Dr. Richard Bentall's critique of biological psychiatry (April 2013)

Richard Bentall, MD, an English psychiatrist, wrote the following in response to recent research on the fruit fly's nervous system which claimed to be relevant understanding the basis of schizophrenia (reported here with full permission of the author, Dr. Bentall), April, 2013

(i) Schizophrenia is a meaningless construct

There is no syndrome of schizophrenia and nobody can agree on who is schizophrenic. To my knowledge, no statistical study has ever identified a cluster of symptoms that correspond to the Kraepelinian concept or its subsequent revisions. Most recent studies have converged on a multidimensional model that incorporates all psychosis diagnoses (schizophrenia, schizoaffective disorder, bipolar disorder, delusional disorder, depression with psychotic features etc) within five dimensions of positive symptoms, negative symptoms, cognitive dysfunction, depression and mania/excitability, or even more complex structural models (Demjaha, A., et al. 2009; Reininghaus, et al in press). In recent field trials, the proposed DSM-V criteria for schizophrenia generated a derisory kappa of 0.46, showing that clinicians working with a precise definition of the disorder and following a diagnostic interview often could not agree on who was schizophrenic and who was not (Regier, D. A., et al. 2013)!

(ii) Heritability coefficients are misleading

It is often forgotten that heritability coefficients are, actually, just fancy correlation coefficients. We all know, or should know, that correlation does not necessarily prove causality. Heritability coefficients are statements about populations and not individuals so that it is wildly misleading to suggest that high heritability = mostly genetically caused (for a detailed discussion of this, see Bentall, R. P. (2009).

In fact, precisely because heritability coefficients are correlations which attempt to parse up the variance in a trait to genetic and environmental causes, low variance in the environment leads to inflation of the apparent effects of genes. This is why, for example, IQ is highly heritable in middle class families (where environmental variation is low) but very low in working class families (where environmental variation is high – Turkheimer, E., et al. (2003). Also, heritability coefficients assume an additive model of genes and environment, which is wildly implausible given what we know about how genes work. Again, assuming an additive model when there are G x E interactions leads to massive inflation of heritability and an underestimate of environmental effects (Dickins, W. T., & Flynn, J. R. 2001). This is probably why, as you know, molecular estimates of heritability are generally much lower than those based on the methods of
classical genetics. The ‘missing’ heritability in these studies is probably phantom heritability.

Incidentally, you will also know from the genetic studies that you cite, that the consensus amongst geneticists is now that many common alleles (perhaps many hundreds) probably each confer a tiny risk of all kinds of severe mental illness. Although some CNVs have much higher association with psychosis, they account for only a small proportion of patients and are also associated with intellectual disabilities and autism (Owen, M. J. 2012). This is further evidence, if ever it was needed, that schizophrenia is a meaningless construct and confirms the impossibility of devising a genetic test for the disorder.

(iii) There is massive evidence that environmental factors are causal in severe mental illness

The implications of ii above are that you can’t estimate environmental influences from heritability estimates – you have to look for them and measure them in their own right. Recent studies have pointed to a wide range of environmental factors associated with psychosis. These include social disadvantage, migration, living in cities and various forms of victimisation. I attach a recent meta-analysis I conducted on the evidence linking childhood adversity to psychosis (Varese, F., et al. (2012). The bare odds ratio between childhood trauma was stable across methodologies (retrospective/prospective) and came in at about 3, much higher than any association with common alleles. More importantly, there is evidence of a dose response effect, with ORs climbing to around 50 for children who have been multiply traumatised. Reaction in the psychiatric community has sometimes been bizarre, with convoluted attempts to explain away the data (see a recent editorial I wrote about this, also attached).

(iv) Brain studies do not provide clear evidence of neurodevelopmental disorder in psychosis

The evidence linking the basal ganglia to psychosis is far from clear cut. The best evidence is from response to antipsychotics, but recent studies suggest that only about 20% of patients show a genuine clinical response (Marques, T. R., et al. 2011). In any case, abnormal basal ganglia activity could just as likely be attributed to environmental factors – animal studies show that chronic victimisation leads to sensitisation of dopamine pathways in this part of the brain (Selten, J.-P., & Cantor-Graae, E. 2005)

Current structural and functional neuroimaging studies of psychosis are probably not to be trusted for a variety of complex methodological reasons (Ioannidis, J. P. A. 2011; Button et al. 2013) – this study [Button et al] estimated that the median statistical power of 461 individual fMRI studies contributing to 41 separate meta-analyses was 8%!), not least the emerging evidence that drugs affect brain structure (Ho, B.-C., et al. 2011).
In any case, the observed abnormalities could well be the consequence of social and environmental factors (Hoy, K., et al. (2011).

(v) A narrow neurodevelopmental approach is damaging to patients

There is little evidence that the biological approach to psychiatry is benefiting patients. Outcomes for patients suffering from ‘schizophrenia’ have not improved since the Victorian age and an increasing number of people are disabled by psychiatric conditions. This is precisely the opposite to what has happened in physical medicine, where genuine advances have led to improved outcomes and reduced disability (see Bentall, 2009, and Whitaker, R. 2005). Just as importantly, although it is often assumed by doctors that promoting a biological understanding of psychosis will reduce stigma, empirical research provides strong evidence that the opposite is the case, and that biological models actually promote stigma (Read, J., et al. 2006; Angermeyer, M. C., et al. (2011).

The claim that biological research (on flies or whatever) will one day lead to a cure for schizophrenia is a common rhetorical trick designed to gain publicity and guarantee grant funding. I have no problem with research on the CNS of flies, which seems valuable in its own right. But linking flies to schizophrenia (whatever that is) is really about self-promotion and is damaging to the interests of patients.

References


Bentall’s latest book is titled *Doctoring The Mind: Is Our Current Treatment Of Mental Illness Really Any Good*?