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General Information

ICAW has developed in 2000 from the interdisciplinary BMBF addiction research network (1996-2001) focusing on neurobiological and behavioral foundations of alcohol-addiction. The objectives are enduring development and encouragement of clinical and neurobiological research on addiction. Advancement of traineeship, teaching, qualification in addiction associated topics, inpatient and outpatient interventions and political decision guidance are additional topics. For this purpose an outpatient and consultation-liaison program for the treatment of alcohol and nicotine addiction has been established at the department of psychiatry, psychosomatics and psychotherapy in 2008 in connection with the reestablishment of a full professor position in psychiatry focusing on addiction medicine (Prof. Fallgatter). Additionally, the Dept. of Psychology I established a full professorship for Interventional Psychology (Prof. A. Kübler) with a focus on addiction research.

Major Research Interests

Neurophysiological assessment of cerebral cue reactivity in substance dependence

(A. J. Fallgatter, M.M. Schecklmann, L. Ernst, A. Dieler, Dept. of Psychiatry)

Event-related potentials (ERP), functional Magnetic Resonance Imaging (fMRI) and Near-Infrared Spectroscopy (NIRS) are used to investigate addiction memory as well as topographical aspects of emotional and cognitive processes in alcohol and tobacco dependency. Other areas of research are the reversibility of disturbances in brain function in alcohol-dependent patients and the application of repetitive Transcranial Magnetic Stimulation (rTMS) in tobacco dependent patients.

Biopsychological mechanisms of nicotine craving

(P. Pauli, R. Mucha, M. Winkler, Department of Psychology)

Within the DFG funded research group (Forschergruppe) "Emotion and Behavior" we examine the addiction specific question how emotional learning processes modulate the significance of environmental cues for craving to smoke. We expect that some environmental cues, especially those asso-

ciated with the beginning of the smoking ritual, increase craving while others, especially those associated with the end of the smoking ritual, inhibit craving. An understanding of the latter process seems especially important since it may help to create environments in which smokers have only little urge to smoke.

Molecular mechanisms of alcohol tolerance in *Drosophila melanogaster*

(A. Scholz, Institute for Genetics and Neurobiology)

With molecular genetic, genetic and anatomical methods we investigate ethanol induced behaviors in the genetic model organism *Drosophila melanogaster*. With our behavioral assays we analyze the influence of learned behavior and/or alcohol preference on the development of alcohol tolerance and alcoholism. We are interested in identifying networks that mediate these behaviors. In addition we try to understand how ethanol affects the brain on the cellular level. Previously we have identified a new cellular mechanism that is important for the development of ethanol tolerance. This mechanism is similar to a cellular stress response. The hangover gene plays an important process in this process and the human homologue of this gene can be associated with clinical alcohol dependence (DFG-Einzelförderung und Graduiertenkolleg, Thyssen Stiftung).

Genetics of alcohol addiction

(K.P. Lesch, Psychiatry, Psychobiology)

Neurobiological and psychobiological processes such as reward-related behavior, cognitive-executive dysfunction, stress coping or anxiety that are involved in the development of alcohol addiction are presumably under the influence of genetic variation. Traits, e.g. impulsivity, sensation seeking, or aggressive behavior, as well as dysfunctional cognitive styles, anxiety, emotional lability, and stress vulnerability are directly or indirectly related to morbidity. As evidenced by a plethora of research, most of these psychobiological domains are modulated by a functional serotonin transporter polymorphism. These findings demonstrate the increasing relevance of translational research and molecular-functional imaging studies in order to describe neurobiological founded endophenotypes, thereby bridging the gap between molecular variation and clinical diagnoses.

The endogenous neurotoxic TaClo

(C. Bringmann, D. Feineis, Institute for Organic Chemistry)

Chemical reactive compounds that people are in contact with due to environmental pollution, drug abuse, medical treatment or workplace conditions are suspected to be involved in the etiology of neurodegenerative processes. The investigations focus upon highly chlorinated tetrahydro-beta-carbolines such as „TaClo“ that originates in man from endogenous tryptamine („Ta“) and chloral („Clo“), e.g., after intake of the hypnotic chloral hydrate, or, due to addiction, after occupational exposure to the industrial solvent trichloroethylene (TRI), or as a consequence of solvent abuse („sniffing“).

ADHD as a risk factor for the development of addiction

(C. Jacob, Dept. of Psychiatry)

60%-80% of the childhood manifestations of ADHD persist into adulthood. There is a variety of co-morbid disorders including substance use disorders. The treatment of ADHD with stimulants is protective against substance use disorders. The clinical research group ADHD which is supported by the DFG performs a multilayered evaluation of the endophenotypes working memory and response inhibition.

Addiction and Mental Disorders

(J. Deckert, Dept. of Psychiatry, Psychosomatics and Psychotherapy)

The relevance of substance abuse and dependence other than alcohol (caffeine, nicotine, amphetamine and cannabis) and its neurobiology for the pathogenesis and therapy of mental disorders has developed as an additional research topic, partly within the context of the SFB-TRR58 on „Fear, Anxiety and Anxiety Disorders“. It focuses on the modulation of mental disorders by substance abuse-related genetic factors and the consequences of substance abuse for the therapy of mental disorders employing drug monitoring as well as genetic and imaging techniques.

Substance and behavioural addiction: executive function and learning

(Kübler, A. Meule, Y. Paelecke-Habermann, Dept. of Psychology I)

a) Addiction as automatic behavior and

failure of executive control

Although the concept of automaticity is not sufficient to explain the emergence and maintenance of addiction, there is no doubt that addictive behavior shows components of automaticity. Addiction could be seen as a failure to instantiate executive control to overcome cue-induced automatic behavior. To investigate this hypothesis, we developed a visual search task that allows us to investigate automatization, automaticity and re-establishment of executive control within few training sessions. In cocaine addicts we could show, that dorsolateral prefrontal cortex is less activated than in healthy subjects when executive control is required after automatization. We are currently adapting the visual search task to specific addictions and eating disorder. (DFG Graduiertenkolleg)

b) Deficits in reward learning as a component of addiction

In addicted subjects positive reinforces such as food, sex, or other pleasurable activities lose their rewarding qualities; the brain reward centres such as the Nucleus accumbens remain silent when confronted with such stimuli. It could thus be hypothesized that a deficit in reward learning could be a component of addiction. In a group of smokers such deficits in implicit and explicit learning could be shown. We are currently investigating whether such deficits can be shown in non-addicted social drinkers, women with restrained eating behavior, addicted smokers, non-smokers and smokers in the state of withdrawal.

Teaching

The seminar „neurobiology of addiction“ is an advanced training for young scientists and students of medicine, psychology and biology. The annual basic and advanced training convention of addiction medicine is an additional teaching activity. Research projects are presented on the annual meetings of the ICAW.

SELECTED PUBLICATIONS

Bringmann G, Feineis D, Münchbach M, God R, Peters K, Peters E-M, Mössner R, Lesch K-P (2006). Toxicity and metabolism of the chloral-derived mammalian alkaloid 1-trichloromethyl-1,2,3,4-tetrahydro-beta-carboline (TaClo) in PC12 cells. *Z. Naturforsch.* 61c, 601-610.

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Kübler A, Dixon V, Garavan H (2006). Automaticity and re-establishment of executive control – an fMRI study. *Journal of Cognitive Neuroscience* 18: 1331-1342.

Lesch KP (2005). Alcohol dependence and gene x environment interaction in emotion regulation: Is serotonin the link? *Eur J Pharmacol.* 5, 13-24.

Schecklmann M, Ehliis AC, Plichta MM, Bouter HK, Metzger FG, Fallgatter AJ (2007). Altered frontal brain oxygenation in detoxified alcohol dependent patients with unaffected verbal fluency performance. *Psychiatry Res.* 15, 129-38.

Schol H, Franz M, Heberlein U (2005). The hangover gene defines a stress pathway required for ethanol tolerance. *Nature* 436, 845-847.