FW Journal Club

This month's Journal Club contribution comes from Natalie Matosin, an NHMRC Early Career Fellow (CJ Martin) at the UNSW and Max Planck Institute of Psychiatry. She studies how our genes and experiences change our brain's molecular makeup, and how this can go wrong to cause psychiatric illness. She is also a surfer, boxer and yogi and often found on the beach with her German Shepherd, Henry.

Matosin N, Fernandez-Enright F, Fung SJ, Lum JS, Engel M, Andrews JL, Huang XF, Weickert CS, Newell KA. Alterations of mGluR5 and its endogenous regulators Norbin, Tamalin and Preso1 in schizophrenia: towards a model of mGluR5 dysregulation. *Acta Neuropathologica.* 2015;130(1):119–129.

What were the aims of this research? Metabotropic glutamate receptor subtype 5 (mGluR5) is a protein essential for healthy brain function, learning and memory. It's been of interest to researchers over the last decade, because when this protein is disrupted in animals, they exhibit schizophrenia-like symptoms. This study aimed to determine whether mGluR5 was affected in postmortem brain samples from people with schizophrenia, specifically in the dorsolateral prefrontal cortex (a region important for cognition).

What are the top 3 take home findings of your research? 1. Although mGluR5 mRNA levels were unchanged, mGluR5 protein levels were over 20% higher in the brains of people who had schizophrenia compared to controls. 2. Proteins that endogenously regulate mGluR5's function were expressed at much lower levels (–30%). 3. mGluR5 protein was significantly correlated with mGluR5 mRNA and protein levels of mGluR5 endogenous regulators in control subjects – but all these associations were lost in the schizophrenia subjects.

How does this research contribute to the field? The cognitive abilities of people with schizophrenia are strongly linked to long-term functional outcomes. Unfortunately, current antipsychotics are mostly ineffective at treating cognitive dysfunction. This work provides the first molecular evidence that the mGluR5 system is dysregulated directly in the schizophrenia dorsolateral prefrontal cortex and supports that mGluR5-targeting drugs may offer a way to improve cognition and quality of life in people with schizophrenia.

Who are your collaborators and how did your work relationship come about? Kelly and Fran were my PhD supervisors; Jeremy, Jess and Martin, who were (at the time) also PhD students, helped me with the experiments; Xu-Feng is director of my PhD lab; and Sam and Cyndi are our collaborators from the Schizophrenia Research Laboratory at NeuRA, UNSW. This collaboration extended from a long-term working relationship between our labs through our common affiliation with the Schizophrenia Research Institute in Sydney.