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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 temporolimbic 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

rare in clinical psychiatric practice. Therefore the next step was to design an effectiveness trial to see whether mental health nurses, without prior experience of CBT could be trained over a short period and then supervised to effectively and safely deliver brief CBT to large numbers of people with schizophrenia in the community. As this involved raters being masked to group allocation, this was therefore not an 'open-label' trial.

In relation to the effect size, it is certainly true that when an antipsychotic is compared with a placebo in drug-naive patients a much larger effect is demonstrable. The patients recruited to this trial were, however, almost entirely stabilised on antipsychotics and had already achieved such improvement from them. The effect size with any psychological treatment added to antipsychotics is always likely to be less than that initially achieved by the medication. We acknowledge that the effect size on symptoms at follow-up is modest but the impact on relapse is significant, clinically and in terms of resource savings, for such a brief intervention.

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doi: 10.1192/bjp.190.3.271b

Contingency management for substance misuse

Petry (2006) provides a welcome review of contingency management in substance misuse settings and expresses surprise that it has not been employed more widely in Europe, particularly given the greater acceptance of 'harm minimisation' here than in the USA, where contingency management has been championed. This is broadly true but some UK drug services are experimenting with interventions informed by reinforcement principles.

The injectable opiate clinic at the Chelsea and Westminster Hospital in London has for some years used reinforcement principles to target illicit opiate and crack cocaine use. Urine samples are regularly tested and the results used alongside clinical judgement to determine the proportion of a client's total daily opiate dose which may be administered intravenously as opposed to orally. In this way, access to injectable rather than oral opiate preparations is the 'reward' for positive behaviour. Staff increase or decrease the injectable proportion of the client's prescription depending on the client's stability.

As a first step towards developing an intervention study (Medical Research Council, 2000) we completed qualitative interviews with staff and clients to assess attitudes towards the further development of reinforcement methods. Staff and clients both cautiously supported reinforcement principles, and staff perceived clients to be more stable and less likely to use illicit substances under the present reinforcement scheme. Nevertheless, challenges were also highlighted. Most staff had reservations about developing voucher-based contingency management, citing possible increased workloads and a potential for damage to staff–client relationships. Despite a strong commitment to harm minimisation strategies at the clinic, some staff also had ethical objections to the development of voucher-based contingency management.

Our study was small and more research is required to explore the feasibility of voucher- or prize-based contingency management. However, as Petry emphasises, contingency management strategies have a good evidence base in a complex and challenging client group where positive outcomes are elusive. It is surely time to evaluate whether contingency management has a place in UK drug treatment services. Our work suggests that debate about the theoretical basis of contingency management and its ethical implications is needed to win support for experimentation among hard-pressed drug treatment workers in the UK.

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doi: 10.1192/bjp.190.3.272

Author's reply: McQuaid *et al* report that clinicians working in their injectable opiate clinic were cautiously supportive of the use of injectable opiates for reinforcement but more hesitant about the use of voucher- and prize-based contingency management procedures.

These perceptions mimic those of clinicians in the USA. Upon initial exposure to contingency management interventions, many clinicians express concerns ranging from hesitation to outright opposition. However, after observing the beneficial effects in practice great shifts in attitude occur. Some who were initially the greatest critics become the strongest supporters of contingency management once they see its benefits with particularly difficult clients.

As in the London programme, critics often evoke 'ethics' to dismiss contingency management. This denunciation is paradoxical, as reinforcement principles upon which contingency management interventions are based are operative in every facet of life. Furthermore, one must wonder about the ethics of withholding an efficacious intervention. It was not long ago that opiate substitution treatment, now considered one of the most effective prevention interventions for HIV transmission, was itself labelled unethical.

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doi: 10.1192/bjp.190.3.272a

Depression and anxiety after myocardial infarction

Dickens *et al* (2006) stress the importance of detection and treatment of anxiety and depression for quality of life after myocardial infarction and point to the mediating role of energy and fatigue.