Research project (possibly Dr. med.) at the Department of Psychiatry and Psychotherapy

The basal forebrain cholinergic nuclei (BFCN) in schizophrenia and bipolar disorder

We are searching for a highly motivated medical student interested in neuroimaging methods and psychotic disorders.

Background:
The basal forebrain cholinergic nuclei (BFCN) are the main source of acetylcholine in the cerebral cortex; they support multiple cognitive functions, ranging from attention to decision-making (Ballinger et al., 2016). Based on this functional relevance, it has been suggested that the BFCN might be altered in schizophrenia and relevant for the patients' cognitive impairments. In support, recent evidence indicates that BFCN structural integrity (i.e., volume) is altered in schizophrenia and associated with patients' attentional deficits (Avram et al., 2021). However, BFCN volume only reflects a rough structural proxy of cholinergic deficits. Other measures might offer a more complete picture on how the cholinergic system is altered in schizophrenia. Therefore, we aim to also investigate the functional connectivity of BFCN in schizophrenia. Furthermore, while there is evidence that abnormal development of the BFCN is a vulnerability factor for schizophrenia (Ross et al., 2013), it is unclear whether BFCN are also altered in other psychotic disorders (e.g., bipolar disorder with psychotic symptoms).

Methodology: We plan to investigate (putative) structural and functional alterations of BFCN in patients with schizophrenia, patients with bipolar disorder with and without psychotic symptoms, and healthy controls. BFCN structure will be assessed by investigating the gray matter integrity of a cytoarchitectonically defined region-of-interest (ROI), via structural magnetic resonance imaging (MRI)–based volumetry. Correspondingly, BFCN function (based on the same ROI) will be investigated by resting-state functional MRI-based functional connectivity. Finally, associations between structural and functional findings as well as between these and clinical/behavioral data (e.g., reflecting cognitive impairment) will be explored with correlation/mediation analyses.

Contact:
If we peaked your interest/ for additional information contact Dr. Mihai Avram (mihai.avram@uksh.de). Prof. Dr. Stefan Borgwardt (stefan.borgwardt@uksh.de) will be the official project supervisor.

Literature:
1. Ballinger EC, Ananth M, Talmage DA, Role LW. Basal forebrain cholinergic circuits and signaling in cognition and cognitive decline. *Neuron*. 2016;91:1199–218.
2. Avram M, Grothe MJ, Meinhold L, Leucht C, Leucht S, Borgwardt S, Brandl F, Sorg C. Lower cholinergic basal forebrain volumes link with cognitive difficulties in schizophrenia. *Neuropsychopharmacology.* (in press). https://doi.org/10.1038/s41386-021-01070-x
3. Ross RG, Hunter SK, McCarthy L, Beuler J, Hutchison AK, Wagner BD, Leonard S, Stevens KE, Freedman R. Perinatal choline effects on neonatal pathophysiology related to later schizophrenia risk. Am J Psychiatry. 2013;170:290–8.