From the Editor's desk

By Kamaldeep Bhui

Translational research in psychiatry

There are many scientific advances in psychiatric interventions. These are mostly new medications with improved safety and tolerability profiles, psychological and social interventions, and models of health service organisation and delivery. Effective interventions acting primarily on biological processes are yet to be realised, albeit exciting advances in neuroscience bring us closer to this aspiration. Translational research in medicine emphasises a move from the laboratory sciences all the way to personalised medicine; the foundations are in studies of molecular mechanisms of disease or immune function, genetic markers and biomarkers for risk stratification, and novel neurotransmitters and receptors implicated in pathophysiology and treatments. Translational medicine encourages studies to progress from laboratory research, to animal models of disease, and then to studies in humans. In the realms of psychiatric care, in addition to these elements, implementation sciences must improve the organisation and delivery of newly discovered interventions and then disseminate these advances to benefit public mental health. Such endeavour requires innovation, disciplined replication, and relentless traction to move interventions along the pipeline towards a clinically effective intervention for an individual patient.

Among the challenges are a lack of sustained funding, the high costs of research, inadequate samples, a need for novel and more precise methods of measuring biomarkers of disease and treatment responsiveness, and conflicts of interest.^{1,2} There are also inherent tensions between service provision studies, and basic and applied research, each with specific time frames for anticipated impact and with differing judgements of acceptability of risks. Fragmented and unstable research infrastructures, shortages of qualified researchers, and incompatible databases are barriers to effective translational psychiatric research.^{3,4} Translational psychiatry also encompasses translation to policy and healthcare guidelines, and the assessment of health policy and usage, and has an impact on global health.⁵ These vast terrains in themselves challenge individual scientists, who must grasp the upstream and downstream implications of their work.⁶

An exciting area of research is that of epigenetics, where modifications such as histone acetylation and deacetylation and DNA methylation can induce lasting changes in gene expression, and are implicated in promoting adaptive behavioural and neuronal changes seen in mental disorders.^{7,8} Epigenetics could explain heterogeneity in study findings.⁹ The challenges and scope of translational psychiatric research are illustrated in this month's *Journal*.

Uher & Weaver's eloquent editorial (pp. 3–5) critiques Perroud *et al*'s (pp. 30–35) study; methylation of the glucocorticoid receptor gene (*NR3C1*) in peripheral blood samples reflects greater experiences of lifetime sexual, physical and emotional traumas among people with bipolar disorder. This study proposes not only a mechanism but also a biomarker for at-risk groups. Mathews *et al*'s (pp. 40–45) cohort study of children and parents implicates prenatal alcohol exposure in Tourette syndrome, but also fails to replicate the findings of previous studies that implicate other risk factors. Disciplined replication studies are important, yet these are less 'glamorous' and may not be attractive to researchers or journal editors. Mataix-Cols *et al* (pp. 77–78) take an intervention that showed promise in

animal studies and test it in humans: post-therapy augmentation with cycloserine was no better than cognitive-behavioural therapy (CBT) alone, so raising questions about the place of animal models. Walterfang & Velakoulis (pp. 9–11) lament the neglect of the corpus callosum as the 'seat of the soul'. This is the largest white matter bundle, and neurobiological investigations of the corpus callosum may yet give us a better understanding of the causes and correlates of, as well as the treatments for, schizophrenia. Collinson *et al* (pp. 55–60) show difference in area and volume of the corpus callosum explained by the chronicity of schizophrenia. Although it may seem optimistic that treatment will restore the area and volume changes, other research of white matter connections suggests that connectivity might be restored by pharmacological treatments.¹⁰

Several other studies reveal potential aetiological factors for future research. Via *et al* (pp. 61–68) find that the severity of aggression/checking and sexual/religious symptoms is associated with heightened amygdala activation in patients with obsessive-compulsive disorder responding to fearful faces, linking clinical symptoms with measurable biological processes. Although negative studies are often less attractive to a readership, Niarchou *et al* (pp. 46–54), investigating 22q11.2 deletion syndrome, demonstrate that psychopathology is unrelated to intellectual impairment, and the two were independent consequences of 22q11.2 deletion syndrome. He *et al* (pp. 36–39) show that *CACNA1C*, which codes for a voltage-dependent calcium channel, is a risk gene for both schizophrenia and major depressive disorder in the Han Chinese population.

At the clinical and legal end of the spectrum, Lepping & Raveesh (pp. 1–2) question whether we lay too much emphasis on patient autonomy. Perhaps this is an unpopular view given that the number of detentions under the Mental Health Act in England is increasing;¹¹ but as argued, we should take more account of a shared value of benefit and what constitutes public good by consulting families and patients and communities, an approach that is better received in other cultural and legal settings.¹² Hollinghurst *et al* (pp. 69–76) emphasise the benefits of CBT for treatment-resistant depression in primary care, and show that it is cost-effective, whereas Jauhar *et al*'s (pp. 20–29) systematic review suggests that CBT produces small gains for patients with schizophrenia. And surprisingly, Koelen *et al* (pp. 12–19) confirm that psychotherapy is effective and better than treatment as usual for severe somatoform symptoms in secondary and tertiary care; however, for psychological symptoms, treatment as usual is as effective.

Studies that link mind and body offer much hope and motivation to develop more effective interventions. Society needs inspired, active and motivated scientists to inform and excite the public with new and promising research leading to psychiatric interventions. This will instil hope, tackle stigma and challenge the popular but mistaken idea that psychiatric disorders are untreatable and not amenable to preventive interventions.^{6,13,14}

- 1 Machado-Vieira R. Tracking the impact of translational research in psychiatry: state of the art and perspectives. *J Transl Med* 2012; **10**: 175.
- 2 Howells DW, Sena ES, Macleod MR. Bringing rigour to translational medicine. *Nat Rev Neurol* 2013; 19 Nov (ePub ahead of print).
- 3 Batson N, Batson L, Peters CK, Wiemken T, Kelley RR, Ramirez J. Collaboration with clinical and translational sciences to improve psychiatry training in research. *Acad Psychiatry* 2013; **37**: 426–8.
- 4 Academy of Medical Sciences. *Strengthening Academic Psychiatry in the UK*. AMS, 2013.
- 5 Licinio J. Translational psychiatry: leading the transition from the cesspool of devastation to a place where the grass is really greener. *Transl Psychiatry* 2011; **1**: e1.

- 6 Belsky DW, Moffitt TE, Caspi A. Genetics in population health science: strategies and opportunities. *Am J Public Health* 2013; **103** (suppl 1): S73–83.
- 7 Mahgoub M, Monteggia LM. Epigenetics and psychiatry. *Neurotherapeutics* 2013; **10**: 734–41.
- 8 El-Sayed AM, Koenen KC, Galea S. Putting the 'epi' into epigenetics research in psychiatry. *J Epidemiol Community Health* 2013; **67**: 610–6.
- 9 Caspi A, Moffitt TE. Gene–environment interactions in psychiatry: joining forces with neuroscience. *Nat Reviews Neurosci* 2006; **7**: 583–90.
- 10 Reis Marques T, Taylor H, Chaddock C, Dell'Acqua F, Handley R, Reinders AATS, et al. White matter integrity as a predictor of response to treatment in first episode psychosis. *Brain* 2013; 19 Nov (ePub ahead of print).
- 11 Keown P, Weich S, Bhui KS, Scott J. Association between provision of mental illness beds and rate of involuntary admissions in the NHS in England 1988–2008: ecological study. *BMJ* 2011; **343**: d3736.
- 12 Dein S, Bhui K. Issues concerning informed consent for medical research among non-westernized ethnic minority patients in the UK. *J R Soc Med* 2005; **98**: 354–6.
- 13 Wasserman D, Terenius L. The role of genetics in promoting suicide prevention and the mental health of the population. Preface. *Eur Psychiatry* 2010; **25**: 249.
- 14 Saxena S, Jane-Llopis E, Hosman C. Prevention of mental and behavioural disorders: implications for policy and practice. *World Psychiatry* 2006; **5**: 5–14.