



## PRESS BRIEFINGS – 26<sup>th</sup> ECNP CONGRESS

### Teasers (short summaries)

#### Press briefing, Sunday 6 October, 12.00-12.50

Moderator: Gitte Knudsen, Denmark

##### **Dopamine in addiction**

*Jocelyne Caboche*

*INSERM-CNRS-Université Pierre et Marie Curie, UMRS 952-UMR7224, Paris, France*

Addiction can be considered as a distortion of reward-controlled plasticity, which depends on dopamine (DA). All drugs of abuse produce, albeit via distinct processes, increases of DA levels within the striatum. Addictive drugs also share the ability to activate the extracellular signal regulated kinase (ERK) cascade in reward-related brain regions through DA-dependent mechanisms. This kinase cascade is well known for its major implications in synaptic plasticity and memory formation in all brain regions. It is also critically involved in the molecular mechanisms underlying reward-controlled plasticity, along with long-lasting behavioural alterations induced by drugs of abuse. Once activated, ERK translocates towards the nucleus where it controls epigenetic and genetic events that are critical for the expression of immediate early genes along with morphological changes and behavioural responses to cocaine. We propose that targeting the ERK pathway may be a promising strategy for therapeutics to alleviate disorders of learning and decision making that arise from compromised striatum function.

##### **Glutamatergic agents as novel treatments for mood and anxiety disorders**

*Gerard Sanacora*

*Yale University, Psychiatry, New Haven, USA*

Although we have made significant advances in the treatment of mood disorders, there is still a lot of room for improvement based on a better understanding of the pathophysiological processes that contribute to the disorders. Mounting evidence now suggests the glutamatergic neurotransmitter system contributes to the pathogenesis of mood and other neuropsychiatric disorders. A series of preclinical and clinical studies now suggest that a novel class of drugs, targeting various components of the glutamatergic neurotransmitter system, may produce rapid and robust antidepressant effects, even in patients who had previously not responded to the standard antidepressant medications. The presentation will briefly review the neurobiological basis for this line of research, presenting specific examples of preclinical rodent data highlighting changes in glutamatergic physiology and the effectiveness of novel glutamatergic drugs in rodent models of mood disorders. It will also include a review of the existing clinical trials including the results of newly completed studies with experimental phase II agents. Specific results from a recently completed phase II trial with a unique non-selective NMDA receptor antagonist (AZD6765) will be included in the presentation.

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**Press briefing, Sunday 6 October, 12.00-12.50**

Moderator: Gitte Knudsen, Denmark

**Epigenetics in ageing and Alzheimer's disease**

*Daniel van den Hove*

*Maastricht University, School for Mental Health and Neuroscience, Department of Translational Neuroscience, Maastricht, The Netherlands*

With the aging of the population, the growing incidence and prevalence of Alzheimer's disease (AD) increases the burden on individuals and society as a whole. To date, the pathophysiology of AD is not yet fully understood. Recent studies have suggested that age-related epigenetic mechanisms such as DNA methylation and histone modifications may play a pivotal role in its pathogenesis. Most of those age-related epigenetic changes were prevented by caloric restriction (dieting/fasting), but not by the certain antioxidants. More recent translational studies on the human hippocampus support the notion that epigenetic regulation is profoundly disturbed in AD subjects. Altogether, these findings indicate that aging and AD are associated with epigenetic dysregulation at various levels although it is not fully clear whether the observed epigenetic changes represent a cause or a consequence of the disease. More research is needed in order to clarify the exact role of epigenetic regulation in the development and course of AD. Research on earlier stages of the disease could provide more insight into its underlying pathophysiology, possibly contributing to the establishment of early diagnosis and the development of more effective treatment strategies.



**Press briefing, Monday 7 October, 08.00-08.50**

Moderator: Hans-Ulrich Wittchen, Germany

**Food addiction: fact or fiction?**

*Suzanne Dickson*

*Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden.*

Obesity has reached global epidemic proportions and creating an urgent need to understand mechanisms underlying excessive and uncontrolled food intake. Almost all circulating gut peptides contribute to the control of food intake by signalling satiety. One important exception is ghrelin. Ghrelin secretion increases before meals and behavioural and electrophysiological evidence shows that ghrelin acts in the hypothalamus to signal hunger and increase food intake and adiposity. Moreover, new data have shown that reward pathways in the brain involved in alcohol and drug addiction are also essential elements of the ghrelin responsive circuit. Based on these and other findings, Dr. Dickson will raise the possibility that obesity is a food addiction.

**New pharmacotherapies for schizophrenia: the case of N-Acetyl Cysteine (NAC)**

*Michael Berk*

*Deakin University, School of Medicine, Geelong, Australia*

Dr. Berk will discuss the evidence base supporting novel approaches to the treatment of so-called negative symptoms in patients with schizophrenia. Positive symptoms (delusions, hallucinations) can be successfully treated, but the treatment of negative symptoms (avolition, anhedonia, blunted affect) is still in its infancy. The glutamate modulator N-acetyl cysteine (NAC) has anti-inflammatory properties, protects against mitochondrial dysfunction, increases neurogenesis, and promotes neuronal survival. NAC has shown efficacy in the treatment of bipolar disorder, autism, smoking, pathological gambling, depression, and in the treatment of obsessive symptoms. Importantly, clinical trial data in schizophrenia also suggests a beneficial effect of NAC on negative symptoms in patients with schizophrenia. Qualitative analysis of the trial data has shown greater improvements in social interaction, insight, self-care, motivation and volition, and mood reactivity. This data supports NAC as a novel adjunctive treatment for schizophrenia.

**Sex hormones and anxiety in women**

*Inger Sundström Poromaa*

*Uppsala University, Department of Women's and Children's Health, Uppsala, Sweden*

Pre-menstrual dysphoric disorder (PMDD) affects approximately 3-5% of women in childbearing ages and is typically manifested by symptoms of anger, irritability, anxiety, and depressed mood that occur only in the luteal phase of the menstrual cycle. PMDD is commonly regarded as a hormonal disorder with psychiatric expression. However, PMDD is also a disorder with a clear-cut relation to altered central serotonergic function. In addition, there are indications for a luteal phase deficit in gamma-aminobutyric acid (GABA)-mediated inhibition. Our findings suggest that anxiety proneness and progesterone levels modulate menstrual cycle related amygdala reactivity in women with PMDD. Dr. Poromaa will discuss the consequences of these findings for our thinking about, and the treatment of, menstrual cycle related mental disorders.



**Press briefing, Monday 7 October, 12.00-12.50**

Moderator: Alessandro Zuddas, Italy

**The pharmacological treatment of adult ADHD**

*Esther Sobanski*

*Central Institute of Mental Health, University of Heidelberg, Mannheim, Germany*

One of the greatest recent successes of psychiatry is the treatment of children with attention deficit/hyperactivity disorder (ADHD) with stimulants like methylphenidate and atomoxetine. However, in many cases, childhood ADHD persists into adulthood and the effect of stimulants in adult ADHD patients is less good and many patients with adult ADHD have persistent symptoms and related impairments in social functions. In this presentation, Dr. Sobanski will present data from two promising proof of concept trials in patients with adult ADHD: one on the nicotine acetylcholine receptor agonist ABT-894 and one on the histamine (H3) receptor antagonist bavisant. While ABT-894 had a significantly better efficacy than placebo, bavisant was not different from placebo and showed a high incidence of adverse events. In addition, Dr. Sobanski will present important data on the impact of atomoxetine on driving, showing that atomoxetine improves the driving performance of adult ADHD patients. These findings are crucial in the treatment and rehabilitation of adult ADHD patients.

**New treatment options for cognitive problems in Down syndrome**

*Benoit Delatour*

*CRICM/ICM, Team Alzheimer's and Prion diseases UPMC/Inserm UMR-S 975, Paris, France*

Down syndrome (DS) is a disorder that causes a lot of individual suffering and high costs to society. It has been suggested that DS is the consequence of an imbalance between inhibitory (GABA) and excitatory (glutamate) neurotransmission. In a mouse model of DS, Dr. Benoit and his colleagues have shown that the GABA-A inverse agonist ( $\alpha 51A$ ) can efficiently restore learning and memory functions. Also,  $\alpha 51A$  enhanced behaviourally-evoked immediate early gene products in specific brain regions and restored levels of gene expression in selected dysregulated brain pathways. These findings support the memory promoting effects and the therapeutic promise for this GABA-A inverse agonist. In the discussion, Dr. Benoit was elaborate on the future role of  $\alpha 51A$  in the prevention and early treatment of DS.

**The anatomy of violence: applications in childhood**

*Adrian Raine*

*Department of Criminology, University of Pennsylvania, Philadelphia, USA*

The rapid developments taking place in neuroscience are providing functional neuroanatomical insights into childhood anti-social behaviour. They are also creating an uncomfortable tension between our concepts of responsibility and retribution on the one hand, and understanding and mercy on the other. Neurocriminology is a new field which is increasingly documenting brain impairments not just in adult offenders, but also in anti-social children. This talk outlines implications of this new research, not just for current crime research, but also for our future conceptualisation of moral responsibility, free will and punishment. If the neural circuitry underlying morality is compromised in psychopaths, how moral is it of us to punish prisoners as much as we do? Should neurobiological risk factors be used to help us better predict future violence? And should we intervene in childhood and adolescence to change the brain to prevent future violent behaviour?



**Press briefing, Tuesday 8 October, 08.00-08.50**

Moderator: Wim van den Brink, The Netherlands

**Classification and diagnosis in psychiatry**

*Wim van den Brink, Academic Medical Center University of Amsterdam, The Netherlands*

*Guy Goodwin, Department of Psychiatry, University of Oxford, United Kingdom*

*Celso Arango, Department of Psychiatry, University Complutense, Madrid, Spain*

*Paul Arteel, Global Alliance of Mental Illness Advocacy networks (GAMIAN Europe)*

In May 2013, the American Psychiatric Association published the fifth version of the Diagnostic and Statistical Manual of Mental Disorder (DSM-5). The launch was accompanied by heated debates both from inside and outside of psychiatry. Some have argued that DSM-5 was lowering disease thresholds resulting in increased prevalence rates of mental disorders, and thus psychiatrisation of normal human behaviour. Others have argued that the developmental process of DSM-5 was not transparent and mainly driven by the interests of the pharmaceutical industry. Again others felt that the new classification failed to take into account recent findings in genetics and neuroscience and that opportunities were missed to make the classification more relevant for treatment and research. In this press briefing, two eminent European psychiatrists, Prof. Guy Goodwin from the UK and Prof. Celso Arango from Spain will answer questions on these and other topics related to DSM-5 and the classification, diagnosis and treatment of mental disorders in general. Mr. Paul Arteel will give his opinion regarding these developments from a patient's representative perspective. The session will be moderated by Prof. Wim van den Brink from the Netherlands.

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