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Taking stock of the present and looking to the future of ADHD research: a commentary on Sonuga-Barke et al. (2022)

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Sonuga-Barke et al. (2022) offer thought-provoking insights on the current and future state of ADHD research. Purposefully designed as a mosaic of different voices from world-leading experts in the field of ADHD, this review provides a clear and up-to-date overview of the state of research, while emphasizing critical and intriguing questions for future investigation. It also highlights the crucial tension between the need to define a coherent conceptualisation of ADHD for clinical and research purposes, while keeping an open mind to new research that challenges, expands or subverts the prevailing consensus. In doing so, this Annual Research Review provides an exceptional roadmap for future research about the nature of ADHD. We are grateful for the opportunity to further consider several cross-cutting ideas discussed in Sonuga-Barke et al. in this commentary, including the heterogeneous nature of ADHD, ensuring equity of translational research across diverse groups, and the importance of participatory research.

As new research expands our understanding of ADHD, a more conventional conceptualization of ADHD is straining at the seams. The classic example of a hyperactive boy with obvious symptoms from early childhood must be expanded to encompass a much more heterogeneous picture – a woman in her 20s who had compensated for childhood ADHD symptoms but is increasingly unable to cope with the demands of adult life; an autistic individual experiencing significant challenges with inattention; an artist who struggled with the demands of traditional schooling but is flourishing in a self-defined creative space. The wealth of research discussed in Sonuga-Barke et al. emphasizes this increasing heterogeneity, both between individuals and within an individual over time.

The availability of population-based cohort studies following children into adulthood has highlighted one source of heterogeneity in ADHD, namely age of onset. ADHD is characterized, both conceptually and explicitly in the DSM, as a neurodevelopmental disorder. Thus, for some, the emergence of evidence for a 'late-onset' presentation of ADHD has called into question this neurodevelopmental conceptualization. However, we would argue that the concept of a neurodevelopmental disorder, like ADHD itself, is more heterogeneous than at first glance. Does 'neurodevelopmental' necessarily imply a start in early childhood? Work in the field of schizophrenia and bipolar disorder sheds light on this seeming incongruity. Despite an average onset in late adolescence/early adulthood, these disorders can be viewed through a neurodevelopmental lens, with some risk factors associated with prenatal/early life exposures, and behavioural and cognitive indicators possibly evident in earlier development (Chien et al., 2022). And indeed, neurodevelopment is not a process restricted to early childhood, with key aspects of brain development – perhaps particularly relevant to ADHD – occurring across adolescence and into young adulthood (Vijayakumar et al., 2018). As longitudinal studies collecting neuroimaging data, like ABCD, IMAGEN and NeuroIMAGE, age into adulthood they will provide key evidence about how these later neurodevelopmental changes may be associated with ADHD during adolescence and early adulthood.

Related issues challenging the conceptualization of ADHD highlighted by Sonuga-Barke and colleagues are the dimensional nature of its symptoms and the frequent co-occurrence with a wide range of neurodevelopmental, mental health and behavioural conditions, possibly due to shared transdiagnostic features and risk factors. Dimensionality and comorbidity contribute to between- and within-person heterogeneity and complicate treatment decisions. In addition to a better understanding of underpinning mechanisms, more dimensional, individual-level and transdiagnostic characterizations may be more valuable than DSM diagnostic categories for guiding treatment selection and prognostication. This could be achieved in clinical practice through closer monitoring of dimensional clinical profiles over time, perhaps leveraging emerging mobile and remote technologies (Denyer et al., 2022). Further, the neurodivergence perspective can help us bring these different features of ADHD jointly under the spotlight. This perspective pushes us to see 'ADHD as part of a wider spectrum of naturally occurring variation' among individuals, going beyond

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traditional diagnostic labels and boundaries (Fletcher-Watson, 2022; Sonuga-Barke et al., 2022). This would help us embrace the complexity of ADHD in terms of different presentations, patterns of co-occurrence, longitudinal trajectories, and preferences regarding treatment and support. A move towards conceptualizing ADHD as neurodivergence may also reduce the stigma around being labelled as 'ADHD' and promote acceptance and awareness of the unique strengths, as well as needs, that characterize each individual.

An additional cross-cutting theme in Sonuga-Barke et al. is the importance of contextual factors in the presentation and course of ADHD. Consideration of context is not new, and has, for example, an important role in diagnosis with the requirement of pervasiveness in the DSM. However, there is increasing attention in ADHD research on situating the individual within social, academic/professional and environmental contexts, apart from establishing pervasiveness. For example, Sonuga-Barke et al. note the impact of 'time-varying developmental demands' in changing the course of ADHD to produce fluctuations around the diagnostic cut-off. Also, in considering the impact of living with ADHD on quality of life more holistically, the authors emphasize the need to focus on environmental influences and constraints. Moreover, the environmental context itself may be shaped by an individual's predisposition: Sonuga-Barke et al. discuss a key area of future research, namely 'active' gene–environment correlation in ADHD, whereby individuals select and change their environment to suit their genetic predisposition. While we may have the intuition that this process occurs, whether and to what extent it does in practice has not been investigated in-depth for individuals with ADHD. Additionally, we know little about the potential triggers and interactions of context and individual-level factors (starting school, leaving school, having children, menopause) that may upset the balance of coping mechanisms and environmental shaping that individuals with ADHD have forged.

As we expand our understanding of the concept of ADHD, so must we expand our research to encompass a broader range of groups across a diversity of characteristics such as gender, age, ethnic group, culture and geographic location. The Annual Research Review emphasizes an increasing focus on women with ADHD, recognizing the possibility of differing presentations by gender and of girls 'masking' ADHD symptoms in younger years – an established concept in autism research that may also have relevance for ADHD. Focusing on the need for more research encompassing diverse age groups, the review notes 'Currently almost nothing is known about later life stages of ADHD developmental trajectories'. Indeed, only a handful of studies assess ADHD in later life, leaving open questions such as the role of ADHD in cognitive functioning and decline in older ages. Reflecting on the interface of these different characteristics we can consider, for example, the interaction of gender and ageing in ADHD: there is significant concern among women with ADHD about the impact of menopause on symptoms and functioning, but there is almost no research on this topic. Differences in ADHD across ethnicity is another important area for future research. A recent meta-analysis found a higher prevalence of ADHD among African-American relative to White youth, in contrast to previous assumptions (Cénat et al., 2021). Additionally, we know little about the cultural factors that may affect ADHD presentation, recognition, treatment and course. For example, recent research in Japan has identified women with ADHD as having more impairment than men, possibly due to gendered cultural expectations of women's behaviour that idealize women as 'quiet, attentive, organized, and patient' (Hayashi et al., 2019). And as the majority of ADHD research focuses on the United States and European samples, future research needs to take a more global view to address settings beyond these few regions.

An important theme of Sonuga-Barke et al. is a focus on translational research – how can we ensure that the work of ADHD researchers is translated into tangible benefit for individuals with ADHD? Although the review does not focus explicitly on ADHD treatments, implications for treatments and approaches to support individuals with ADHD are discussed across several sections. As the authors note, inter-individual variability in treatment response represents an additional aspect of heterogeneity within the ADHD population, currently requiring a process of trial and error before an effective treatment is found on an individual basis. As this is ubiquitous in psychiatry and true for available ADHD treatments (e.g. stimulant medication is not effective or tolerated by about a third of people with ADHD), it will likely also be true for new pharmacological or non-pharmacological treatments that may be developed in the future. More explicit consideration of this issue will be required in the design of future clinical trials, in order to move away from exclusive testing of group-level effects and towards a more targeted approach focused on individual characteristics to delineate subpopulations of individuals with ADHD who may benefit from different treatments (i.e. personalized medicine). While behavioural and clinical characteristics alone have typically yielded inconsistent findings and poor ability to predict treatment outcomes, there is considerable interest in the identification of biomarkers, such as neural measures, that may parse heterogeneity in treatment response and aid treatment decision making. Much of this research has focused on candidate biomarkers from structural and functional magnetic resonance imaging (MRI), guided by the rich neuroimaging literature discussed in the review. Additionally, initial promising findings based

on candidate electroencephalography (EEG) biomarkers, if replicated in pragmatic trials and supported by cost–benefit analyses, may be clinically translatable at scale (Michelini et al., 2022).

Another key point to highlight in relation to treatment is that while treatment outcomes have generally been quantified in terms of reductions of ADHD symptoms or remission, more holistic views are also emerging that emphasize the need to consider additional or alternative outcomes. As highlighted in the review, such treatment approaches recognize the preferences of those with ADHD, who may see the focus on ADHD symptoms as stigmatizing and give more importance to improvement in quality of life and general mental health. For example, Sonuga-Barke et al. discuss the possibility of targeting broad and transdiagnostic phenotypes, such as emotion dysregulation, as a way of improving long-term outcomes and reducing co-occurring mental health problems. The neurodivergence perspective and emerging research on the positive aspects and strengths of ADHD is also likely to assist the design of new holistic interventions (Bölte et al., 2021), such as approaches aiming to implement reasonable environmental adjustments and helping individuals find environments in which they can thrive.

A crucial aspect to consider for translational research is equity – that the benefits of new scientific developments are not concentrated among those with the most privilege. Indeed, while there are standards of care that are widely agreed upon in the ADHD field, many across the world lack access to these consensus best practices. Our task as ADHD researchers is not only to provide insights into the nature of ADHD but also to increase access to care across geographic, social and economic boundaries. While we know the importance of timely intervention in ADHD, many individuals will experience long waitlists for assessment and treatment, or may not be able to access treatment at all (e.g. stimulant medication remains unavailable to large swathes of the world). For research to truly translate into practice, we also need to focus on on-the-ground access issues that prevent people from receiving effective, timely and personalized care.

Finally, a central theme mentioned across several sections in the review is the importance of involving individuals with ADHD in the co-design, co-production and co-dissemination of research. Such participatory approaches, inspired by a stronger tradition of advocacy and participatory research in neighbouring fields (e.g. autism research), are starting to be applied more often in certain areas of ADHD research, such as the development of novel interventions (French et al., 2020), but perhaps less so in mechanistic research. We agree with Sonuga-Barke et al. that involving people with ADHD in future research will be vital, and encourage researchers to employ participatory research approaches across the full spectrum of ADHD research, including its more basic science branches. In doing so, it will be important to ensure that all voices in the ADHD community are heard, recognizing the heterogeneity and diversity mentioned in earlier paragraphs. By focusing our attention on matters important to those with ADHD and embracing the diversity of their lived experiences, views and preferences, participatory approaches are likely to facilitate the future translation of ADHD research findings into equitable and acceptable applications and clinical practices for all individuals with ADHD.

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Key points

- Sonuga-Barke et al. (2022) offer thought-provoking insights on the current and future state of ADHD research.
- Designed as a mosaic of different voices from world-leading experts in the field of ADHD, the review by Sonuga-Barke et al. provides a clear and up-to-date overview of the state of research, while emphasizing critical and intriguing questions for future investigation.
- In our commentary, we further consider several cross-cutting ideas discussed in Sonuga-Barke et al. including the heterogeneous nature of ADHD, ensuring equity of translational research across diverse groups, and the importance of participatory research.

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