

age 16 were more likely to be described as clumsy. Delays in learning to stand, walk or speak are linearly related to later risk of schizophrenia (Isohanni *et al*, 2001) as also was delay in potty-training, a finding that corresponds to an increased incidence of failures of continence observed in the NCDS cohort.

Each of these findings suggests some commonality between features of pervasive developmental disorders (including Asperger syndrome) and those that precede schizophrenia, notwithstanding obvious differences in methods of data collection. There remains the question of time course to which Asperger drew attention – the features of Asperger syndrome are present early, whereas those of schizophrenia show an element of progression. This difference is exemplified by a progressive decrease in language scores preceding the onset of schizophrenia (Fuller *et al*, 2002).

The key question is why does this constellation of features come together? One finding from the NCDS sample points to the neurological substrate. At age 7, children who, in adulthood, develop schizophrenia were more likely to be rated as ambidextrous for handwriting by their mothers and were less lateralised on a square ticking task at age 11. There is evidence that lateralisation is a major determinant of the acquisition of words as well as of other aspects of cognitive ability (Crow *et al*, 1998). We propose that development of hemispheric dominance for the components of language is relevant to the similarities of the conditions described by the term Asperger syndrome and those that precede the onset of schizophrenic psychoses, as well as to differences in their time course. Thus, language – the core characteristic of the species – with its context in social interaction and its matrix in the lateralisation to the two hemispheres, is the function that varies between individuals and accounts for the similarities between the early developmental anomalies that were identified by Asperger and those that can now be seen as precursors to psychotic illness.

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### Genetics of early-onset depression

We were very interested to read the recent, thought-provoking editorial by Andrews *et al* (2002) on the prevention of depression in young people. However, we are concerned that they have understated the important role of genetics in early-onset depression. Contrary to their assertion that the children of parents with depression are likely to be at heightened risk for psychological rather than genetic reasons, available evidence suggests that childhood-onset depression represents a strongly genetic subtype of affective disorder (Neuman *et al*, 1997; Sullivan *et al*, 2000). Up to 50% of prepubertal children with depression eventually develop bipolar disorder (Geller *et al*, 2001) and recurrent, early-onset depression (defined as two or more episodes before age 25) is recognised as a malignant form of affective disorder characterised by high genetic loading, frequent recurrence and poor long-term outcome (Zubenko *et al*, 2001). Furthermore, one recent study suggests that the inheritance of depression in these families is compatible with a single major locus (Maher *et al*, 2002).

Preliminary findings from our own study of early-onset depression in a university population support the view that early age at onset defines a subgroup at very high genetic risk. Using the Family Interview for Genetics Studies (FIGS; National Institute of Mental Health, 1999), 76% of the subjects seen so far (36 out of 47) report at least one first-degree relative with affective disorder, with 87% (41 out of 47) reporting either a first- or second-degree relative affected. The mean age at onset in this group is 15.6 years (s.d.=2.6).

Population-based interventions are unlikely to reduce the prevalence of depression in young people as long as we have an incomplete understanding of how genetic and non-genetic risk factors interact to bring about the depressive phenotype. Interventions such as the cognitive therapy programme described by Clarke and colleagues (Clarke *et al*, 2001) might be cost-effective strategies if they can be targeted to high-risk groups. Unfortunately, we are not yet in a position to reliably identify those individuals at high risk.

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