

Correspondence

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Child sexual abuse and schizophrenia

The authors of a recent study concluded that it 'gave no support to child sexual abuse being associated with schizophrenic disorders later in life' (Spataro *et al*, 2004). Despite numerous acknowledged limitations that 'reduce the probability of finding a positive association between [child sexual abuse] and mental disorders', males who had suffered child sexual abuse were 1.3 times, and abused females 1.5 times, more likely to have been subsequently treated for schizophrenic disorders than the general population. However, the researchers missed a crucial additional limitation. Because the abused subjects were drawn from police and court records many will have been removed from the abusive situation and received early support. The researchers warned, specifically in relation to schizophrenia: 'Care must be taken in interpreting this and other negative findings'; we agree.

The researchers also claimed 'the findings to date do not support an association between child sexual abuse and schizophrenia', adding that this hypothesis 'has claimed considerable public, if not professional, attention'. It seems professional attention has been somewhat selective.

There are many studies demonstrating the powerful relationship between child abuse (sexual and otherwise) and schizophrenia (reviewed by Read *et al*, 2004). Studies of specific psychotic symptoms reveal that the relationship is particularly strong with hallucinations (Hammersley *et al*, 2003; Read *et al*, 2003, 2004). When mediating variables are controlled for, the relationship, with both clinician-rated symptoms (e.g. Read *et al*, 2003) and research measures of psychosis (e.g. Janssen *et al*, 2004), remains significant.

One of the most robust of these studies was a prospective general population study ($n=4045$), controlling for age, gender,

education, unemployment, urbanicity, ethnicity, discrimination, marital status, drug use, and psychotic symptoms or psychiatric care in first-degree relatives. On the three measures of psychosis, people who had suffered child abuse were 2.5, 7.3 and 9.3 times more likely to have psychosis. As in previous studies (e.g. Read *et al*, 2003), there was a 'dose-response' relationship. Those who had experienced severe child abuse were 48 times more likely than the general population to have 'pathology level' psychosis (Janssen *et al*, 2004).

Hammersley, P., Dias, A., Todd, G., et al (2003) Childhood traumas and hallucinations in bipolar affective disorder: preliminary investigation. *British Journal of Psychiatry*, **182**, 543–547.

Janssen, I., Krabbendam, L., Bak, M., et al (2004) Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavica*, **109**, 38–45.

Read, J., Agar, K., Argyle, N., et al (2003) Sexual and physical assault during childhood and adulthood as predictors of hallucinations, delusions and thought disorder. *Psychology and Psychotherapy: Theory, Research and Practice*, **76**, 1–22.

Read, J., Goodman, L., Morrison, A., et al (2004) Childhood trauma, loss and stress. In *Models of Madness: Psychological, Social and Biological Approaches to Schizophrenia* (eds J. Read, L. Moshier & R. Bentall), pp. 223–252. Hove: Brunner-Routledge.

Spataro, J., Mullen, P. E., Burgess, P. M., et al (2004) Impact of child sexual abuse on mental health: prospective study in males and females. *British Journal of Psychiatry*, **184**, 416–421.

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Author's reply: John Read appears to feel we were less than generous in our paper to the hypothesised relationship between child sexual abuse and schizophrenia. One of the many frustrations which beset researchers is that having chosen an analytical method and set the level of significance, you just have to live with your

results, equivocations around trends notwithstanding. You certainly cannot, as John Read does in his letter, state about our results that 'males who suffer child sexual abuse were 1.3 times, and abused females 1.5 times, more likely to have been subsequently treated for schizophrenic disorders', when those relative risks were non-significant. I can assure your readers that had we been able to squeeze out a significant association between schizophrenia and child abuse from our data we would have done so. After all, dramatic and unexpected results tend to acquire that coveted accolade of citation more frequently than do the mundane and predictable. As we hopefully made clear, our study did not exclude an association between schizophrenia and child abuse – how could it – but simply failed to support such an association.

Dr Read refers to the associations found in a number of studies between endorsing symptoms which can occur in psychotic disorders and prior sexual abuse. I would suggest this is not quite the same thing as associations with schizophrenic illness. It should also be emphasised that correlations do not necessarily reflect causal relationships even if you chose to describe them as 'powerful relationships'.

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Social development, urban environment and psychosis

Van Os (2004) persuasively argues for a greater recognition of the urban environment as a justifiable and empirically sound aetiological factor in psychotic illness. The unanswered question, however, remains about the mechanism through which this environment increases the risk for psychosis. It seems necessary to suggest that perhaps psychiatric illness cannot be assessed under the generally accepted cause and effect rubric that defines other medical illnesses. This is mostly because there are no definitive or specific markers that can define the presence of the illness and, although genetic factors are associated with the risk for developing psychosis, the expression of illness is clearly an interaction with environmental factors (Tsuang *et al*, 2001).

Van Os notes that the medium of risk exposure is likely to be widespread and

cumulative over the course of development. This further suggests that the presentation of psychosis represents a culmination of an ongoing interaction between an individual and his/her environment. This remains the only reasonable explanation for the variation in incidence rates, particularly those reported for migrant populations in Britain and Europe (Hutchinson & Haasen, 2004). Interactions between perceptions of self, cognitive processes and the features of a modern urban environment underlie social development. The relative weighting of vulnerability and resilience factors is a function of this interaction and must in turn be affected by wider social issues such as racism, socioeconomic opportunity and perceived social isolation. There is also the generational transfer of unfulfilled expectations and distrust of institutional structures. The problems in mental health for migrants in Britain are mirrored in the education and criminal justice systems (Modood *et al*, 1997). This suggests a developmental trajectory that is affected by social and generational realities and at the same time increases the risk of presentation with psychotic symptoms.

This would mean that the risk exposure for psychosis lies not specifically in the urban environment but in the way this environment generates and/or facilitates a life course that ultimately disadvantages those whose vulnerability is not compensated for by the support of their social environment. This is also influenced by the individual's perception of the negative experiences of the ethnic and socio-cultural groups with which they identify in both the narrow family and community sense as well as the wider national and international sense.

There might therefore be a need to reconstruct the neurodevelopmental model which has led to a preoccupation with the biology of psychosis to include a social developmental model that can demonstrate how the neurobiological endpoint of psychosis can have both biological and social origins.

Hutchinson, G. & Haasen, C. (2004) Migration and schizophrenia. The challenges for European psychiatry and implications for the future. *Social Psychiatry and Psychiatric Epidemiology*, **39**, 350–357.

Modood, T., Berthoud, R., Lakey, J., et al (1997) *Ethnic Minorities in Britain: Diversity and Disadvantage*. London: Policy Studies Institute.

Tsuang, M. T., Stone, W. S. & Faraone, S. V. (2001) Genes, environment and schizophrenia. *British Journal of Psychiatry*, **178** (suppl. 40), s18–s24.

Van Os, J. (2004) Does the urban environment cause psychosis? *British Journal of Psychiatry*, **184**, 287–288.

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Van Os (2004) discusses the implication from the epidemiological research by Sundquist *et al* (2004) that psychosis may indeed be due to urban toxicity. The dose–response increase in urbanicity with schizophrenia does incline to an explanation of causation rather than association. The discussion of a set of environmental factors acting between birth and the onset of psychosis (child and adolescence) should have led to a discussion of the role that cannabis plays in the early onset of psychosis. This link between substance use and urbanicity was, however, not discussed in the editorial.

The clue to an ecological exposure lies in the early use of cannabis. Arseneault *et al* (2002) in a prospective study found an association between early use of cannabis (by the age of 15) and an increased risk of psychosis for 1037 children born in New Zealand. This aetiological factor interacts with the increased social fragmentation, social inequality and social isolation found with greater urbanicity. The cognitive vulnerabilities for psychosis have a strong social environmental aetiology, and a link needs to be made between models of urban toxicity and increased early cannabis use.

Arseneault, L., Cannon, M., Poulton, R., et al (2002) Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ*, **325**, 1212–1213.

Sundquist, K., Frank, G. & Sundquist, J. (2004) Urbanisation and incidence of psychosis and depression. Follow-up study of 4.4 million women and men in Sweden. *British Journal of Psychiatry*, **184**, 293–298.

Van Os, J. (2004) Does the urban environment cause psychosis? *British Journal of Psychiatry*, **184**, 287–288.

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Memantine as a neuroprotective treatment in schizophrenia

Phospholipid metabolism occurs in cell (including neuron) membranes and

although regional differences are described by Jensen *et al* (2004), these are not neurotransmitter-specific. This research suggests increased phospholipid metabolism in the anterior cingulate area of people with schizophrenia.

Jensen *et al* suggest that this is supportive evidence for a neurodegenerative mechanism in schizophrenia. They also review the effects of neuroleptic and anxiolytic (including benzodiazepine) medications on brain phosphorus metabolism.

Memantine is a drug currently licensed for use in people with moderate to severe Alzheimer's dementia. It is a non-competitive, low-affinity *N*-methyl-D-aspartate (NMDA) antagonist. (The NMDA receptor is a class of glutamate receptor.) Glutamate-mediated excitotoxicity and/or receptor dysfunction is involved in the pathogenesis of several neuropsychiatric and neurological disorders. Memantine partially blocks these NMDA receptors, preventing a neurotoxic influx of calcium. Theoretically, it is neuroprotective for glutamate-receiving neurons.

Given its mode of action, it should theoretically be more effective in the early stages of neurodegenerative disorders such as Alzheimer's dementia. On these theoretical grounds it may also be neuroprotective for people with schizophrenia.

Jensen, J. E., Miller, J., Williamson, P. C., et al (2004) Focal changes in brain energy and phospholipid metabolism in first-episode schizophrenia: ³¹P-MRS chemical shift imaging study at 4 Tesla. *British Journal of Psychiatry*, **184**, 409–415.

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Authors' reply: Memantine, as described by Dr Rands, would appear to be a suitable candidate as a neuroprotective agent for people with schizophrenia, based on its NMDA-receptor-blocking properties. This drug is currently in use as a treatment for people with moderate to severe Alzheimer's dementia.

As shown by Theberge *et al* (2002, 2003), glutamate levels in first-episode schizophrenia are higher than normal in the anterior cingulate and lower than normal in this same region in the chronic stages of illness. As shown in this same work, *N*-acetylaspartate levels correlate negatively