DR. MANDY JOHNSTONE

Biography

Mandy Johnstone *BSc (Hons), MB ChB, PhD, MRCPsych* (mandy.johnstone@ed.ac.uk). Dr M. Johnstone completed her PhD in Developmental Neurobiology at King's College London. She qualified in Medicine at the University of Glasgow and then went on to train as a psychiatrist at The Institute of Psychiatry/South London and The Maudsley and then in Edinburgh on the South East Scotland Rotation. She is currently a Clinical Lecturer in Psychiatry at The University of Edinburgh. Her research interests are in the clinical and molecular genetics of schizophrenia and affective disorders and currently she is investigating whether copy number variants (CNVs) contribute to susceptibility in families multiply affected with schizophrenia and bipolar affective disorder. Her research is funded by grants from The Academy of Medical Sciences & The Wellcome Trust and from The RS MacDonald Charitable Trust.

Research Interests

Prior to commencing my medical and psychiatric studies I trained and worked as a post-doctoral neuroscientist in both academia and industry. My PhD was an investigation of MAP1B phosphorylation during neuronal development, carried out in the laboratory of Professor Phillip Gordon-Weeks at King's College London. Axon growth is crucially dependent on the assembly and organisation of microtubules and their associated proteins (MAPs) in axons and growth cones, where they function both as substrate for axonal transport and to maintain the structural integrity of the axon. MAP1B is the first MAP expressed in the developing nervous system, where the phosphorylated forms predominate in axonogenesis and play a critical role in neurite outgrowth. My post-doctoral research involved elucidating the neuroinflammatory events in Alzheimer's disease (AD)(Johnstone *et al*, 1999) and demonstrated that beta-amyloid activates glia to produce chemokines which serve as potent in vitro microglial and macrophage chemoattractants. This research was one of the first studies to propose that beta-amyloid-mediated astrocyte activation initiates an inflammatory cascade which could be targeted for therapeutic intervention in AD. My research also established cell-based assays to screen compounds that inhibit beta-amyloid production. We were able to screen, identify and patent specific drug candidates that inhibited the secretase enzymes which aberrantly process amyloid precursor protein (APP) to produce neurotoxic beta-amyloid- a major focus for pharmaceutical intervention in AD.

During my psychiatric training I have been struck by the devastating effects that schizophrenia has on those afflicted and their families and would like to gain a greater understanding of the development of the disorder with the principal goal of improving treatment and patient care. Schizophrenia is a common and severe mental illness often running in families, some showing a particularly strong inheritance of the disorder. Determining the molecular aetiology has proved challenging because of its genetic complexity. Familial inheritance can be caused in some cases by microscopically visible physical changes in the DNA architecture e.g. chromosomal translocations. Although these are rare associates of schizophrenia, they have proved to be valuable in identifying susceptibility genes such as DISC1. Recent studies have shown that smaller submicroscopic chromosomal rearrangements, known as copy number variants (CNVs), are present in a much greater proportion of suffers from schizophrenia. CNVs are defined as genomic DNA

duplications, insertions or deletions between 1kb and 3Mb in size and have been shown to alter risk in familial and sporadic forms of illness. CNVs may contribute towards pathology by disrupting gene structure at their endpoints or by changing the mRNA expression level. An association between CNVs and the inheritance of mental illness in families, would provide a powerful tool for the discovery of genes associated with the disorder and will further knowledge of the biological causes of schizophrenia. Ultimately, this will allow us to elucidate and target aberrant molecular and cellular pathways underpinning the disorder with the goal of developing better future treatments.

Top 6 Publications

Pickard, B.S., Van Den Bossche, M.J.A., Malloy, M.P., **Johnstone, M.**, Lenaerts, A.S., Nordin, A., Goossens, D., St Clair, D., Muir, W.J., Nilsson, L-G., Bernard S, Adolfsson, R., Blackwood, D.H.R., and Del-Favero, J. (2011). MAQ screening the *ABCA13* gene for copy number variation in schizophrenia and bipolar disorder. *Psychiatric Genetics* (in press).

Johnstone, M., Thomson, P. A., Hall, J., McIntosh, A., Lawrie, S. M. & Porteous, D. J. (2011). DISC1 in schizophrenia: Genetic mouse models and human genomic imaging. *Schizophrenia Bulletin*, **37**: 14-20.

Johnstone, M., Gearing, A. J. H. & Miller, K. M. (1999). A central role for astrocytes in the inflammatory response to β-amyloid: chemokines, cytokines and reactive oxygen species are produced. *Journal of Neuroimmunology*, **93**:182-193.

Johnstone, M., Goold, R. G., Bei, D., Fischer, I. & Gordon-Weeks, P. R. (1997). Localisation of microtubule-associated protein 1B phosphorylation sites recognised by monoclonal antibody SMI-31. *Journal of Neurochemistry*, **69**:1417-1424.

Johnstone, M., Goold, R. G., Fischer, I. & Gordon-Weeks, P. R. (1997). The neurofilament antibody RT97 recognises a developmentally regulated phosphorylation epitope on microtubule-associated protein (MAP) 1B. *Journal of Anatomy*, **191**:229-244.

Gordon-Weeks, P. R., Mansfield, S. G., Alberto, C., **Johnstone, M**. & Moya, F. (1992). A phosphorylation epitope on MAP1B that is transiently expressed in growing axons in the developing rat nervous system. *European Journal of Neuroscience*, **5**:1302-1311.

QUALIFICATIONS

• BSc(Hons) Biochemistry	Stirling	1992
• PhD in Developmental Neurobiology	King's College London	1997
• MB ChB	Glasgow	2004
• MRCPsych	Royal College of Psychiatrists	2008