

5.2.5 Interdisciplinary Centre for addiction research (ICAW)

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General Information

ICAW has developed in 2000 from the interdisciplinary BMBF addiction research network (1996-2001) focusing neurobiological and behavioral foundations on 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.

Major Research Interests

Neurophysiological assessment of cerebral cue reactivity in substance dependence

(A. Fallgatter, M.M. Richter, M. Schecklmann, 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 associated 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 at *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 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).

Functional and structural cerebral neurodegeneration in alcohol dependency

(A. Bartsch, Department of Neuroradiology)

Chronic alcohol abuse results in morphological, metabolic, and functional brain damage which may, to some extent, be reversible with early effects upon abstinence. We investigated global and local brain volume changes in a longitudinal two-time point study with T1-weighted MRI at admission and after short-term (6-7 weeks) sobriety follow-up in 15 uncomplicated, recently detoxified alcoholics. Volumetric brain gain was related to metabolic and neuropsychological recovery. On admission and after short-term abstinence, structural image evaluation using normalization of atrophy (SIENA), its voxelwise statistical extension to multiple subjects, proton MR spectroscopy (1H-MRS), and neuropsychological tests were applied. The increase of concentration of choline was proved as a matter of a detectable increase of the brain volume. The increase of NAA, a product of the metabolism of the white matter and the neurons, is directly connected with an increased concentration.

Genetic of alcohol addiction

(K.P. Lesch, Psychiatry, Psychobiology)

Neurobiological and psychobiological processes such as reward-related behavior,

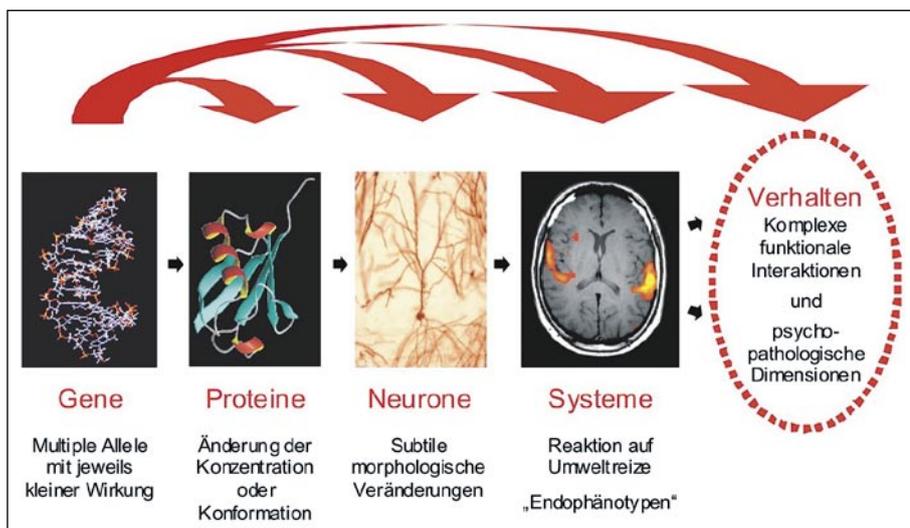


Fig. 1: Molecular imaging of complex behavior and psychopathology.

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 of the development of addiction

(J. Böning, C. Jacob, A. Schmidtke, 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.

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 and teaching of modules of the qualification addiction medicine are additionally activities. Research projects are presented on the annual meetings of the ICAW.

SELECTED PUBLICATIONS

Bartsch AJ, Homola G, Biller A, Smith SM, Weijers HG, Wiesbeck GA, Jenkinson M, De Stefano N, Solymosi L, Bendszus M (2007). Manifestations of early brain recovery associated with abstinence from alcoholism. *Brain*. 130, 36-47.

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.
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, Ehlig 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.

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