

**Authors' reply:** Patra & Balhara point to limitations of retrospective designs. However, it should be noted that our data were collected prospectively and thus not open to recall bias. They also stress that many factors are important when choosing occupation, many of which are in turn influenced by psychiatric disorders. There are indeed a plethora of determinants of occupational choices, but we addressed the bias of psychiatric disorder *per se* by also investigating the patient's healthy relatives, where we found a stronger association with creative occupations than among the patients themselves.

We agree with Patra & Balhara that using the term occupation is likely to miss creative activity unrelated to economic production, and therefore commented in the paper that schizophrenia might be associated with creative avocational rather than vocational activities. The aim of our study was, however, not to problematise the concept of occupation, but to use these validated occupations as a proxy for creativity. Thus, those with creative occupations are on average more creative than other people.

Schmechel gives an interesting reference regarding alpha-1-antitrypsin polymorphisms and both artistic avocations and occupations, adding to the list of recently found polymorphisms associated with increased creativity as well as to observations of alterations in white matter integrity in both psychopathology and creativity.<sup>1</sup> Indeed, if we believe that the association between creativity and psychopathology is contingent on genetic factors, we should give high priority to elucidate the specific genetic mechanism.

Kirov & Miller point out the paradox of high heritability and low fertility combined with a stable prevalence of schizophrenia, which was early noted by the Swedish psychiatrist Essen-Möller.<sup>2</sup> These findings have been repeatedly demonstrated in schizophrenia and to some extent, although with conflicting results, in bipolar disorder.<sup>3</sup> However, fertility rates may be biased and it has been argued that reduced fertility in patients with schizophrenia and their relatives does not constitute evidence against sexual selection on susceptibility genes for schizophrenia.<sup>4</sup>

We agree that mutation selection is one likely mechanism by which the persistence of psychiatric disorder can be explained, albeit some discrepancy between different psychiatric disorders seems warranted. This does not, however, rule out the presence of balancing selection. To cite Keller & Miller:<sup>5</sup> 'The normal range of creativity may be nearly neutral (or under balancing selection). Most of the genetic risk of mental disorders comes from harmful mutations. High creativity has negative effects on fitness when coupled with a high mutation background because it increases the risk of mental disorders, but it has positive effects when in a low mutation background.' In fact, 'creativity could be a sexually selected signal, designed to partially reveal one's mutation load: only those with a low mutation load can afford the cost of being creative.'<sup>5</sup> In this way, these authors have elegantly explained both the age-old observation of genius and madness, while preceding future results of next-generation sequencing studies.

- 1 Jung RE, Grazioplene R, Caprihan A, Chavez RS, Haier RJ. White matter integrity, creativity, and psychopathology: disentangling constructs with diffusion tensor imaging. *PLoS One* 2010; **5**: e9818.
- 2 Essen-Möller E. Mating and fertility patterns in families with schizophrenia. *Eugen Quart* 1959; **6**: 142–7.
- 3 Uher R. The role of genetic variation in the causation of mental illness: an evolution-informed framework. *Mol Psychiatry* 2009; **14**: 1072–82.
- 4 Del Giudice M. Reduced fertility in patients' families is consistent with the sexual selection model of schizophrenia and schizotypy. *PLoS One* 2010; **5**: e16040.
- 5 Keller MC, Miller G. Resolving the paradox of common, harmful, heritable mental disorders: which evolutionary genetic models work best? *Behav Brain Sci* 2006; **29**: 385–404; discussion 405–52.

**Simon Kyaga**, MD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden. Email: [simon.kyaga@ki.se](mailto:simon.kyaga@ki.se); **Paul Lichtenstein**, PhD, **Niklas Långström**, MD, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; **Mikael Landén**, MD, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, and Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden

doi: 10.1192/bjp.200.4.348