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

Angermeyer, M. C., et al. (2011). Biogenetic explanations and public acceptance of mental illness: systematic review of population studies. *British Journal of Psychiatry*, 199, 367-372.

Bentall, R. P. (2009). *Doctoring the mind: Why psychiatric treatments fail*. London: Penguin.

Button, K., Ioannidis, J., Mokrysz, C., Nosek, B., Flint,J., Robinson , E., & Munafò, M (2013) Power failure: why small sample size undermines the reliability of neuroscience *Nature Reviews Neuroscience* doi:10.1038/nrn3475

Demjaha, A., et al. (2009). Combining dimensional and categorical representation of psychosis: the way forward for DSM-V and ICD-11? *Psychological Medicine*, 39, 1943-1955

Dickins, W. T., & Flynn, J. R. (2001). Heritability estimates versus large environmental effects: The IQ paradox resolved. *Psychological Review*, 108, 346-369)

Ho, B.-C.,et al. (2011). Long-term antipsychotic treatment and brain volumes. *Archives of General Psychiatry*, 68, 128-137

Hoy, K., et al. (2011). Childhood trauma and hippocampal and amygdalar volumes in first–episode psychosis. *Schizophrenia Bulletin*. doi: 10.1093/schbul/sbr085

Ioannidis, J. P. A. (2011). Excess significance bias in the literature on brain volume abnormalities. *Archives of General Psychiatry*, 68, 773-780

Marques, T. R., et al. (2011). The different trajectories of antipsychotic response: antipsychotics versus placebo. *Psychological Medicine*, 41, 1481-1488

Noë, A. (2009) *Out of our Heads: Why you are not your brain, and other lessons from the biology of consciousness*. New York, Hill and Wang.

Owen, M. J. (2012). Implications of genetic findings for understanding schizophrenia. *Schizophrenia Bulletin*, 38, 904-907. doi: 10.1093/schbul/sbs103

Read, J., et al.(2006) *Acta Psychiatrica Scandinavica*, 114, 303-318;

Regier, D. A., et al. (2013). DSM-5 field trials in the United States and Canada, Part II: Test-retest reliability of selected categorical diagnoses. *American Journal of Psychiatry*, 170, 59-70)

Reininghaus, U., Priebe, S., & Bentall, R. P. (in press). Testing the psychopathology of psychosis: Evidence for a general psychosis dimension. *Schizophrenia Bulletin*, available online

Selten, J.-P., & Cantor-Graae, E. (2005). Social defeat: Risk factor for psychosis? *British Journal of Psychiatry*, 187, 101-102

Turkheimer, E., et al. (2003). Socioeconomic status modifies heritability of IQ in young children. *Psychological Science*, 14, 623-628

Van Orden, G. & Paap, K (1997) Philosophy of Science 64, Supplement. Proceedings of the 1996 Biennial Meetings of the Philosophy of Science Association. Part II: Symposia Papers (Dec., 1997), pp. S85-S94

Varese, F., et al. (2012). Childhood adversities increase the risk of psychosis: A meta-analysis of patient-control, prospective and cross-sectional cohort studies. *Schizophrenia Bulletin*, 38, 661–671. doi: 10.1093/schbul/sbs050.

Whitaker, R. (2005). Anatomy of an epidemic: Psychiatric drugs and the astonishing rise of mental illness in America. *Ethical Human Psychology and Psychiatry*, 7, 23-35

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

- Bentall, Richard (2009). *Doctoring the mind: is our current treatment of mental illness really any good?*. NYU Press. ISBN 0-8147-9148-4. (The UK title is *Doctoring the Mind: Why Psychiatric Treatments Fail*)[5]
- Read, J; Bentall, RP; Fosse, R (October–December 2009). "Time to abandon the bio-bio-bio model of psychosis: Exploring the epigenetic and psychological mechanisms by which adverse life events lead to psychotic symptoms". *Epidemiologia e Psichiatria Sociale* 18 (4): 299–310. PMID 20170043.
- Varese, F; Smeets, F; Drukker, M; Lieverse, R; Lataster, T; Viechtbauer, W; Read, J; van Os, J et al. (29 March 2012). "Childhood Adversities Increase the Risk of Psychosis: A Meta-analysis of Patient-Control, Prospective- and Cross-sectional Cohort Studies". *Schizophrenia Bulletin*. doi:10.1093/schbul/sbs050. PMID 22461484. Retrieved 13 April 2012. Citation uses old-style implicit et al. for authors
- Morrison, A. P. & Renton, & J & French P & Bentall, R. P. (2008) *Think You're Crazy? Think Again: A Resource Book for Cognitive Therapy for Psychosis* London: Routledge. ISBN 978-1-58391-837-1
- Bentall, R. P. (2003) *Madness Explained: Psychosis and Human Nature* London: Penguin Books Ltd. ISBN 0-7139-9249-2
- Bentall, Richard (1999). Why There Will Never Be a Convincing Theory of Schizophrenia. In S. Rose (ed). *From brains to consciousness? Essays on the new sciences of mind* London: Penguin Books.
- Bentall, R. P. & Slade, P. D. (eds) (1992) *Reconstructing Schizophrenia* London: Routledge. ISBN 0-415-01574-X
- Bentall, R. P. & Slade, P. D. (1988) *Sensory Deception: A Scientific Analysis of Hallucination* Johns Hopkins University Press. ISBN 0-8018-3760-X