

Prof. (apl.) Dr. med. Mathias Zink

Molecular schizophrenia research

1. Narrative academic profile

Dr. Zink started his medical studies with a primary interest in psychiatry and in particular psychotic disorders at Ruprecht-Karls-University of Heidelberg and finished them at Ludwig-Maximilians-University of Munich in 1998, supported by scholarships of the state of Bavaria and the German National Academic Foundation. After a short family break he invested two and a half years into basic research at the Max-Planck-Institute of Neurobiology with methods of molecular and cellular biology as well as animal models. He analysed differential gene expression during terminal differentiation in the chicken's peripheral nervous system and described transcription factors (zinc-finger-protein-encoding genes) under regulation of neurotrophic factors and their receptors. Trained both as a physician and neurobiologist he changed positions to work at the CIMH in Mannheim in order to finish the clinical specialization in Psychiatry and Psychotherapy. At the same time he organized research collaborations within the CIMH. Most important fields of research were dedicated to animal models of perinatal ethanol toxicity in rats, learned helplessness in rats as a model of human depression and effects of antipsychotic treatment on gene expression. These approaches resulted in his habilitation thesis on plasticity of brain development.

Meanwhile his clinical research into basic neurobiological mechanism and treatment interventions in humans was established. Over a period of 16 years he was involved in a broad range of clinical studies, ranging from the investigation of pharmacovigilance, the pathogenesis and treatment of delirium in general medical hospitals, critical evaluation of psychometric test systems, sleep and neurocognition to treatment of mood disorder including electroconvulsive therapy (ECT). More recently, he took part in a multicentre trial testing a SMART-phone intervention to prevent relapse in alcohol dependency. Dr. Zink started investigator initiated trials as principal investigator and finally lead international clinical trials as LKP. His central interest was dedicated to psychotic disorders, most importantly early detection and intervention in individuals with an increased risk for the development of psychotic disorders (at risk mental state: ARMS) and the neurobiology and treatment of first episode psychosis (FEP). Under his guidance and within national and international collaborations, his research group investigated alterations of functional brain activation, neurocognitive and metacognitive deficits in ARMS, as well as the efficacy of pharmacological and psychotherapeutic interventions in ARMS and FEP. Another research interest focused on comorbidity in psychotic disorders. Besides treatment of comorbid major depressive episodes with innovative antidepressive pharmacotherapy, studies addressed comorbid obsessive compulsive syndromes (OCS). Theses investigated the epidemiology, clinical profiles, and interaction of OCS and psychotic symptoms, as well as genetic disposition, functional imaging correlates, pharmacodynamic mechanism and therapeutic interventions.

The research group 'molecular schizophrenia research' successfully applied for grants from several companies, peer reviewed international foundations and the german research foundation (DFG).

In addition he holds the position of chief physician at Bezirksklinikum Ansbach, a large hospital for psychiatry, psychotherapy and psychosomatics with at present 324 inpatients, 10 patients in home treatment (StäB), 70 day clinic places and four large outpatient departments. In collaboration with other large hospitals in Bavaria he currently designs approaches and applications on key questions of psychopathology, comorbidity of several psychiatric disorders,

pharmacological interventions as well as aspects of gender-specific, cultural sensitive and migration-dependent psychiatric treatment.

2. Key output

The multidisciplinary research group has reached different academic milestones: Several members achieved a Bachelor- and Masterthesis in Psychology, a MD-thesis in veterinary and human medicine, and in 2022 a habilitation in human medicine (PD Dr. Susanne Englisch).

New MD-projects investigate the course of comorbid OCS within the interventional PREVENT study, particularly focusing on longitudinal changes of OCS in dependence of pharmacological and psychotherapeutic interventions.

The former group member Dr. Frederike Schirmbeck facilitated the collaboration with her current research at the University Medical Center in Amsterdam, the Netherlands. This resulted in joined publications on comorbid OCS in the large Genetic Risk and Outcome of Psychosis study (GROUP). At present further collaboration studies are planned.

New research collaborations were established with the research group of Prof. Berking at the Friedrich-August-University Erlangen and with the Bavarian multicentre database on pharmacological and epidemiological variables BIDAQ.

Established research interests were pursued and led to review articles and book chapters, e.g. pathogenesis and treatment of comorbid OCS in psychotic disorders (Nerventarzt 2022, Therapiehandbuch Zwangsstörungen 2022).

The analysis of collaborative imaging data was the basis for high-impact publications within consortia. In 2020 we contributed to:

Elvsåshagen T, Bahrami S, van der Meer D, Agartz I, Alnæs D, Barch DM, Baur-Streubel R, Bertolino A, Beyer MK, Blasi G, Borgwardt S, Boye B, Buitelaar J, Bøen E, Celius EG, Cervenka S, Conzelmann A, Coyne D, Di Carlo P, Djurovic S, Eisenacher S, Espeseth T, Fatouros-Bergman H, Flyckt L, Franke B, Frei O, Gelao B, Harbo HF, Hartman CA, Håberg A, Heslenfeld D, Hoekstra PJ, Høgestøl EA, Jonassen R, Jönsson EG, Karolinska Schizophrenia Project (KaSP) consortium, Kirsch P, Kłoszewska I, Lagerberg TV, Landrø NI, Le Hellard S, Lesch KP, Maglanoc LA, Malt UF, Mecocci P, Melle I, Moberget T, Nordvik JE, Nyberg L, Connell KSO, Oosterlaan J, Papalino M, Papassotiropoulos A, Pauli P, Pergola G, Persson K, de Quervain D, Reif A, Rokicki J, Van Rooij D, Shadrin AA, Schmidt A., Schwarz, Ph.D E, Selbæk G, Soininen H, Sowa P, Steen VM, Tsolaki M, Vellas B, Wang L, Westman E, Ziegler GC, Zink M, Andreassen OA, Westlye LT, Kaufmann T. The genetic architecture of human brainstem structures and their involvement in common brain disorders. **Nat Commun.** 2020 11(1):4016.

The recruitment and treatment of patients within large interventional trials made several important publications possible. Several time, secondary endpoints were specifically analysed the the research group. This is also in a phase of conceptualization within the COMBINE trial. The main result of this intervention has been recently published:

Schmidt-Kraepelin C, Feyerabend S, Engelke C, Riesbeck M, Meisenzahl-Lechner E, Verde PE, Correll CU, Kluge M, Makiol C, Neff A, Lange C, Englisch S, Zink M, Langguth B, Poepl TB, Reske D, Gouzoulis-Mayfrank E, Gründer G, Hasan A, Brockhaus-Dumke A, Jäger M,

Baumgärtner J, Leucht S, Cordes J, COMBINE Study Group . Amisulpride and olanzapine combination treatment versus each monotherapy in acutely ill patients with schizophrenia in Germany (COMBINE): a double-blind randomised controlled trial. **Lancet Psychiatry**. 2022 9(4):291-306.