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doi: 10.1192/bjp.190.3.270a

### Hippocampal and amygdala volume reductions in first-episode schizophrenia

Steen *et al* (2006) performed a systematic review and meta-analysis of cross-sectional and longitudinal magnetic resonance imaging (MRI) studies of brain volumes in patients with first-episode psychosis and healthy controls. Despite some methodological differences, the findings were in line with a recent meta-analysis performed by our group (Vita *et al*, 2006).

A significant decrease in hippocampal but not amygdala volumes was found in patients at illness onset in both reviews. Another relevant paper reporting amygdala and hippocampal volumes in a large sample of patients with first-episode schizophrenia was published after these two meta-analyses (Velakoulis *et al*, 2006). Thus we considered it worthwhile to conduct a new set of meta-analyses including these MRI data.

The results of the new meta-analyses for hippocampus (7 studies, 290 patients, 355 controls) and amygdala (5 studies, 218 patients, 175 controls) confirmed our previous findings. Even with the inclusion of the study of Velakoulis *et al* (2006), the composite effect sizes for the hippocampus remained significant ( $d=0.357$ , 95% CI 0.208–0.541 for the right hippocampus and 0.574, 95% CI 0.405–0.742 for the left hippocampus) whereas those for the amygdala were not ( $d=-0.046$ , 95% CI  $-0.247$  to 0.154 for the right amygdala and 0.025, 95% CI  $-0.175$  to 0.226 for the left amygdala).

These results, in line with those of Steen *et al* (2006), support the hypothesis of

different patterns of involvement of tem-porolimbic structures over the course of schizophrenia, with the hippocampus affected earlier than the amygdala. In our opinion, these findings have important implications for future neurobiological studies of schizophrenia and emphasise the importance of longitudinal studies to address the issue of different times of occurrence and progression of brain abnormalities in people with first-episode schizophrenia.

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doi: 10.1192/bjp.190.3.271

### Effectiveness of cognitive-behavioural intervention by mental health nurses in schizophrenia

Turkington *et al* (2006) report on outcomes of an effectiveness trial of brief cognitive-behavioural therapy (CBT) by mental health nurses in schizophrenia. Unfortunately there are flaws in the methodology, which casts major doubts on the validity of the study (Quitkin *et al*, 2000). First, although the authors claim to have a control group, it seems that patients in the control group did not have a placebo-like intervention; for example, the nurses could have spent the same amount of time with the patients without providing the CBT intervention. What is more surprising is that the study was powered to give a 90% chance of detecting only a 25% level difference in overall symptoms at the 0.01 level of significance. A 25% difference between a treatment and non-intervention group can easily be accounted for by a placebo effect. It is well known that the placebo response rate is usually around 30% in

psychiatric trials. For over 50 years the inclusion of a placebo control group has been the standard for determining the efficacy of an intervention. Without an adequate comparison group and without adequate comparison conditions, it is impossible to differentiate any specific effects from other 'non-specific' factors, including chance variation, regression to the mean, healthcare provider attention, treatment credibility and rationale, persuasion, patient expectancy effects, researcher allegiance effects, effort justification, spontaneous remission, demand characteristics, etc. (Lohr *et al*, 1999).

Given the lack of a true control group this study would be called nothing but an open-label trial. Open-label trials require at least a 50% level difference in overall symptoms between baseline and post-intervention response; moreover they do not require huge numbers of patients to show a tendency towards improvement.

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doi: 10.1192/bjp.190.3.271a

**Authors' reply:** We believe that Dr Alam has misunderstood the difference between efficacy and effectiveness research. The national guidelines on the clinical management of schizophrenia (National Institute for Clinical Excellence, 2002) confirmed CBT to be an evidence-based treatment for persistent symptoms of schizophrenia. However, that decision was based almost entirely on efficacy trials where CBT was given by expert therapists to highly selected samples of people with schizophrenia without comorbidities and using an active comparator such as befriending or supportive counselling (e.g. Sensky *et al*, 2000). Expert therapists and uncomplicated patients are