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Language lateralisation in schizophrenia

Dr Sommer and colleagues (2004) reported decreased language lateralisation measured with functional magnetic resonance imaging (fMRI) in 12 monozygotic twin pairs discordant for schizophrenia compared with 12 healthy monozygotic twin pairs. The authors did not find significant differences in language lateralisation between affected twins and their co-twins without schizophrenia. In the December 2003 issue of the Czech peer-reviewed psychiatric journal *Psychiatrie*, we published preliminary data from a study (supported by grant NF 6794-3/2001 from the Internal Grant Agency of the Czech Republic) that examined hemispheric dominance for language processing by means of fMRI in four monozygotic twin pairs discordant for schizophrenia. Although the activation paradigm (a verbal fluency task) differed from the one employed by Dr Sommer *et al*, the lateralisation index was calculated according to the same method within identical volumes of interest. The results indicated that language processing was significantly less lateralised in affected twins compared with their co-twins without schizophrenia ($P<0.05$, Wilcoxon signed ranks test, robustness assessed by analysis of 10 000 Monte Carlo permutations; mean laterality index 0.90 (s.d.=0.12) for unaffected twins and 0.73 (s.d.=17) for affected twins). There were no statistical differences in the laterality index during the verbal fluency paradigm between unaffected twins from the discordant monozygotic twin pairs and the four control monozygotic twin pairs (unpublished data). The explanation of the discrepancies could lie in the participants enrolled in our study. Since the aim of our work was to assess relative contribution of non-genetic factors in previously reported decreased language lateralisation in schizophrenia, the exclusion criterion was (in contrast to Dr Sommer's study) any family history of schizophrenia or other major psychiatric disorder. This particular study strategy allowed selection of an extreme population presumably represented by sporadic forms of the disease. In addition, stringent diagnostic criteria were used in that only participants with schizophrenia were enrolled in the study. The occurrence of psychiatric disorders in co-twins without schizophrenia and the fact that the participants were not controlled for family history of psychosis suggest a substantial degree of genetic predisposition for schizophrenia in unaffected co-twins expressed as overall decrease in language lateralisation within the discordant twin group studied by Dr Sommer and her colleagues.

Sommer, I. E. C., Ramsey, N. F., Mandl, R. C. W., *et al* (2004) Language activation in monozygotic twins discordant for schizophrenia. *British Journal of Psychiatry*, **184**, 128–135.

Španiel, F., Tintera, J., Hájek, T., *et al* (2003) Language lateralization in monozygotic twins discordant for schizophrenia. Evidence from functional MRI. *Psychiatrie*, **4**, 301–303.

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Authors' reply: We read with interest the results of the study by Dr Španiel *et al*. In parallel to our findings, they reported decreased language lateralisation in (twin) patients with schizophrenia compared with healthy (twin) controls. However, they did not report whether the decreased lateralisation in the patients resulted from increased activation of the right hemisphere, or from decreased activation of the left hemisphere. This is an essential point, since decreased activation of frontal, temporal and parietal language areas in the left hemisphere of schizophrenia patients is frequently associated with decreased task performance (as reported by Artiges *et al*, 2000). Increased language-related activation of right cerebral areas, in contrast, may reflect a failure to establish cerebral dominance, which may be a genetic predisposition to develop schizophrenia.

In our study (Sommer *et al*, 2004), the language tasks employed were selected to be very simple in order not to cause a difference in performance between patients and healthy subjects. Left hemispheric language activation was not lower in patients than in their co-twins, which, in our opinion, reflects equal task performance.

In the Španiel *et al* study, a verbal fluency task was employed, which is known to generate a difference in performance between schizophrenia patients and controls, and generally yields decreased activation of left frontal areas in patients (Curtis *et al*, 1999). This may explain why Španiel *et al* found lower lateralisation in patients compared with their co-twins.

Španiel *et al* mentioned that selection of co-twins without schizophrenia and of control pairs may have caused the difference between their results and ours, since the control twin pairs in their sample were selected not to have relatives with schizophrenia. This was, however, also the case in our sample. The second point of difference raised by Španiel *et al* is that the co-twins in their study had no psychiatric disorder. However, in our article we described an additional analysis comparing twins with schizophrenia with their co-twins after exclusion of all pairs from which the co-twins had psychiatric pathology, which yielded the same results as the analysis including the entire sample.

In sum, we find Dr Španiel *et al*'s study an interesting contribution; in our opinion it is differences in the language activation tasks, rather than differences in sample selection, that are the cause of the differences in outcome between the studies.

Artiges, E., Martinot, J. L., Verdys, M., *et al* (2000) Altered hemispheric functional dominance during word generation in negative schizophrenia. *Schizophrenia Bulletin*, **26**, 709–721.

Curtis, V. A., Bullmore, E. T., Morris, R. G., *et al* (1999) Attenuated frontal activation in schizophrenia

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may be task dependent. *Schizophrenia Research*, **37**, 35–44.

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Cognitive–behavioural interventions in schizophrenia

Hodgins & Müller-Isberner (2004) in their clinical implications assert that schizophrenia patients with antisocial behaviour 'require cognitive–behavioural interventions aimed at changing antisocial behaviours . . .', yet the paper itself can only quote evidence of effectiveness of these techniques in offenders who are not mentally ill (McGuire, 1995). It therefore seems unclear why they then suggest that these techniques will be effective in reducing antisocial behaviours in people with schizophrenia and should be regarded as 'required'. Unfounded assumptions like these may be quoted by others referencing this paper and lead people to assume, mistakenly, an evidence base for this assertion. Providing cognitive–behavioural therapy to this client group may therefore provide no benefit but divert resources that may have benefited others. While I agree that reducing antisocial behaviour in this client group is desirable, we should not hasten to assume, in the absence of evidence, that cognitive–behavioural therapy will provide a panacea.

Hodgins, S. & Müller-Isberner, R. (2004) Preventing crime by people with schizophrenic disorders: the role of psychiatric services. *British Journal of Psychiatry*, **185**, 245–250.

McGuire, J. (1995) *What Works: Reducing Reoffending. Guidelines from Research and Practice*. Chichester: John Wiley & Sons.

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Authors' reply: Thank you for your interest in our work. It is important to note that we proposed that cognitive–behavioural interventions that have been shown to reduce offending could be adapted to treat a subgroup of offenders with schizophrenia. This sub-group shares with the offenders who have benefited from these interventions a history of antisocial behaviour since childhood, and antisocial attitudes and ways of thinking.

Dr Huda makes the presumption that interventions proven to reduce offending would not have a similar effect among offenders with schizophrenia. In our view, this presumption is unfounded. For example, treatments for medical conditions proven to be effective in people without schizophrenia are used with equal success with those with schizophrenia. We also disagree with Dr Huda's presumption because, generally, effective treatments target specific problems, not a disorder. This is true in the case of schizophrenia where different treatments have been shown to have a positive impact on positive and negative symptoms, substance misuse, life skills, social skills and employment skills (Bloom *et al*, 2000).

As we noted, compliance with medication is a prerequisite to participating in interventions aimed at reducing offending. Furthermore, these interventions need to be adapted for use with people with schizophrenia and their effectiveness evaluated. This has been done recently, for example, with interventions that targeted substance misuse. Programmes that were adapted to patients with schizophrenia and integrated with their other treatments are reported to be effective (Mueser *et al*, 2003).

We agree with Dr Huda that evidence for the effectiveness of cognitive–behavioural programmes in reducing offending among persons with schizophrenia is still sparse. It is presently limited to naturalistic follow-up studies with non-random assignment of participants (T. Fahy, personal communication, 2004; Kunz *et al*, 2004). In our view, however, the available evidence is encouraging and sufficient to undertake randomised controlled trials of these interventions with the sub-group of offenders with schizophrenia who display a stable pattern of antisocial behaviour from an early age. Given the potential of these interventions to prevent criminal activity, improve the individual patient's life, and reduce costs to both the health and criminal justice system, such trials are urgently needed.

Bloom, J. D., Mueser, K. T. & Müller-Isberner, R. (2000) Treatment implications of the antecedents of criminality and violence in schizophrenia and major affective disorder. In *Violence among the Mentally Ill: Effective Treatments and Management Strategies* (ed. S. Hodgins), pp. 145–169. Dordrecht: Kluwer Academic.

Kunz, M., Yates, K. F., Czobor, P., *et al* (2004) Course of patients with histories of aggression and crime after discharge from a cognitive–behavioral program. *Psychiatric Services*, **55**, 654–659.

Mueser, K. T., Noordsy, D. L., Drake, R. F., *et al* (2003) Research on integrated dual-disorder treatment. In *Integrated Treatment for Dual Disorders: A Guide to Effective Practice* (ed. D. H. Barlow), pp. 301–321.

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Suicide and antidepressant sales

Helgason *et al* (2004) reported that the dramatic increase in the sales of antidepressants in Iceland had not had any impact on suicide rates. While the sales of antidepressants increased fivefold from 14.9 defined daily doses per 1000 persons per day in 1989 to 72.7 in 2000, the suicide rate remained quite stable (around 11/1000 000 persons per year). The data were, however, not analysed separately by gender.

Based on the World Health Organization database on national suicide rates, Levi *et al* (2003) compared the periods 1980–84 and 1995–99, and found that suicide rates in Iceland decreased by 1.7% in males during the whole period (17.9 to 17.6) and by 46.7% in females (from 6.0 to 3.2). In spite of the fact that the time periods investigated by Helgason *et al* (2004) and Levi *et al* (2003) are not exactly identical, the general trends should be similar. Given this extremely great (27-fold) difference in the decrease in suicide rates between males and females, it would be interesting to see the data on the use of antidepressants in Iceland between 1989 and 2000 for males and females separately. Perhaps the increase in the use of antidepressants was more pronounced in women than in men, as for example in Australia (Hall *et al*, 2003)?

A significant negative correlation between antidepressant prescription and national suicide rates has been reported from Sweden, Denmark, Finland and Norway (Isacsson, 2000) as well as from Hungary (Rihmer, 2004), countries where suicide rates have been traditionally high. Statistical association, of course, does not necessarily imply causality, but considering the strong relationship between untreated depression and suicide, the national trends mentioned above point in the expected direction. On the other hand, however, if a marked increase in antidepressant

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