

the lesser goal of showing core pathology (in other words, the Venn diagram intersection). Coreness of pathology allows for diversity, without having to reconcile everything.

Second, we note that the secondary analysis was performed to dissect out the effects of the disorder from that of illness duration and treatment. The authors achieved this by using fractional anisotropy scores extracted from the principal analysis, which were then used to compare chronically with briefly medicated patients. Perhaps newly diagnosed, antipsychotic-naïve patients help most to partition out these effects² but they are not essential. An alternative approach is voxel-based ANOVA covarying for illness duration and atypical antipsychotic duration/dosage since this can help maximise anatomical coverage (particularly in the striatum where antipsychotic effects are detectable at even 2–3 weeks of treatment^{3,4}).

- 1 Kanaan R, Barker G, Brammer M, Giampietro V, Shergill S, Woolley J, et al. White matter microstructure in schizophrenia: effects of disorder, duration and medication. *Br J Psychiatry* 2009; **194**: 236–42.
- 2 Cheung V, Cheung C, McAlonan GM, Deng Y, Wong JG, Yip L, et al. A diffusion tensor imaging study of structural dysconnectivity in never-medicated, first-episode schizophrenia. *Psychol Med* 2008; **38**: 877–85.
- 3 Szeszko PR, Ardekani BA, Ashtari M, Kumra S, Robinson DG, Sevy S, et al. White matter abnormalities in first-episode schizophrenia or schizoaffective disorder: a diffusion tensor imaging study. *Am J Psychiatry* 2005; **162**: 602–5.
- 4 Chua SE, Deng Y, Chen EY, Law CW, Chiu CP, Cheung C, et al. Early striatal hypertrophy in first-episode psychosis within 3 weeks of initiating antipsychotic drug treatment. *Psychol Med* 2009; **39**: 793–800.

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Authors' reply: We agree that the process of establishing a definitive extent of white matter disruption in schizophrenia, and its relationship with illness duration and antipsychotic medication, is likely to be a lengthy one – larger studies such as ours notwithstanding. But we would like to clarify our reasoning

with respect to Chua & McAlonan's comments and the methodological alternatives they suggest.

First, we suspect that a 'core pathology' for white matter abnormalities in schizophrenia may be rather more elusive than the reconciliation we attempted. Although the recent meta-analysis by Ellison-Wright & Bullmore¹ has found areas of most common difference in the 15 studies they examined, it should be noted that only a fraction of the studies they looked at shared these differences – and the history of diffusion tensor imaging in schizophrenia is full of such conflicts.² Although there may indeed be areas of greater difference, the evidence is against any difference that is common to all.

Second, with regard to distinguishing the effects of duration of illness and antipsychotic medication, drug-naïve cohorts clearly offer enormous potential as the authors acknowledge. Such cohorts are difficult to obtain in high-income countries however, and the alternative approach they suggest – of ANOVA with covariation – has similar difficulties, since duration of treatment and illness will be so strongly correlated in most samples. We also note that the studies they cite as demonstrating the effectiveness of this approach either did not covary for medication exposure³ or did not use diffusion tensor imaging.⁴

- 1 Ellison-Wright I, Bullmore E. Meta-analysis of diffusion tensor imaging studies in schizophrenia. *Schizophr Res* 2009; **108**: 3–10.
- 2 Kanaan RA, Kim JS, Kaufmann WE, Pearlson GD, Barker GJ, McGuire PK. Diffusion tensor imaging in schizophrenia. *Biol Psychiatry* 2005; **58**: 921–9.
- 3 Szeszko PR, Ardekani BA, Ashtari M, Kumra S, Robinson DG, Sevy S, et al. White matter abnormalities in first-episode schizophrenia or schizoaffective disorder: a diffusion tensor imaging study. *Am J Psychiatry* 2005; **162**: 602–5.
- 4 Chua SE, Deng Y, Chen EY, Law CW, Chiu CP, Cheung C, et al. Early striatal hypertrophy in first-episode psychosis within 3 weeks of initiating antipsychotic drug treatment. *Psychol Med* 2009; **39**: 793–800.

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Corrections

Differential efficacy of escitalopram and nortriptyline on dimensional measures of depression. *BJP*, **194**, 252–259. The two last-named authors, Dr K.J. Aitchison and Professor P. McGuffin, are the GENDEP Principal Investigators and contributed equally to the work. In addition, Dr Aitchison's qualifications include MRCPsych.

Caption for cover picture, April 2009. *BJP*, **194**, A14. The text and image were submitted by Wojtek Wojcik; edited by Allan Beveridge.

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