

Institute for Children and Young People's Mental Health

at King's College London & Maudsley Hospital

ADHD is the most common mental health condition assessed and treated in our CAMH services, making it a research and policy priority. Our group conducts research on impulse and attention control difficulties including attention-deficit/hyperactivity disorder and its prodromal precursors with goal of identifying bio-markers and new treatment targets to promote therapeutic innovation. Our work also attempts to understand the overlap between ADHD and comorbid conditions such as conduct disorder, anxiety, autism and obsessive-compulsive disorder. Our current work is divided into three themes.

1. **Genes, Environment & Development:** Using longitudinal cohort and registry studies we explore the role of genetic and environmental risk factors, and their interplay, in the aetiology of attention and impulse control problems and their development during childhood and adolescence. Recent studies have identified measured genetic risk markers in genome wide association studies, epigenetic processes regulating gene expression and the effects of early childhood adversity on the emergence and persistence of attention problems. There is a special focus on identifying early childhood markers (including infancy) of later disorder to promote timely identification and intervention.
2. **Pathophysiology:** Our search for biomarkers and disorder precursors is based on studies of structural and functional alterations in brain systems and their neuropsychological sequelae across a range of different ages and from a range of different perspectives. We currently employ experimental approaches coupled with individual and comparative structural and functional MR neuroimaging, pharmacological fMRI, PET and electrophysiology EEG and ERPs. We are particularly interested in decomposing the role of executive and reward pathways in ADHD pathophysiology, along with other systems such as the default mode network, in causal heterogeneity in ADHD.
3. **Therapeutics:** We aim to translate our basic research findings into therapeutic benefit for children and adolescents with attention and impulse control problems including ADHD. As part of this we are undertaking a major initiative in health informatics to improve the phenotypic information available to families and clinicians to enhance therapeutic precision in ADHD. This employs artificial intelligence methods to combine and extract childhood ADHD data from clinical and non-clinical public service systems. Our treatment portfolio includes proof of concept studies for new and innovative approaches as well as large scale RCTs to promote evidence-based interventions. Our work extends from medication to psycho-social interventions such as parent training and cognitive behaviour therapy and neurotherapies. There is a strong focus on early intervention. We have recently been awarded a programme grant to study how to deliver parent training using on-line approaches. Our novel cutting edge neuro-therapeutic approaches include fMRI neurofeedback, transcranial direct current stimulation (tDCS) combined with cognitive training and gaze-controlled training in infancy.

Clinical and research foci are completely integrated in the work of the group with clinicians bringing new therapeutic insights to inform scientific goals and researchers exploring the clinical relevance of their work with clinical colleagues.

In the next five years we will work closely together as a scientific and clinical team to strengthen further the synergy between science and clinical practice by focusing on five science themes of explicit therapeutic significance.

Early identification & intervention - We plan to conduct longitudinal studies of early risk predictors to mental illness and to develop early cost effective interventions to reduce those risks.

Identifying new treatment targets - We plan to move beyond the study of established brain systems such as executive control to target novel brain systems increasingly known to be implicated in the causes of ADHD.

Evaluating novel treatments - We plan to evaluate novel cutting-edge neurotherapeutics including fMRI neurofeedback, transcranial direct current stimulation (tDCS), and trigeminal nerve stimulation (TNS). We also plan to evaluate novel non-pharmacological treatments such as Cannabidiol.

Precision medicine - We plan to validate neuro-psychological subtypes to guide treatment decisions. We will also investigate predictors of treatment response for future individualised therapy development.

Digital innovations to improve existing services – We focus on increasing the acceptability and utility, and evaluating the efficacy of digital parent training and behaviour therapy applications and work out the best way to exploit remote monitoring technology to speed up the diagnosis of ADHD to improve the monitoring of treatment.

Key Publications

Genes, Environments & Development

- Barker E. et al. (in press). Do ADHD and BMI have shared polygenic and neural correlates? *Molecular Psychiatry*,
- Demontis D et al (2019). Discovery of the first genome-wide significant risk loci for attention-deficit/hyperactivity disorder. *Nature Genetics*, 51, 63–75.
- Kennedy M, et al (2016). Early severe institutional deprivation is associated with a persistent variant of adult attention-deficit/hyperactivity disorder (ADHD): Clinical presentation, developmental continuities and life circumstances in the English and Romanian Adoptees study. *Journal of Child Psychology & Psychiatry*, 57, 1113-1125.

Pathophysiology

- Lambek R, et al (2018). Are there distinct cognitive and motivational sub-groups of children with ADHD? *Psychological Medicine*, 48, 1722-1730.
- Norman LJ et al. (2016) Structural and functional brain abnormalities in ADHD and OCD: A comparative meta-analysis. *JAMA Psychiatry*, 73, 815-82.
- Sidlauskaite J et al (2016). Default mode network abnormalities during state switching in attention-deficit/hyperactivity disorder. *Psychological Medicine*, 46, 519-528.

Therapeutics

- Alegria et al (2017) Real-time fMRI neurofeedback in adolescents with attention deficit hyperactivity disorder. *Human Brain Mapping*. 38, 3190-3209.
- Sonuga-Barke EJS, et al (2018). The clinical effectiveness and cost of specialised individually-delivered and generic, group-based parenting programmes for preschool attention-deficit/hyperactivity disorder: A multi-centre, randomised controlled-trial comparing the New Forest Parenting Programme and Incredible Years. *European Child Adolescent Psychiatry*, 27, 797-809.
- Westwood S, Radua J, Rubia K (2020) Non-invasive brain stimulation in children and adults with ADHD: A systematic review and meta-analysis, *Journal of Psychiatry and Neuroscience*, in press.