More broadly, it remains unclear whether the effects of antipsychotics on the brain are damaging or alternatively protective. The possibility of a protective effect of antipsychotics on brain would be supported by evidence, from animal models of schizophrenia, that antipsychotics positively affect neurogenesis, and prevent the insurgence of brain structural changes later in life (Keilhoff *et al*. 2010; Piontkewitz *et al*. 2010). By relating longitudinal information on brain structure and function, and exposure to antipsychotic, to clinical improvement, we may be able to elucidate which of these alternatives is true.

### Declaration of Interest

None.

### References

**Cahn W, van Haren NE, Hulshoff Pol HE, Schnack HG, Caspers E, Laponder DA, Kahn RS** (2006). Brain volume changes in the first year of illness and 5-year outcome of schizophrenia. *British Journal of Psychiatry* **189**, 381–382.

**Dazzan P, Morgan KD, Orr KG, Hutchinson G, Chitnis X, Suckling J, Fearon P, McGuire PK, Mallett RM, Jones PB, Leff J, Murray RM** (2005). Different effects of typical and atypical antipsychotics on grey matter in first episode psychosis: the ÆSOP study. *Neuropsychopharmacology* **30**, 765–774.

**Ebdrup BH, Glenthoj B, Rasmussen H, Aggernaes B, Langkilde AR, Paulson OB, Lublin H, Skimminge A, Baare W** (2010). Hippocampal and caudate volume reductions in antipsychotic-naive first-episode schizophrenia. *Journal of Psychiatry and Neuroscience* **35**, 95–104.

**Keilhoff G, Grecksch G, Becker A** (2010). Haloperidol normalized prenatal vitamin D depletion-induced reduction of hippocampal cell proliferation in adult rats. *Neuroscience Letters* **476**, 94–98.

**Moncrieff J, Leo J** (2010). A systematic review of the effects of antipsychotic drugs on brain volume. *Psychological Medicine*. Published online: 20 January 2010. doi:10.1017/S0033291709992297.

**Navari S, Dazzan P** (2009). Do antipsychotic drugs affect brain structure? A systematic and critical review of MRI findings. *Psychological Medicine* **39**, 1763–1777.

**Piontkewitz Y, Arad M, Weiner I** (2010). Risperidone administered during asymptomatic period of adolescence prevents the emergence of brain structural pathology and behavioral abnormalities in an animal model of schizophrenia. *Schizophrenia Bulletin*. Published online: 3 May 2010. doi:10.1093/schbul/sbq040.

**Scheef L, Manka C, Daamen M, Kuhn KU, Maier W, Schild HH, Jessen F** (2010). Resting-state perfusion in nonmedicated schizophrenic patients: a continuous arterial spin-labeling 3.0-T MR study. *Radiology* **256**, 253–260.

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### The authors reply

We are not as convinced as Dr Dazzan that 'schizophrenia is associated with volume changes in several brain areas' (Dazzan, 2010). As we showed in our systematic review, a large majority of studies with drug-naive patients with psychosis or schizophrenia have not found any differences in global brain or grey-matter volumes, or in total CSF or ventricular volumes between patients and controls (Moncrieff & Leo, 2010). Although some of these studies reported differences in the volumes of specific structures, such as the thalamus and the caudate nuclei, others found no differences and multiple testing suggests some of the results may be false positives.

We do agree that disentangling the effects of drug treatment and underlying pathology are difficult, but we feel that, following the Hippocratic mandate to 'first do not harm', it should be assumed that the drugs rather than the disorder are causing the effects, until proven otherwise. Similarly, although it is not impossible that antipsychotic-induced brain alterations are beneficial, it seems more prudent to assume that they might be harmful, and to direct research into assessing this possibility.

### References

**Dazzan P** (2010). Are antipsychotics good or bad for the brain? A comment on Moncrieff & Leo (2010). *Psychological Medicine*. Published online: 1 September 2010. doi:10.1017/S0033291710001698.

**Moncrieff J, Leo J** (2010). A systematic review of the effects of antipsychotic drugs on brain volume. *Psychological Medicine* **40**, 1409–1422.

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### Letter to the Editor

### Early intervention in psychosis: a response to McGorry *et al*. (2010)

The Commentary of McGorry *et al*. (2010) on our Editorial in the March 2010 edition of the Journal

(Bosanac *et al*. 2010), used the opportunity to promote the early intervention agenda. Unfortunately it did not adequately address the challenges we raised. It is instead an example of how the early intervention agenda has been so successful in influencing policy – a simple solution to a complex problem, argued with passion.

The fact remains that there is no evidence that we can ameliorate the longer term course of psychosis with existing early intervention programmes. The Lambeth Early onset Group in the UK (Gafoor *et al*. 2010), the Danish OPUS study (Bertelsen *et al*. 2008) and an early intervention study from The Netherlands (Linszen *et al*. 1998) all show no overall beneficial effects of early intervention programmes in the medium term (5 years). We also know that most patients continue to have symptoms well beyond the early phases, despite the very best early care. For example, in the EPPIC 7-year follow-up study, only 14.9% of the schizophrenia/schizophreniform patients achieved social/vocational and symptomatic remission (Henry *et al*. 2010). It may be, as McGorry and colleagues suggest, that the interventions have been too short and hence early gains have not been maintained. But this surely undermines the rationale for a primary emphasis on early intervention in enhancing the longer term trajectory of illness. Rather it points to a need for better integration of early intervention programmes into the mainstream of psychiatric care so that the beneficial elements of the intervention can be continued. To focus exclusively or even predominantly on early intervention rather than promote continuity of quality care across the lifespan of psychotic illness seems unjustifiable given this evidence on the loss of early gains.

McGorry *et al*. (2010) suggested that we wish to maintain the *status quo* regarding the management of schizophrenia; that we 'deserve censure' and 'cause real harm by delaying care' and are 'manufacturing a hopelessness that is by no means justified by the facts'. We do not believe that this is so. Rather than labelling generic services as 'pessimistic' (McGorry *et al*. 2010, p. 402) we should be engaging generic services in the provision of a coherent and comprehensive response to people with schizophrenia whatever their stage of illness. Stand-alone early intervention services have their own problems, including silo effects, the potential de-skilling of the generalized workforce in the area of early psychosis and the difficultly of transitions between services for patients, their families and clinicians. Transition between services is associated with loss and other adjustment problems (Friis, 2010). And it is not true that generic services cannot deliver good care: they can meet all the fidelity guidelines for early psychosis within generic structures as long as they are resourced and structured to do so.

We have yet much to learn about the care and treatment of people with psychotic illnesses such as schizophrenia. The main lesson to date from the early intervention field, namely that timely and comprehensive care is beneficial to patients whilst it is being delivered, is important. Further research into whether it may be possible fundamentally to change illness trajectories through intervention early in its course, remains important. Without such evidence, however, a predominant focus on early intervention seems a step too far.

## References

**Bertelsen M, Jeppesen P, Petersen L, Thorup A, Ohleschlager J, le Quach P, Christensen TO, Krarup G, Jorgensen P, Nortentoft M** (2008). Five year follow-up of a randomised multicenter trial of intensive early intervention vs standard treatment for patients with a first episode of psychotic illness: the OPUS trial. *Archives of General Psychiatry* **65**, 762–771.

**Bosanac P, Patton GC, Castle DJ** (2010). Early intervention in psychosis: faith before facts? *Psychological Medicine* **40**, 353–358.

**Friis S** (2010). Early specialised treatment for first-episode psychosis: does it make a difference? *British Journal of Psychiatry* **196**, 339–340.

**Gafoor R, Nitsch D, McCrone P, Craig TKJ, Garety PA, Power P, McGuire P** (2010). Effect of early intervention on 5-year outcome in non-affective psychosis. *British Journal of Psychiatry* **196**, 372–376.

**Henry LP, Amminger P, Harris MG, Yuen HP, Harrigan SM, Prosser AL, Schwartz OS, Farrelly SE, Herrman H, Jackson HJ, McGorry PD** (2010). The EPPIC follow-up study of first-episode psychosis: longer-term clinical and functional outcome 7 years after index admission. *Journal of Clinical Psychiatry* **71**, 1–14.

**Linszen D, Lenior M, DeHaan L, Dingemans P, Gersons B** (1998). Early intervention, untreated psychosis and the course of early schizophrenia. *British Journal of Psychiatry* **172** (Suppl. 33), 84–89.

**McGorry P, Johanessen JO, Lewis S, Birchwood M, Malla A, Nordentoft M, Addington J, Yung A** (2010). Early intervention in psychosis: keeping faith with evidence-based health care [Commentary]. *Psychological Medicine* **40**, 399–404.

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