Universität Basel

Research Project

Linking synaptic dysfunction to disease mechanisms in schizophrenia - a multi-level investigation (SYNSCHIZ) ERA-NET

Third-party funded project

Project title Linking synaptic dysfunction to disease mechanisms in schizophrenia - a multi-level investigation (SYNSCHIZ) ERA-NET
Principal Investigator(s) Borgwardt, Stefan ;
Organisation / Research unit
Bereich Psychiatrie (Klinik) / Neuropsychiatrie (Borgwardt)
Departement Psychologie / Cognitive and Decision Sciences (Mata)
Department
Project start 01.08.2019
Probable end 31.07.2022
Status Completed

Schizophrenia (SZ) is a severe mental illness characterized by a wide range of defective cognitive function and a complex set of symptoms including halluccinations and delusions. SZ represents one of the major challenges for society, with large unmet patient needs and substantial health care costs for the European community. Various studies on the genetic risk architecture and aberrant brain functional connectome of SZ have implicated synaptic dysfunction in the pathophysiology, yet the precise mechanisms remain elusive. The complex nature of SZ can only be unveiled in an integrative transdisciplinary research framework which involves several research disciplines collaborating on the same topic from different perspectives. To integrate and maximally exploit the transdisciplinarity benefits, the SYNSCHIZ project implements a vertical synergy approach, where synaptic dysfunction is targeted at multiple levels of investigation, from a genetic level to the neuron level to the level of brain network dysfunction.The main aims of SYNSCHIZ are to:-uncover the genetic architecture that increases the risk for synaptic dysfunction in SZ using large international cohorts and running multi-site replication studies.-integrate the identified genes into the development of novel, biophysically detailed computational models of synapse dysfunction.-validate these computational models experimentally in neuronal cell cultures derived from stem cells and create new knowledge on mechanisms underlying synaptic dysfunction in SZ-link gene- and neuron-level discoveries to brain network level (dysconnectivity) in SZ patients focusing on the SZ prodrome and in individuals at ultra-high risk for psychoses in a clinical setting.The vertical structure will maximize synergy by at least four features:-identification of novel genes will improve the accuracy of computational models-experimental verification will allow refinement of the computational models-gene-level and neuron-level discoveries can be used to predict effects observable at brain level-brain-level dysconnectivity discoveries can be used to link synapse dysfunction to symptoms.The multi-level approach aims to identify clinically useful biomarkers, required for early detection and prognostic predictions in SZ, e.g. by using pluripotent stem cells as a screening tool. SYNSCHIZ therefore implements a strong translational component that will immediately transfer scientific discoveries into clinical application for targeted treatment and care. To reach these ambitious aims, SYNSCHIZ gathers a consortium of international scientific experts, ensuring synergy across various disciplines and with access to critical infrastructure. The SYNSCHIZ approach will substantially improve our understanding of the SZ pathophysiology and simulate new developments for treatment that we will take into immediate clinical testing and promotion for market uptake.

Keywords schizophrenia; gene level; translational level; neuronal level; synaptic disfunction; brain network level

Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners