matter volume in the left anterior cingulate cortex in 66 Italian patients with schizophrenia, and greater grey matter volume in the left anterior cingulate cortex in 37 Italian controls.

In terms of providing evidence that the *CNNM2* variant would contribute to social cognition and its neural underpinnings, it is a very interesting study. However, the study has a very important limitation. The reported risk allele was incorrect: the risk allele at rs7914558 is not minor 'A' but major 'G'. Therefore, interpretation of these associations was opposite.

At almost the same time, we reported that the rs7914558 variant was associated with grey matter volume in the orbital region of the bilateral inferior frontal gyri in 173 Japanese patients with schizophrenia and 449 healthy individuals.[4] Those with the risk G/G genotype of rs7914558 had reduced grey matter volume in the bilateral inferior frontal gyri compared with carriers of the non-risk A allele. Interestingly, the orbital region of the inferior frontal gyrus also plays an important role in social functioning. Taken together, the variant was associated with reduced grey matter volume in putative social cognition-related regions, including the temporal pole, anterior cingulate and inferior frontal cortices, which were reduced in patients with schizophrenia, although the detailed regions were not consistent among the different populations studied.

Furthermore, a recent study has indicated that mutations in the *CNNM2* gene are associated with intellectual disability, and the knockdown of *Cnnm2* isoforms in zebrafish has resulted in disturbed brain development.[5] These findings suggest that the *CNNM2* variant might play a role in the social cognition and social functioning impairments noted in patients with schizophrenia through the volumetric vulnerability of these grey matter regions.

1 Ripke S, Sanders AR, Kendler KS, Levinson DF, Sklar P, Holmans PA, et al. Genome-wide association study identifies five new schizophrenia loci. *Nat Genet* 2011; **43**: 969–76.

2 Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. *Nature* 2014; **511**: 421–7.

3 Rose EJ, Hargreaves A, Morris D, Fahey C, Tropea D, Cummings E, et al. Effects of a novel schizophrenia risk variant rs7914558 at *CNNM2* on brain structure and attributional style. *Br J Psychiatry* 2014; **204**: 115–21.

4 Ohi K, Hashimoto R, Yamamori H, Yasuda Y, Fujimoto M, Umeda-Yano S, et al. The impact of the genome-wide supported variant in the cyclin M2 gene on gray matter morphology in schizophrenia. *Behav Brain Funct* 2013; **9**: 40.

5 Arjona FJ, de Baaij JH, Schlingmann KP, Lameris AL, van Wijk E, Flik G, et al. CNNM2 mutations cause impaired brain development and seizures in patients with hypomagnesemia. *PLoS Genet* 2014; **10**: e1004267.

Kazutaka Ohi, MD, PhD, Department of Psychiatry, Osaka University Graduate School of Medicine, Suita, Osaka, Japan. Email: ohi@psy.med.osaka-u.ac.jp

doi: 10.1192/bjp.206.4.343b

Authors' reply: Dr Ohi is correct that the risk allele at the locus rs7914558 is the major G allele; throughout the paper we had incorrectly identified the risk allele as being the major A allele.[1] We have submitted a corrigendum to state that the G allele is both the major allele and the risk allele.

However, while the tables and text have incorrectly named the risk allele as the A allele, the analysis undertaken, and its interpretation, are correct, as we based our analysis on the major allele being the risk allele. As we state in our study, the risk allele was associated with reduced self-serving bias, and increased grey matter volume in regions relevant to social cognition in both the Irish and Italian samples. Dr Ohi, therefore, seems to be incorrect in asserting that the results are consistent with data from his group's study, in which the risk allele was associated with reduced grey matter volume in the orbitofrontal cortex. Although both regions are associated with social cognition, they are also implicated in other cognitive processes, which might explain the differences in results. While both sets of results will require replication in independent samples before firm conclusions are drawn, the availability of a replication sample in our study enabled us to provide additional support for our results, despite their counterintuitive nature.

We also take this opportunity to disagree with Dr Ohi's assertion that this variant rs7914558 is necessarily associated with *CNNM2*. Although the title of our paper notes that this variant is located at the same locus as *CNNM2*, and named as such in the PGC GWAS study, we highlight in our discussion that linkage disequilibrium from this variant extends to three other genes over a region of several hundred kb, any one of which could potentially be associated with this signal. In fact, the most recent study by the PGC[2] suggests, based on eQTL analysis, that the single-nucleotide polymorphism most strongly associated with schizophrenia in this region (rs11191419) is associated with altered expression of the *AS3MT* gene.

1 Rose EJ, Hargreaves A, Morris D, Fahey C, Tropea D, Cummings E, et al. Effects of a novel schizophrenia risk variant rs7914558 at *CNNM2* on brain structure and attributional style. *Br J Psychiatry* 2014; **204**: 115–21.

2 Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. *Nature* 2014; **511**: 421–7.

Gary Donohoe, PhD, Trinity College Dublin and National University of Ireland; **Emma Rose**, PhD, Trinity College Dublin and RTI International, Baltimore; **Derek Morris**, PhD, Trinity College Dublin.
Email: gary.donohoe@nuigalway.ie

doi: 10.1192/bjp.206.4.344