Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

A multi-scale neurocircuitry for modeling drug effects

Autor: Judith Schöttler
Institut / Klinik: Zentralinstitut für Seelische Gesundheit (ZI)
Doktorvater: Prof. Dr. R. Spanagel

Neuropsychiatric disorders account for 14% of the global burden of diseases, however the existing compounds (> 150) achieve only modest treatment success due to our incomplete understanding of brain functioning. Therefore, it is critical to gain insights on the underlying pathophysiological processes, which can be manipulated by pharmacological interventions. The brain topology is a manifold composition of networks/neurocircuitries at different spatiotemporal scales. Thus, it is vital to characterize the network comprising components and the neuronal interactomes. While recent in silico and experimental approaches (*HumanBrainProject*) attempt to shed light on the human brain topology, there is not yet sufficient data for systematic characterization of the neurocircuitries. In preclinical research, rodent brain is considered as an appropriate translational model for human neurobiology. A number of previous studies have investigated the rodent neurocircuitries, but a robust and systematic understanding of the rat's connectome is still missing. In particular, the already established neurocircuitries are often not hypothesis-free and empirical and lack consistencies in terms of scales, methodology and species (i.e. the networks were obtained from a mixture of cat, primate and rodent studies).

Therefore, the goal of this thesis is to establish a consistent multi-scale assumption-free neurochemical connectome of the rat brain using high-end systematic data mining and statistical methods. In total, track tracing, autoradiography, immunohisto- and cytochemical, in situ hybridization data and biological factors (such as gender, strain, weight/age etc.) from 1560 original research articles (36464 rats) were extracted. The resulting neurocircuitry is comprised by 125 anatomically distinct brain regions (forebrain, midbrain and brain stem), 2931 chemically-defined projections and represents a dynamical extension of the previously developed *neurocircuitry for modeling drug effects*. It provides a unique comprehensive framework for understanding the topological network properties of the healthy rat brain and constitutes a robust reference for future in vitro, in vivo and in silico neuropsychiatric studies.