

Declan Murphy MD, FRCPsych

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Biographical Information

Professor Murphy is the Mortimer D Sackler Professor of Translational Neurodevelopment, and Director of the Sackler Institute of Translational Neurodevelopment, Institute of Psychiatry (IOP), King's College London. He is also Head of Department of Forensic and Neurodevelopmental Sciences (IOP), and Director of the Behavioural and Developmental Psychiatry Clinical Academic Group, King's Health Partners, King's College London. In the latter role his team comprises 600 people who see many thousands of patients a year, and they deliver both Local and National services for people with autism and ADHD, various genetically determined neurodevelopmental disorders (e.g. SHANK3 and 22Q abnormalities),

His overarching mission is to translate research from 'bench to bedside' and develop new diagnostic approaches and treatments. The research work undertaken in his laboratory currently links to stem cells and animal models through to neuropsychological studies and neuroimaging, and clinical trials (including behavioral interventions) and Health Services research.

Professor Murphy undertook his undergraduate training in Medicine at University College (London) and his postgraduate training in psychiatry at the Maudsley Hospital and IOP (London). His research training was first at the IOP and then at NIH (Bethesda). He returned from NIH to the UK in order to establish a 'translational' research program in neurodevelopment.

In autism Professor Murphy, together with colleagues in Oxford and Cambridge, established the MRC UK AIMS multicenter imaging network – the first in Europe. He also leads an NIHR funded program grant on the health and service needs of individuals with autism as they 'transition' from childhood to adulthood. Additionally he leads the European Union Innovative Medicines Initiative in autism (EU-AIMS <http://www.eu-aims.eu/>). This is a novel collaboration between organizations representing affected individuals and their families (Autism Speaks), academia (14 academic centers) and Industry - who for the first time in the world have come together to develop the infrastructure underpinning the discovery of new treatments for autism.

Presentation Abstract (4:30 pm presentation)

Translating findings 'from bench to bedside' rapidly – can it be done?

Discovering novel treatments for any neurodevelopmental and neuropsychiatric disorder is an enormous task. As an example I will describe new 'translational' efforts in Autism Spectrum Disorder (ASD). However the same model can be applied to many other disorders.

ASD is a particularly difficult challenge. Its aetiology and pathology are unknown, the condition shows wide clinical diversity, and case identification is still solely based on symptomatology. Hence clinical trials typically include samples of biologically heterogeneous patients. Nevertheless, recent reports suggest that new opportunities are emerging. Risk gene variants have been identified, some linked to synaptic function and neural connectivity. Also, animals modelling these genetic traits mimic behavioural and neuroanatomical/chemical phenotypes associated with ASD; and it is possible that these behavioural/biological ASD phenotypes could be rescued by targeted molecular treatment. Further, potential biomarkers to aid clinical stratification have emerged from recent neuroimaging, eye tracking, and electrophysiological studies (including adults). In addition, abnormalities have been observed in neurochemical/peptide pathways that may link to abnormalities in brain development and behaviour. There is, therefore, now an opportunity to make progress on the development of new therapies for ASD, including both children and adults

For example, our preliminary results suggest that; 1) differences in brain maturation and function are present very early in 'at risk infants'; 2) people with ASD have abnormalities in the glutamatergic and serotonergic

systems; 3) these are recapitulated in some (but not all) ‘genetic’ and ‘environmental’ rodent models of ASD that; 4) by targeting underpinning molecular mechanisms we can translate work from rodent to human (and back); and 5) modulate differences in brain development (in rodents) and function (in humans).

This initial work, is now being brought together with that of academic and industrial partners across the European Union in the basic and clinical sciences to develop a new platform for drug discovery (European Autism Interventions – A Multicentre Study for Developing New Medications; EU-AIMS) as part of the EU Innovative Medicines Initiative. Our aim is to: a) develop cellular assays and animal models based on confirmed genetic risks, and utilise these models to focus on translational endophenotypes for facilitating new drug discovery; b) validate biomarkers and patient group stratification to optimise conditions for clinical trials; and c) develop a sustainable EU-wide clinical infrastructure to promote research and development of new drugs. We will couple this integrated research effort with the development of new training opportunities and the implementation of new analytical approaches.