1007/s12402-012-0086-2.

246. Tye C, Johnson KA, Kelly SP, Asherson P, Kuntsi J, Ashwood KL, ... McLoughlin G. Response time variability under slow and fast-incentive conditions in children with ASD, ADHD and ASD + ADHD. J Child Psychol Psychiatry. 2016;57(12):1414–23. https://doi.org/10.1111/jcpp.12608.

247. Uddin LQ. (2020). Brain mechanisms supporting flexible cognition and behavior in adolescents with autism spectrum disorder. *Biological Psychiatry, pre-proof.* https://doi.org/10.1016/j.biopsych.2020.05.010.

248. Ujlarevic M, Hamilton A. Recognition of emotions in Autism: A formal meta-analysis. J Autism Dev Disord. 2013;43(7):1517–26. https://doi.org/10.1007/s10803-012-1695-5.

249. van der Plas E, Dupuis A, Amold P, Crosbie J, Schachar R. Association of Autism Spectrum Disorder with Obsessive-Compulsive and Attention-Deficit/Hyperactivity traits and response inhibition in a community sample. J Autism Dev Disord. 2016;46(9):3115–25. https://doi.org/10.1007/s10803-016-2853-y.

250. van der Sluis S, Posthuma D, Nivard MG, Verhage M, Dolan CV. Power in GWAS: Lifting the curse of the clinical cut-off. Mol Psychiatry. 2013;18(1):2–3. https://doi.org/10.1038/mp.2012.65.

251. van der Sluis S, Verhage M, Posthuma D, Dolan CV. (2010). Phenotypic complexity, measurement bias, and poor phenotypic resolution contribute to the missing heritability problem in genetic association studies. PLoS ONE, 5(11). https://doi.org/10.1371/journal.pone.0013929.

252. van Ewijk H, Heslenfeld DJ, Zwiers MP, Buitelaar JK, Oosterlaan J. Diffusion tensor imaging in attention deficit/hyperactivity disorder: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2012;36(4):1093–106. https://doi.org/10.1016/j.neubiorev.2012.01.003.

253. van Ouden HEM, Daw ND, Fernandez G, Elshout JA, Rijpkema M, Hoogman M, ... Cools R. Dissociable effects of dopamine and serotonin on reversal learning. Neuron. 2013;80(4):1090–100. https://doi.org/10.1016/j.neuron.2013.08.030.

254. Van Rooij D, Anagnostou E, Arango C, Auzias G, Behrmann M, Busatto GF, ... Buitelaar JK. Cortical and subcortical brain morphometry differences between patients with autism spectrum disorder and healthy individuals across the lifespan: Results from the ENIGMA ASD working group. Am J Psychiatry. 2018;175(4):359–69. https://doi.org/10.1176/appi.ajp.2017.17010100.

255. Van Steijn DJ, Richards JS, Oerlemans AM, De Ruiter SW, Van Aken MAG, Franke B, ... Rommelse NNJ. The co-occurrence of Autism Spectrum Disorder and Attention-Deficit/ Hyperactivity Disorder symptoms in parents of children with ASD or ASD with ADHD. J Child Psychol Psychiatry. 2012;53(9):954–63. https://doi.org/10.1111/j.1469-7610.2012.02556.x.

256. Verbruggen F, Logan GD. Response inhibition in the stop-signal paradigm. Trends in Cognitive Sciences. 2008;12(11):418–24. https://doi.org/10.1016/j.tics.2008.07.005.

257. Verbruggen F, Logan GD, Stevens MA. STOP-IT: Windows executable software for the stop-signal paradigm. Behav Res Methods. 2008;40:479–83. https://doi.org/10.3758/brm.40.2.479. (2 LB-Verbruggen2008).

258. Vogan VM, Francis KE, Morgan BR, Smith M, Lou, Taylor MJ. Load matters: Neural correlates of verbal working memory in children with Autism Spectrum Disorder. Journal of Neurodevelopmental Disorders. 2018;10(1):1–12. https://doi.org/10.1186/s11689-018-9236-y.
259. Waddington F, Hartman C, de Bruijn Y, Lappenschaar M, Oerlemans A, Buitelaar J, ... Rommelse N. An emotion recognition subtyping approach to studying the heterogeneity and comorbidity of Autism Spectrum Disorders and Attention-Deficit/Hyperactivity Disorder. Journal of Neurodevelopmental Disorders. 2018a;10(1):31. https://doi.org/10.1186/s11689-018-9249-6.

260. Waddington F, Hartman C, de Bruijn Y, Lappenschaar M, Oerlemans A, Buitelaar J, ... Rommelse N. Visual and auditory emotion recognition problems as familial cross-disorder phenomenon in ASD and ADHD. Eur Neuropsychopharmacol. 2018b;28(9):994–1005. https://doi.org/10.1016/j.euroneuro.2018.06.009.

261. Walton KM. Leisure time and family functioning in families living with Autism Spectrum Disorder. Autism. 2019;23(6):1384–97. https://doi.org/10.1177/1362361318812434.

262. Wang E, Sun L, Sun M, Huang J, Tao Y, Zhao X, ... Song Y. Attentional selection and suppression in children with Attention-Deficit/Hyperactivity Disorder. Biological Psychiatry: Cognitive Neuroscience Neuroimaging. 2016;1(4):372–80. https://doi.org/10.1016/j.bpsc.2016.01.004.

263. Wang X, Xu Q, Bey AL, Lee Y, Jiang YH. Transcriptional and functional complexity of Shank3 provides a molecular framework to understand the phenotypic heterogeneity of SHANK3 causing autism and Shank3 mutant mice. Molecular Autism. 2014;5(1):1–14. https://doi.org/10.1186/2040-2392-5-30.

264. Waszczyk MA, Eaton NR, Krueger RF, Shackman AJ, Waldman ID, Zald DH, ... Kotov R. Redefining phenotypes to advance psychiatric genetics: Implications from Hierarchical Taxonomy of Psychopathology. J Abnorm Psychol. 2020;129(2):143–61. https://doi.org/10.1037/abn0000486.

265. Wechsler D. Wechsler Adult Intelligence Scale - Fourth Edition Australian and New Zealand Language Adapted Edition. Sydney: Pearson; 2008.

266. Wechsler D. Wechsler Intelligence Scale for Children, Fifth Edition: Australian and New Zealand Standardised Edition. Sydney: Pearson: Fifth; 2016.

267. Group WHOQOL, W. WHOQOL-BREF: Introduction, administration, scoring and generic version of the assessment. Geneva: WHO; 1996.

268. Wiig EH, Secord WA, Semel E. CELF-5 Screening Test. Sydney: Pearson Clinical; 2013.

269. Wiig EH, Semel E, Secord WA. Clinical Evaluation of Language Fundamentals Australian and New Zealand - Fifth Edition (CELF-5). Sydney: AU: Pearson Clinical; 2017.

270. Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of Attention-Deficit/Hyperactivity Disorder: A meta-analytic review. Biol Psychiat. 2005;57(11):1336–46. https://doi.org/10.1016/j.biopsych.2005.02.006.

271. Wodka EL, Mahone EM, Blankner JG, Larson JCG, Fotedar S, Denckla MB, Mostofsky SH. Evidence that response inhibition is a primary deficit in ADHD. J Clin Exp Neuropsychol. 2007;29(4):345–56. https://doi.org/10.1080/10803390600678046.

272. Wright L, Lipszyc J, Dupuis A, Thayaparajah SW, Schachar R. Response inhibition and psychopathology: A meta-analysis of Go/No -Go task performance. 2014;123(2):429–39. https://doi.org/10.1037/a0036295.

273. Yang J, Wray NR, Visscher PM. Comparing apples and oranges: Equating the power of case-control and quantitative trait association studies. Genet Epidemiol. 2010;34(3):254–7. https://doi.org/10.1002/gepi.20456.

274. Yip BHK, Bai D, Mahjani B, Klei L, Pawitan Y, Hultman CM, ... Sandin S. Heritable variation, with little or no maternal effect, accounts for recurrence risk to Autism Spectrum Disorder in Sweden. Biol Psychiat. 2018;83(7):589–97. https://doi.org/10.1016/j.biopsych.2017.09.007.

275. Zablotsky B, Bramlett MD, Blumberg SJ. (2017). The co-occurrence of Autism Spectrum Disorder in children with ADHD. Journal of Attention Disorders, 1087054717713638. https://doi.org/10.1177/1087054717713638.

276. Zamboulis C, Reid JL. Withdrawal of Guanfacine after long-term treatment in essential hypertension. Eur J Clin Pharmacol. 1981;19:19–24.
277. Zhou ZW, Fang YT, Lan XQ, Sun L, Cao QJ, Wang YF, … Zhang H. Inconsistency in abnormal functional connectivity across datasets of ADHD-200 in children with Attention Deficit Hyperactivity Disorder. Front Psychiatry. 2019;10(SEP):1–15. https://doi.org/10.3389/fpsyt.2019.00692.

278. Ziegler S, Pedersen ML, Mowinckel AM, Biele G. Modelling ADHD: A review of ADHD theories through their predictions for computational models of decision-making and reinforcement learning. Neurosci Biobehav Rev. 2016;71:633–56. https://doi.org/10.1016/j.neubiorev.2016.09.002.

279. Zimmerman IL, Steiner VG, Pond RE. Preschool Language Scales - Fifth Edition (PLS-5) (Fifth). Bloomington: Pearson; 2011.