

Re-Conceptualizing Neuropsychiatric Diseases with Meta-Analytical Data Mining

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Overview

Numerous neuroimaging studies have elucidated the neural underpinnings of neuropsychiatric diseases in the last two decades. Although the current fifth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) - published in 2013 - introduced dimensional approaches, the ambitious aim to include reliable biomarkers failed so far. Now it is time to harvest knowledge from these numerous small sample neuroimaging studies and to extract their essence to provide convergence of studies as reliable diagnostic support. Here, we want to discuss how meta-analytical approaches can crucially accelerate the conceptualization of neuropsychiatric diseases and optimize therapy by providing reliable and clinically applicable biomarkers.

The symposium is designed in the following way. The first talk by Veronika Müller will introduce meta-analytical imaging approaches and demonstrate their potential in elucidating the underpinnings of psychiatric disorders using as a model the disease depression and personality traits and disease. The second talk by Su Lui will focus on another psychiatric disorder, i.e. schizophrenia, and will discuss data-driven approaches to subtype schizophrenia. The third talk by Franziska Albrecht will discuss how meta-analytic approaches can contribute to the early and accurate diagnosis of atypical Parkinsonian syndromes, in particular corticobasal syndrome and progressive supranuclear palsy. For these syndromes the dissociation from typical Parkinson's disease is of paramount interest to initiate adequate treatment. The last talk by Matthias Schroeter will show how clinical symptoms can be predicted not only in diseases such as frontotemporal dementia, but even in single patients when meta-analytical approaches are combined in patients and healthy cohort data. The symposium will give a comprehensive overview how meta-analytical approaches can revolutionize the understanding and

therapy of neuropsychiatric diseases, and, by doing so, pave the road to incorporate imaging biomarkers into diagnostic systems.

Lecture 1: *The hidden treasures of neuroimaging: Meta-analyses as a tool to better understand brain functioning*

Veronika Müller Presenter

Over the last two decades, neuroimaging has evolved into a widely used method to investigate functional neuroanatomy and the pathophysiology of brain disorders. However, despite this success, results of individual studies are limited as they often suffer from low statistical power and limited replicability. Neuroimaging meta-analyses constitute a potent approach to capitalize on the wealth of neuroimaging research and identify regions robustly involved in specific mental processes and their developmental or pathological changes. The talk will introduce the method and strengths and pitfalls of coordinate-based meta-analysis (Neurosci Biobehav Rev 2018;84:151-161. doi: 10.1016/j.neubiorev.2017.11.012), how it can investigate brain function and organization, and its role in understanding the neural mechanisms associated with mental disorders. These issues will be illustrated by exemplary use cases dealing with the consistency of aberrant brain activity in depression (JAMA Psychiatry 2017;74(1):47-55. doi: 10.1001/jamapsychiatry.2016.2783) and the use of meta-analytically defined networks for predicting personality traits and disease (Brain Struct Funct 2018;223(6):2699-2719. doi: 10.1007/s00429-018-1651-z; Hum Brain Mapp 2017;38(12):5845-5858. doi: 10.1002/hbm.23763; Biol Psychiatry 2021;89:308-319. Doi: 10.1016/j.biopsych.2020.09.024).

Lecture 2: *Meta-analytic imaging findings in schizophrenia and data-driven approaches to subtype schizophrenia patients*

Su Lui Presenter

Numerous imaging studies have made effort to explore brain abnormalities in first-episode or long-term illness of schizophrenia and their relations with the clinical symptoms, illness duration, or predictive values for the outcome. Here, the consistent meta-analysis findings of structural and functional imaging biomarkers of schizophrenia will be discussed and how these imaging findings can be used for individual diagnosis based on our clinical experience (Am J Psychiatry 2016;173(3):232-43. doi: 10.1176/appi.ajp.2015.15050641; J Psychiatry Neurosci 2018;43(2):131-142. doi: 10.1503/jpn.160219). Then, the talk will discuss how data-driven approaches that cross conventional diagnostic categories can explain individual differences in clinical symptoms (Mol Psychiatry 2021; doi: 10.1038/s41380-021-01308-6; Schizophr Bull 2021;sbab110. doi: 10.1093/schbul/sbab110; JAMA Psychiatry 2015;72(7):678-86. doi: 10.1001/jamapsychiatry.2015.0505).

Lecture 3: *Disentangling atypical Parkinsonian syndromes & predicting symptoms individually*

Franziska Albrecht Presenter

Using meta-analytical approaches, we present a new conceptual framework to understand atypical Parkinsonian syndromes, and distinguish between their clinical features (i.e. corticobasal syndrome) and underlying histopathology (i.e. corticobasal degeneration) (npj Parkinson's Disease 2017;3:12. doi:10.1038/s41531-017-0012-6). Further the talk outlines how these findings can be used for individual clinical syndrome prediction of alien/anarchic limb phenomena which are frequent in corticobasal syndrome (Cortex 2019;117:33-40. doi.org/10.1016/j.cortex.2019.02.015 & Ann Neurol 2020;88(6):1118-1131. doi: 10.1002/ana.25901). Another atypical parkinsonian syndrome - progressive

supranuclear palsy - is presented as a model to validate systematically a well-known disease hallmark (midbrain atrophy) with whole-brain meta-analyses identifying disease-related atrophy (Neuroimage Clin 2019;22:101722. doi.org/10.1016/j.nicl.2019.101722). Results support the incorporation of structural MRI data, particularly disease-specific structures, into revised diagnostic criteria.

Lecture 4: *From correlational approaches to meta-analytical symptom reading in single subjects*
Matthias Schroeter Presenter

Recent approaches base diagnosis and therapy mainly on clinical assessments of patients. Here, we show, in particular for frontotemporal dementia, that meta-analytical approaches can not only extract disease-specific prototypical networks, but also predict specific symptoms associated with these diseases. Herewith, diseases can be re-conceptualized in the framework of cognitive neuropsychiatry when meta-analyses on diseases and meta-analyses in healthy subjects are combined (Cortex 2014;57:22-37. doi: 10.1016/j.cortex.2014.02.022; Neurosci Biobehav Rev 2020;112:164-212. doi: 10.1016/j.neubiorev.2020.01.023; & 2021;128:592-620. doi: 10.1016/j.neubiorev.2021.05.028). Meta-analytical tools can even predict symptoms in single patients if information is used from comprehensive functional imaging databases on healthy subjects (so called Meta-Analytical Reading of Symptoms, MARS, see Cortex 2020;128:73-87. doi: 10.1016/j.cortex.2020.03.010). The latter personalized stance can even be used to tailor therapy for patient's needs.