Lecture 2: Monday, July 9

Neuroimaging & neurophysiological investigations into schizophrenia

Kiyoto Kasai
Department of Neuropsychiatry, The University of Tokyo

Abstract

Psychiatric research has been limited in reciprocally translating findings between rodent models and human neuroimaging. Here we propose a concept of “translatable” brain markers (Okano et al., 2016) and describe cutting-edge efforts by illustrating research on schizophrenia as a representative example. The onset of schizophrenia is usually at adolescence and young adulthood, and the cognitive dysfunction persists for life-long in some patients. Structural MRI studies have shown progressive decrease of neocortical gray matter volume in early stages of schizophrenia that was coupled with an abnormality of neurophysiological index of glutamatergic neurotransmission called auditory mismatch negativity (MMN) (Kasai et al., 2003; Salisbury et al., 2007; Nagai et al., 2013; 2017). Patients show abnormal auditory steady state gamma-band oscillations (ASSR) (Tada et al., 2016), which is thought to be associated with dysfunction in GABA interneurons. On the other hand, rodent model and human postmortem studies have indicated that insult to dendritic spines through glutamatergic/GABAergic dysfunction may underlie the peri-onset progressive pathology in schizophrenia. However, there has been no direct evidence of synaptic dysfunction in schizophrenia, a missing link between animal/postmortem and in vivo human studies. To bridge the gap, “translatable” brain markers should be developed using neuroimaging and electrophysiological indices that can be commonly measured in animals and humans. We here present MMN and gamma oscillation data on primates, humans, and patients with schizophrenia. The bidirectional animal and human research using the translatable brain markers such as MMN/ASSR will facilitate identification of effective molecular targets for early intervention for schizophrenia. We will also present findings from our recent multi-center MRI study of subcortical regions in patients with schizophrenia (ENIGMA-SZJ; Okada et al., 2016), which will facilitate neuro-circuit explorations in primate models.