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Narrative academic profile

I am managing assistant medical director, consultant psychiatrist, head of the inpatient unit for schizophrenia and psychosis, head of the inpatient unit for transition psychiatry and head of the outpatient clinic for individuals at ultra-high risk for developing psychosis at the Department of Psychiatry and Psychotherapy at the Central Institute of Mental Health in Mannheim (CIMH), Germany. Further, I am also actively involved in neuroscientific and neuropharmacological research and a group leader of the *"Clinical Neuroscience of Motor Behavior"* research group at the CIMH. The goal of my work is to facilitate the development of prognostic biomarkers for early detection of psychotic disorders (e.g., schizophrenia, catatonia, schizoaffective disorder, depression and bipolar disorder with psychotic features) and sensorimotor side effects associated with antipsychotic medication, to develop novel psychopharmacological models, and to identify neurobiologically plausible target sites for non-invasive brain stimulation. My group is doing this through four interrelated research themes: **(1)** We use state-of-the-art neuroimaging methods (e.g. multivariate data fusion techniques for multimodal MRI data) and behavioral assessments to characterize the neural correlates of sensorimotor abnormalities (e.g. neurological Soft Signs, parkinsonism and catatonia) across the psychosis spectrum; **(2)** We develop and validate next-generation instrumental assessments (via ecological momentary assessment and qualitative real-time motion monitoring/capture) based on sensorimotor mechanisms to predict the onset and outcome of psychotic disorders; **(3)** We conduct prospective studies that follow a range of sensorimotor abnormalities to identify young adults exhibiting clinical high risk of psychosis, and **(4)** In collaboration with colleagues at multiple institutions (at CIMH: Prof. M. Leweke and Prof. G. Gründer), we conduct clinical trials examining the efficacy of novel pharmacological and non-pharmacological approaches for treatment-resistant positive, negative and cognitive symptoms in psychotic disorders.

In a large-scale clinical trial, which started in May 2022, as a PI (together with Dr. Urs Braun, RG Complex systems in psychiatry), I will evaluate the efficacy and safety of oxytocin combined psychosocial interventions (Soteria [community-based social milieu therapy] and cognitive-behavioral therapy/family intervention) for improving psychopathology and social skills in patients with schizophrenia spectrum disorders across the life span. In the coming months, together with the clinical RG of Prof. Peter Gass (CIMH) and the translational neuroimaging RG of Prof. Alexander Sartorius and Dr. Wolfgang Weber-Fahr (CIMH), we seek to develop a (transgenic) rodent model of catatonia that reflects crucial clinical psychomotor abnormalities and can be used to study anatomical and molecular features of pathogenesis and therapy. On a long run, the consistent pursuit of a domain-based approach, taking into account other important dimensions, such as the cognitive and affective domains (e.g. within the framework of the PsyMIND study in collaboration with Dr. E. Schwarz, RG Translational bioinformatics in psychiatry, CIMH), will, I believe, promote further significant contributions to the nosology and neurobiological model development of psychotic disorders. In addition, my hope is also that *propsychotherapeutic psychopharmacology* approach will lead to the development of effective adjuvants to psychosocial therapies that helps patients with schizophrenia spectrum disorders to improve their social skills.

Key output of the years 2020-now

In the last two years, my group used a number of neuroimaging methods including multivariate data fusion techniques for multimodal MRI data to investigate patterns of aberrant intrinsic neural activity and gray matter volume in schizophrenia spectrum disorders patients with neurological Soft Signs, parkinsonism and catatonia. In particular, we provided novel neuromechanistic insights into catatonia suggesting co-altered structure/function-interactions in neural systems subserving coordinated visuospatial functions and motor behavior. These investigations resulted in numerous publications (selected publications):

Hirjak, D., Rashidi, M., Kubera, K. M., Northoff, G., Fritze, S., Schmitgen, M. M., Sambataro, F., Calhoun, V. D., & Wolf, R. C. (2020). Multimodal Magnetic Resonance Imaging Data Fusion Reveals Distinct Patterns of Abnormal Brain Structure and Function in Catatonia. *Schizophrenia bulletin*, *46*(1), 202–210. https://doi.org/10.1093/schbul/sbz042

Fritze, S., Harneit, A., Waddington, J. L., Kubera, K. M., Schmitgen, M. M., Otte, M. L., Geiger, L. S., Tost, H., Meyer-Lindenberg, A., Wolf, R. C., & **Hirjak, D**. (2021). Structural alterations in brainstem, basal ganglia and thalamus associated with parkinsonism in schizophrenia spectrum disorders. *European archives of psychiatry and clinical neuroscience*, *271*(8), 1455–1464. https://doi.org/10.1007/s00406-021-01270-y

Wolf, R. C., Rashidi, M., Fritze, S., Kubera, K. M., Northoff, G., Sambataro, F., Calhoun, V. D., Geiger, L. S., Tost, H., & **Hirjak, D**. (2020). A Neural Signature of Parkinsonism in Patients With Schizophrenia Spectrum Disorders: A Multimodal MRI Study Using Parallel ICA. *Schizophrenia bulletin*, *46*(4), 999–1008. https://doi.org/10.1093/schbul/sbaa007

Wasserthal, J., Maier-Hein, K. H., Neher, P. F., Northoff, G., Kubera, K. M., Fritze, S., Harneit, A., Geiger, L. S., Tost, H., Wolf, R. C., & **Hirjak, D.** (2020). Multiparametric mapping of white matter microstructure in catatonia. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, *45*(10), 1750–1757. https://doi.org/10.1038/s41386-020-0691-2

In a longitudinal study on sensorimotor dysfunction, we showed that neurological Soft Signs are significant predictors of poor clinical outcome in schizophrenia at baseline and >6 months after an acute psychotic episode (reduction of PANSS positive and negative scores).

Sambataro, F., Fritze, S., Rashidi, M., Topor, C. E., Kubera, K. M., Wolf, R. C., & **Hirjak, D**. (2020). Moving forward: distinct sensorimotor abnormalities predict clinical outcome after 6 months in patients with schizophrenia. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*, *36*, 72–82. https://doi.org/10.1016/j.euroneuro.2020.05.002

In another multimodal MRI study, we also showed that neurological Soft Signs and intrinsic neural activity of the inferior parietal lobule were significant predictors of auditory verbal hallucinations in schizophrenia.

Wolf, R. C., Rashidi, M., Schmitgen, M. M., Fritze, S., Sambataro, F., Kubera, K. M., & **Hirjak, D**. (2021). Neurological Soft Signs Predict Auditory Verbal Hallucinations in Patients With Schizophrenia. *Schizophrenia bulletin*, *47*(2), 433–443. https://doi.org/10.1093/schbul/sbaa146

In the last 2 years I have also been working on theoretical and historical concepts of catatonia. The results of these investigations and in-depth analyses have also been published in the meantime:

Hirjak, D., Wolf, R. C., Landwehrmeyer, G. B., & Northoff, G. (2022). Catatonia: looking back and moving forward. *Brain : a journal of neurology*, awac196. Advance online publication. https://doi.org/10.1093/brain/awac196 3

Hirjak, D., Foucher, J. R., Ams, M., Jeanjean, L. C., Kubera, K. M., Wolf, R. C., & Northoff, G. (2022). The origins of catatonia - Systematic review of historical texts between 1800 and 1900. *Schizophrenia research*, S0920-9964(22)00208-0. Advance online publication. https://doi.org/10.1016/j.schres.2022.06.003

Last nut not least, I am also a founding member of a new systematic collaboration of experts in the sensorimotor domain in schizophrenia and other psychoses, the *"European collaboration on movement and sensorimotor/psychomotor functioning in schizophrenia and other psychoses"* (ECSP). I am also the last author of two consensus articles published in *European Neuropsychopharmacology* in 2020 and 2021 describing (a) a common conceptual framework for standards for clinical classification and research on sensorimotor functioning in schizophrenia and other psychoses, and (b) the historical development of the terms "catatonia" and "psychomotor phenomena".

Walther, S., van Harten, P. N., Waddington, J. L., Cuesta, M. J., Peralta, V., Dupin, L., Foucher, J. R., Sambataro, F., Morrens, M., Kubera, K. M., Pieters, L. E., Stegmayer, K., Strik, W., Wolf, R. C., & **Hirjak, D.** (2020). Movement disorder and sensorimotor abnormalities in schizophrenia and other psychoses - European consensus on assessment and perspectives. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*, *38*, 25–39. https://doi.org/10.1016/j.euroneuro.2020.07.003

Foucher, J. R., Jeanjean, L. C., de Billy, C. C., Pfuhlmann, B., Clauss, J., Obrecht, A., Mainberger, O., Vernet, R., Arcay, H., Schorr, B., Weibel, S., Walther, S., van Harten, P. N., Waddington, J. L., Cuesta, M. J., Peralta, V., Dupin, L., Sambataro, F., Morrens, M., Kubera, K. M., … **Hirjak, D.** (2022). The polysemous concepts of psychomotricity and catatonia: A European multi-consensus perspective. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*, *56*, 60–73. https://doi.org/10.1016/j.euroneuro.2021.11.008