

**ECNP Targeted Expert Meetings (TEMs)
27-28 August 2010, Amsterdam, The Netherlands**

**Report on the TEM Child and Adolescent Neuropsychopharmacology
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The Targeted Expert Meeting on Child and Adolescent Neuropsychopharmacology was focused on Attention Deficit Hyperactivity Disorder (ADHD).

The first series of three presentations discussed new molecular pathways in ADHD and their basic, translational and clinical implications. Barbara Franke reviewed the results of the association studies of classic candidate genes, linkage studies and the newer generation of genome-wide association studies (GWAS). Although GWA studies in ADHD have reported few so far, if any, genome-wide significant findings, many interesting and potentially useful genetic variants may be found among the top findings. These do not support the involvement of the classic neurotransmitter genes (e.g. of the dopaminergic, serotonergic or noradrenergic neurotransmission) but genes involved in basic processes like cell division, adhesion (especially via cadherin and integrin systems), neuronal migration, and neuronal plasticity. One of the newer candidate genes is *CDH13*. The GWAS results point further to the relevance of shared genetic factors across multiple psychiatric disorders as well as shared genes between psychiatric disorders like ADHD and somatic conditions such as diabetes mellitus and cardiovascular disease. Recent papers also indicate that in an as yet unknown number of cases ADHD is due to major rare variants such as copy number variations. Strategies for the future are to perform whole genome or exon sequencing to understand the prevalence of the rare variations, to perform translational studies in animal and cell models, and intensify bioinformatic analyses to integrate the various findings. Phil Asherson drew upon further implications of these newer findings, and Klaus-Peter Lesch illustrated the value of using knock-out models of these newer candidate genes in ADHD and of studying the functional consequences of these genes in an imaging genetics approach.

The second series of presentations was about brain imaging in ADHD and its translational aspects. Kerstin Konrad first commented on some practical issues, such as that the sample of ADHD children recruited for brain imaging studies may not be representative of the larger clinical population of ADHD patients, since more severe patients tend not to be selected or tend to drop out. Findings of brain anatomy indicate widespread abnormalities in structural brain development with both regional decrease and increase of grey matter and decrease of white matter. Most of the differences appear to be stable over age. A new idea is that functional abnormalities such as attentional lapses and other cognitive impairments in ADHD are due to an abnormal default-mode network (DMN), i.e. a DMN that stays activated while performing on a task or interferes with task performance. Most exciting are newer data of patterns of abnormal connectivity between neural systems in ADHD, and beneficial effects of both medication and intensive cognitive training on these connectivity problems. Sarah Durston stressed the importance of making brain imaging findings clinically meaningful. She showed that different cognitive subtypes of ADHD (deficits in control, reward, timing and speed-accuracy tradeoff) had a distinctive brain imaging profile. Nikos Makris made a close connection to this presentation in his talk about a neural systems analysis of ADHD in adults.

The third component in this TEM was about the use and clinical applications of animal models of ADHD. Terje Sagvolden extensively discussed the merits of the spontaneous hypertensive rat (SHR) model of ADHD and explained the Developmental Dynamic Theory of ADHD that emphasises impairment of reinforcement delay gradients. Jeffrey Glennon provided a critical appraisal of the SHR and argued that we need a variety of animal models that reflect the clinical heterogeneity of ADHD. Trevor Robbins discussed a neural-systems approach based on a refined dissection of the various fronto-striatal circuits in animals and functional psychopathology approaches in humans.

All presentations gave rise to lively and interesting discussions and debate, and to various new ideas for research and translation studies. These will be described in a road map that identifies critical gaps in current knowledge and present priorities in research.