Advanced Diffusion Analyses and Data Harmonization Methods for Improving Sensitivity and Specificity of Diffusion MRI Studies in Psychosis

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Diffusion MRI acquisition and analyses often suffer from poor reproducibility due to lack of standardization in acquisition and analysis approaches, heterogeneity of subject populations with regard to demographics, clinical presentation, medication confounds, and/or, importantly, statistically underpowered samples to detect subtle abnormalities. In addition, common diffusion metrics reflect non-specific signals associated with numerous microstructural changes, which could also vary as a function of illness-related processes.

Over the last two decades, our laboratory has been developing and applying novel strategies to overcome the above challenges as well as using them to study white matter disruptions in schizophrenia. In this talk, I will present three novel approaches to generate reliable and valid lifespan neuroimaging trajectories in psychosis. I will demonstrate the use of advanced diffusion MRI acquisition and analysis methods that produce measures with improved specificity, in order to help disentangle the effects of co-occurring pathologies. I will then describe novel procedures to harmonize and to analyze data across multiple studies. Finally, I will present findings from harmonized data from multiple studies, leading to a large dataset consisting of 1092 subjects (600 patients and 492 controls), derived from 13 different studies. Importantly, subjects were recruited at different disease stages, and across a wide age-range (14-65). We report on lifespan trajectories from this Big-Data and compare these findings to previously hypothesized trajectories.

Our approach identifies co-occurring cellular and extracellular abnormalities, which fluctuate as a function of age and disease progression. The Big-Data harmonization approach provides superior statistical power, enables cross-sectional studies comprising homogeneous populations, and when combined with the use of specific imaging markers, improves our capacity to detect reliable and valid information regarding the pathophysiology of psychosis, and ultimately resulting in refined and robust estimation of lifespan trajectories associated with various imaging markers.

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Neuroscience Research Building (NRB 132)
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