Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Seminar

Discovering the Biology of Major Psychiatric Illness

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Major psychiatric illnesses (MPIs) are highly heritable, yet the search for replicable genetic and neurobiological mechanisms has proven highly challenging. Studying large numbers of multiplex families with affected members having several psychiatric illnesses, and unaffected relatives, would provide the most statistically robust method for the identification of neurocognitive endophenotypes that cut across traditional diagnostic boundaries. The Centre for Brain and Mind is an effort in this direction, which creates a clinical longitudinal cohort and a biorepository of such individuals. The study sample included patients diagnosed with five MPIs namely schizophrenia, bipolar disorder, obsessive compulsive disorder, substance use disorder, and Alzheimer's dementia, their unaffected first-degree relatives (FDRs), and population healthy controls (PHCs). All individuals underwent detailed clinical assessments and a blood sample was drawn for isolation of DNA and peripheral blood mononuclear cells (PBMCs). Several additional intermediate phenotype/ endophenotype measures [Magnetic Resonance Imaging (MRI), Cognition, Eye movement tracking, Functional near Infra-Red Spectroscopy (FNIRS), Electroencephalography (EEG)], with the intention of conducting repeated measurements every alternate year were also performed. PBMCs from a subset were used to generate lymphoblastoid cell lines and subsequently induced pluripotent stem cells (IPSCs), and whole exome sequencing (WES) was performed. So far, we have screened 5000+ families and recruited 900 families with multiple affected members, with deep endophenotype assessments performed in 600 families. A total of 3000 individuals have been assessed in person till date, with ongoing follow-ups. WES (N=300) and IPSC generation (N=100) was performed for a subset of individuals. WES has identified rare damaging variants in several genes related to neurodevelopment, and subsequent preliminary studies in IPSC derived neural precursors/ organoids identified cell migration and proliferation deficits in individuals who also had MRI abnormalities. As a clinical counterpart, transdiagnostic neurodevelopmental endophenotypes were identified in both patients and FDRs.

Tuesday, Aug 27th 2024

16:00 Hrs (Tea / Coffee 15:45 Hrs)

Auditorium, TIFR-H