SPECIAL SECTION

The neuroscience of ADHD: multidisciplinary perspectives on a complex developmental disorder

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The neuroscience of Attention Deficit Hyperactivity Disorder (ADHD) is at a particularly fascinating stage in its development. On the one hand, there are great opportunities for increasingly sophisticated and detailed analyses of the neurobiological underpinnings of the disorder afforded by powerful neuroimaging and genetic techniques. On the other hand, there is the challenge of trying to conceptualize a complex, heterogeneous and 'fuzzy' developmental disorder in a coherent and neurobiologically plausible way so that these opportunities can be exploited. In this Special Section, we have brought together a group of leading international scientists in ADHD from the fields of child psychiatry, paediatrics, experimental and developmental psychology, neurology, psychopharmacology and neuroscience to grapple with this challenge. Their goal was to work in groups across disciplinary boundaries, not to provide exhaustive reviews of the field (although, where reviews are included in papers they are authoritative and wide ranging), but rather to bring their particular points of view to bear on some of the key issues associated with the conceptualization of ADHD and, in so doing, to provide direction for future study. Through the European Network on Hyperkinetic Disorder (Eunethydis), of which most are long-standing associates, the contributors have a track record of undertaking collaborative studies integrating multiple levels of analysis (neuroanatomy, genetics, neuropsychology, neurophysiological and clinical) in an attempt to forge theoretical links between clinical and fundamental science. Thus they are perfectly placed to provide the type of 'state-of-play' review required.

In the first paper, Coghill and colleagues provide a broad examination of the current standing of the science of ADHD in terms of its capacity to develop and test neuroscientifically plausible causal models. These authors conclude that, while a number of such models have been proposed, their accuracy has not been demonstrated empirically. They go on to argue that if this situation is to change, a number of specific barriers need to be overcome. These include the need to properly characterize the ADHD phenotype for genetic and neurobiological studies; to break down disciplinary boundaries to allow work integrating concepts across multiple levels of analysis, using multiple methods; to recognize the existence of neuroscientific complexity both in terms of substantial heterogeneity within ADHD samples and significant overlap between ADHD samples and samples of children with other conditions; and to use developmental approaches that integrate environmental factors into models of genetic and neurobiological influence on ADHD. In many ways, this paper represents a manifesto for the future of research in the neuroscience of ADHD. Its relevance is highlighted by the way its agenda resonates with the contents of the remaining papers, as these themes are picked up and discussed from different points.

Stevenson and colleagues address the issue of the ADHD phenotype. Up to this point, the genetic study of ADHD has made considerable progress with relatively broad and unsophisticated phenotypic measures (e.g. rating scale measures). The authors argue that these measures may need to be refined if further progress is to be made, especially in the area of gene identification. A major concern in this regard is to reduce genetic heterogeneity and identify genetic variation that is shared with other disorders and that which is specific to ADHD. They recommend that both categorical and dimensional measures should be employed, defined on the basis of information from multiple sources. They also conclude that, despite their potential value for segregating heterogeneity, attempts to identify endophenotypes (intermediate processes that

mediate the causal pathway between susceptibility genes and the clinical exophenotype) have so far met with limited success. The authors, while encouraging continuation of this strategy suggest extending such studies beyond the cognitive underpinnings of ADHD to include physiological and metabolic markers. Oades and colleagues ground a discussion of these issues within a broad overview of the neurochemistry and psychopharmacology of the catecholamine-based behavioural systems implicated in ADHD. They highlight the complex role played by catecholamine neurotransmission in ADHD, as studied in rodent and primate models and in the clinical condition. Research in the neuropathology of ADHD has mainly concentrated on pre-frontal executive processes as modulated by dopamine. The authors remind us of two things that emphasize the complexity and potential neurobiological heterogeneity of the condition. First, that dopamine plays a critical roles in the regulation of many neural pathways linking sub-cortical with cortical regions, which play separate and distinct roles in areas other than executive functioning, for instance in the regulation of reward-related behaviours and the regulation of the cognitive energetic state. Second, that norepinephrine, as well as dopamine, plays a key role in modulating these brain circuits and that an understanding of dopamine × norepinephrine interactions is likely to be vital in models of ADHD. Banaschewski and colleagues focus on the issue of specificity of causal processes by comparing the neuropsychological, neurobiological and genetic characteristics of ADHD with other disorders (including Oppositional Defiant Disorder, learning disability, autism and schizophrenia). Critically, they provide a case against executive dysfunction as a specific cause of ADHD. They argue that there needs to be concerted and systematic study of the role of other candidate processes such as timing deficits, motivational characteristics and state regulation in the neuropathology of ADHD. Finally, Sonuga-Barke and colleagues highlight the importance of placing ADHD within its developmental context. They do this by exploring the developmental roots of the condition in the preschool period. By doing this, they highlight the importance of identifying pathways between risk and later ADHD. Once again these authors emphasize the developmental complexity and heterogeneity of the condition.

While the focus in all five papers is on basic science, the broader framework is translational. The underlying motivation is to apply findings from the basic sciences to the clinical condition in a way that facilitates a more appropriate and informative taxonomy and eventually more effective treatments for ADHD. The picture that emerges of ADHD as a disorder with a complex, heterogeneous and 'fuzzy' psychopathophysiology challenges current diagnostic conceptualizations regarding the internal structure of the disorder (e.g. the existence of neuropsychological subtypes) and its distinctiveness from other disorders. At the same time, it presents a stimulus for further multidisciplinary work to address these emerging issues.