psychopathology. We addressed limitations of the meta-analyses in our original paper. We suggest that careful and comprehensive examination of the diverse phenotypes associated with neuropsychiatric illness may be a more fruitful approach.

Second, Dr Crow cites his own review of the linkage literature to suggest that most of the candidate genes reported by our group, and many others, are not supported by linkage studies and thus should be discounted. This reasoning is based on a flawed understanding of the role of linkage in complex disorders and is inconsistent with a large body of recent empirical evidence in complex genetics. In other complex disorders, a majority of susceptibility loci that have been unambiguously replicated in association studies fall outside of previously identified areas of even suggestive linkage (e.g. Barrett *et al*[1]). Therefore, an argument utilising non-significant linkage data to invalidate a subsequent candidate gene association is erroneous.

Third, Dr Crow notes the productivity of our lab over the past several years as a source of concern for him. In so doing he mischaracterises our papers. First, he is simply incorrect in stating that only one paper reports strictly negative results (see Fubke *et al*[2] and Hodgkinson *et al*[3]). Moreover, many of our papers report complex relationships that are not so simplistically reduced to 'positive' *v.* 'negative'. More importantly, Dr Crow fails to mention that most of our papers are not simply analyses of association to schizophrenia diagnosis, but instead examine alternative phenotypes. For example, our study of *DRD2* assessed the relationship between a functional promoter region polymorphism and clinical response to olanzapine and risperidone in the context of a randomised controlled clinical trial in first-episode schizophrenia.[4] Therefore, it is not surprising that our *DRD2* results were not 'replicated' in either linkage studies or the association study of Sanders *et al*,[5] as these papers were restricted to mere association to diagnosis.

Although Dr Crow is entitled to his opinions, the field of psychiatric genetics may be better served by more constructive discussion leading towards a better understanding of the complexities of these devastating disorders.

1 Barrett JC, Hansoul S, Nicolae DL, Cho JH, Duerr RH, Rioux JD, et al. Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *Nat Genet* 2008; **40**: 955–62.

2 Funke BH, Lencz T, Finn CT, DeRosse P, Poznik GD, Plocik AM, et al. Analysis of TBX1 variation in patients with psychotic and affective disorders. *Mol Med* 2007; **13**: 407–14.

3 Hodgkinson CA, Goldman D, Ducci F, DeRosse P, Caycedo DA, Newman ER, et al. The FEZ1 gene shows no association to schizophrenia in Caucasian or African American populations. *Neuropsychopharmacology* 2007; **32**: 190–6.

4 Lencz T, Robinson DG, Xu K, Ekholm J, Sevy S, Gunduz-Bruce H, et al. DRD2 promoter region variation as a predictor of sustained response to antipsychotic medication in first-episode schizophrenia patients. *Am J Psychiatry* 2006; **163**: 529–31.

5 Sanders AR, Duan J, Levinson DF, Shi J, He D, Hou C, et al. No significant association of 14 candidate genes with schizophrenia in a large European ancestry sample: implications for psychiatric genetics. *Am J Psychiatry* 2008; **165**: 497–506.

Todd Lencz, The Zucker Hillside Hospital, Psychiatry Research, 75–59 263rd Street, Glen Oaks, New York 11004, USA. Email: lencz@lij.edu; **Robert H. Lipsky**, Laboratory of Neurogenetics, National Institute on Alcohol Abuse and Alcoholism, Bethesda; **Pamela DeRosse**, Division of Psychiatry Research, The Zucker Hillside Hospital; **Katherine E. Burdick**, Center for Translational Psychiatry, Feinstein Institute for Medical Research and Division of Psychiatry Research, The Zucker Hillside Hospital, New York; **David Goldman**, **Colin Hodgkinson**, Section of Human Neurogenetics, National Institute on Alcohol Abuse and Alcoholism, Rockville; **John M. Kane**, Center for Translational Psychiatry, Feinstein Institute for Medical Research and Department of Psychiatry, The Zucker Hillside Hospital, New York; **Anil K. Malhotra**, Center for Translational Psychiatry, Feinstein Institute for Medical Research and Division of Psychiatry Research, The Zucker Hillside Hospital, New York, USA

doi: 10.1192/bjp.195.2.179a

Outcome of group psychoeducation for stabilised bipolar disorders

The article by Colom *et al*[1] further enhanced our understanding about the role of psychoeducation in the management of bipolar disorders. The study draws its strengths from the fact that it included an active control group and individuals with bipolar disorder and Axis II comorbidity, follow-up rates were excellent and the authors assessed the outcome in the form of the number and type of recurrences, time to recurrence, time spent ill and number of hospitalisations at 5 years. However, some of the issues require further clarification.

When one looks at the article reporting 2-year follow-up of the same cohort,[2] the authors report that individuals with Axis I comorbidity were excluded, but at 5-year follow-up the authors report that only those with severe Axis I diagnosis were excluded. Further, the authors do not define 'severe'. Individuals with bipolar disorder can have a high rate of comorbidity, hence clarification of this fact is very important from the perspective of generalisability of the study findings. In addition, Colom *et al* do not provide details of status and/or type of Axis I/II comorbidities and whether the drop-out rate and the number of completers made any difference with regard to clinical and demographic features.

Another important aspect is the way the authors defined recurrence based on rating scale scores. This type of definition in the true sense does not include the subsyndromal symptoms and can influence almost all the outcome measures such as time spent ill, time to recurrence and the number of recurrences, especially when the cohort is being followed up at a frequency of every 2 weeks. Similarly, although the study included the number and duration of hospitalisations as an outcome measure, the authors have not discussed the criteria for hospitalisation.

Another important aspect which needs clarification is the analysis of data. In many places Colom *et al* have used parametric tests to compare the numerical variables, although the standard deviation is more than the mean. Similarly, mean values are given for the number of recurrences without standard deviations, and comparison statistics are given as *F*-values. In Table 2,[1] again the authors compare the mean values using Fisher *F* statistics and demonstrate that there was a significant difference in the number of days spent in each episode for all types of episodes. However, when one looks at the data, it is difficult to understand this contention. In the same table when one adds the mean number of days spent in each episode for the control group, the data regarding each episode and the total duration do tally, but the same is not the case for the psychoeducation group.

1 Colom F, Vieta E, Sánchez-Moreno J, Palomino-Otiniano R, Reinares M, Goikolea JM, et al. Group psychoeducation for stabilised bipolar disorders: 5-year outcome of a randomised clinical trial. *Br J Psychiatry* 2009; **194**: 260–5.

2 Colom F, Vieta E, Martinez-Aran A, Reinares M, Goikolea JM, Benabarre A, et al. A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. *Arch Gen Psychiatry* 2003; **60**: 402–7.

Navendu Gaur, Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Email: drsandeepg2002@yahoo.com; **Sandeep Grover**, Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh, India

doi: 10.1192/bjp.195.2.180

Authors' reply: We would like to provide some clarifications in response to Gaur & Grover's queries.

First, only those patients with 'severe' Axis I comorbidity diagnoses were excluded. This means that patients were excluded if

https://doi.org/10.1192/bjp.195.2.180 Published online by Cambridge University Press