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).


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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 disadvantage 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.


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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.


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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.


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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
with duration of positive symptoms. This work, as well as the phosphorus work by our team (Jensen et al, 2000, 2002), suggests a gradual neurodegenerative process in the anterior cingulate in schizophrenia, possibly initiated by an early neurodevelopmental anomaly involving basal ganglia–thalamocortical neuronal circuits or the structures which regulate these circuits. As Dr Rands points out, memantine would partially block the NMDA receptors preventing excitotoxic damage in the anterior cingulate and connected structures, thus slowing the progression of symptoms. However, there are other considerations. There is evidence that excitotoxicity is linked to non-NMDA receptors (Tsai & Coyle, 2002) which may not be affected by this approach. Furthermore, another NMDA-blocker, phencyclidine, can actually cause a paradoxical increase in glutamate activity which could aggravate the condition.

In summary, we agree that treatment options for schizophrenia should begin to focus more on this neuroprotective strategy. Although current medications may alleviate positive symptoms, they are relatively ineffective for negative symptoms and are often inadequate in preventing the psychosocial deterioration seen in chronic schizophrenia. Treatment with memantine could theoretically slow the progression of negative symptoms when administered to patients in the early stages of schizophrenia but the overall effects of these drugs are difficult to predict and it is our view that some caution is indicated in planning long-term trials of these medications in people with schizophrenia.


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Testing for diabetes

Taylor et al (2004) report on the differences in testing for diabetes among 606 patients receiving antipsychotics, observing that patients receiving atypical antipsychotics were more likely to have been tested than those receiving older agents. Moreover, this appeared to be significant specifically for clozapine, olanzapine, and antipsychotic polypharmacy.

It is noteworthy that very similar results were found by our group when examining hospitalised patients in New York State (Citrome et al, 2003, 2004). Among 1154 patients in 2000–2002 with no known prior history of receiving anti-diabetic medications, those receiving clozapine, olanzapine, or more than one atypical antipsychotic had a significantly higher frequency of blood glucose testing than those receiving only typical antipsychotics (Citrome et al, 2004). Moreover, those receiving risperidone had a frequency of testing similar to those receiving only older agents, resulting in the conclusion that there are clear differences in surveillance for diabetes mellitus among even the newer agents.

Investigators performing pharmaco-epidemiological studies examining the risk of association between antipsychotics and diabetes mellitus need to be mindful of this surveillance bias.

Declaration of interest

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Taylor et al (2004) found very low rates of monitoring for diabetes in their study population. Less than 50% were tested, and the testing rates varied with the antipsychotic prescribed.

So why is this the case? This probably reflects the lack of a clear consensus in this area. There is currently no consistent direction for doctors regarding the need for monitoring for diabetes. The conflicting evidence in the literature is abundant. For example, the British National Formulary is probably the most widely used reference for prescribers in the UK. The current edition makes no mention of blood sugar abnormalities with typical antipsychotics, quetiapine and risperidone. Concerns are mainly highlighted with olanzapine and clozapine. This is despite studies showing increased risks with typical and atypical antipsychotics. Furthermore, the recent Maudsley Guidelines give some suggestions of the type and frequency of tests, focus mainly on olanzapine and clozapine but contradict the British National Formulary in suggesting testing for all antipsychotics.

So is testing important? Evidence is mounting of an association between schizophrenia and diabetes. Ryan & Thakore (2002) give schizophrenia as an independent risk factor for diabetes even in antipsychotic-naive patients. The PORT study (Dixon et al, 2000) gives a prevalence of 15% in this population compared with 3% in the general population (Bennett et al, 1995). Several studies suggest an even higher risk of diabetes in those prescribed atypical antipsychotics (Bushe & Leonard, 2004). Therefore, it appears that people with schizophrenia are a high-risk group for developing diabetes and its potential consequences.
Our patients may have little contact with other doctors and diabetes can be a silent illness which could be easily missed. Psychiatrists are well placed to monitor this high-risk population and should be encouraged to adopt a holistic approach. There is a need for clear consensus to avoid any confusion among psychiatrists. Guidelines are needed to help clinicians to decide which patients should be tested, the type of test to use and how often. The Royal College of Psychiatrists is well placed to publish the necessary guidelines.


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One hundred years ago

The asylum medical service

To the Editors of The LANCET

SIRS, – I am glad to see by the letter of “M.B.” in your issue of Dec. 31st, 1904, p. 1888, that at least one assistant medical officer has the courage to protest against the treatment which is meted out to his colleagues in the asylum service. The present unsatisfactory state of affairs has gone on quite long enough and in the interest not only of the medical staff but also of the patients committed to their charge a change is desirable, even essential. As long as the medical staff of asylums are content to exist under their present conditions it is useless to insinuate that the fault lies at the door of those in authority, be they Commissioners in Lunacy, visiting committees, or even medical superintendents. The fault and the remedy lie in their own hand. But how few will ever take the trouble to place their views on paper. There are three distinct classes of assistant medical officers in asylums: (1) those who on entering it intend to remain in the service, devoting their lives to the study and treatment of mental diseases and thus in time becoming specialists; (2) those who, newly qualified, seek a asylum appointment in order that they may read for some further examination, on the passing of which they have set their ambition; or (3), those who unable to afford to enter general practice immediately they become qualified take an asylum post with the intention of waiting for a suitable opening in some district which may be known to them. When the opportunity presents itself they leave and are succeeded by colleagues with possibly similar views. To such as these an asylum appointment is but a means to an end. The end having been attained they depart and as a rule trouble no more about lunacy or asylums unless they be called on to certify a patient in the course of their general practice.

In the case of an assistant medical officer who enters the asylum service with the intention of remaining permanently in it the case is very different. He starts full of enthusiasm and hope with an initial salary of anything from £120 to £150 per annum with the usual allowances. Three or four years pass by and he finds himself with some knowledge of mental diseases in addition to the general knowledge of his profession with which he started, but it suddenly occurs to him that notwithstanding his increased experience in a special science he is still drawing the same salary as when he entered the asylum service fresh from the hospital. His colleagues who are senior to him have little, if any, prospect of promotion in the future. True, they have had more years of service and consequent experience, but their salaries are very little in excess of what was considered sufficient remuneration for him when he entered the service without any special knowledge of lunacy. Then come weary years of waiting, hoping that one of his seniors may be promoted to one of the few vacant medical superintendencies which may chance to occur at rare intervals, and in most cases with resulting disappointment. His senior colleague, should he be unsuccessful in obtaining the post of medical superintendent in some other asylum, is in, if possible, a more hopeless plight. He has given the best years of his life to the study of mental diseases. What is his reward? A salary of perhaps £250 or £300 per annum and should he be over 40 years of age the probability that he may expect no further promotion or increase of salary. Moreover, there is a rule that no assistant medical officer can be married. (I believe there are one or two cases in which the senior assistant medical officer can do so if he likes.)

To the junior members of the staff, this is not such a hardship as to their seniors. The pay and accommodation of a junior assistant medical officer put matrimony out of the question but when a senior comes to the age of, say, 40 years he may have some desire to have a home of his own after living for years in two rooms. With all respect for the authorities who govern asylums I would ask, What has a man done who has given the best years of his life to their service that he should be debarred from entering the matrimonial state should he so desire? As far as I can ascertain there is no other branch of the public service in which such a restriction is imposed on the permanent medical staff. It may be argued by those who favour the present system of enforced celibacy in the case of asylum assistant medical officers that a similar rule is in force in the hospitals and Poor-law infirmaries. To them I would point out that in neither case do the medical officers accept their appointments as a permanency. They, as a rule, leave after longer or shorter periods and enter general
practice or one of the services, the experience which they gained during their term of office being of immense value to them in their future careers. With the asylum medical officer the case is absolutely different. After some years, as “M.B.” correctly states, spent in the treatment of mental diseases a man has become a specialist and is thus more or less unfitted for general practice. The special experience he has gained in the asylum is of comparatively little use to him outside the walls, his duty for years having been more to treat mental diseases than physical ailments. Therefore there is no analogy between the cases.

With regard to the striking differences between the salaries paid to medical superintendents as compared with those of senior assistants I do not for a moment suggest that the medical superintendent, who is according to the Lunacy Act the chief responsible official of an asylum, is paid too much, but I maintain that there is far too great a drop from the medical superintendent to the senior assistant medical officer who has discharged the duties of medical superintendent in addition to his own routine work. It must be obvious that in these days of huge asylums the duties and responsibilities which were formerly personally discharged by the medical superintendent have now to be deputed to the assistant medical officers.

The Commissioners in Lunacy in their last report strongly condemned the erection of these huge places, but despite this, committees ignore the recommendations of a body whom the public look upon as experts in such matters and still continue to erect enormous costly “houses for the detention of the insane” – one really cannot call them hospitals for the treatment of mental diseases.

The question of leave is also the source of much complaint in asylums. The medical superintendent gets one month or in some cases six weeks annually, the assistant medical officers 28 days or perhaps in a few cases 31 days. Occasional leave is grudgingly accorded and then only one night can be spent outside the asylum gates unless a special appeal is made to the chairman of the committee who, unless there is some special reason given for wanting leave other than annual, may refuse it. Anyone with common sense must appreciate the fact that constant association with the insane is not conducive to exhilaration. Therefore a change of short duration at fairly frequent intervals, exclusive of annual leave, becomes not only desirable but even necessary to those who have charge of them. If the best men are to be attracted to the study of lunacy, which is becoming daily a more and more alarming factor in our social system, it behoves the authorities to amend the conditions of service of the assistant medical officers who have served them so long uncomplainingly. By this means alone can good men be induced to enter the asylum service as a permanency. Under the present system the junior post in asylums is usually sought after as a temporary abiding place where examinations may be read for or as a pleasant resting place until some better or more congenial employment turns up.

I am, Sirs, yours faithfully,
A.M.O.

REFERENCE

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