

2002). Although parental psychiatric disorder might increase the chance that children become looked after, this is not inevitable and there are many other reasons why children may enter the care system. In fact, only 6% of the children participating in the survey on which our analysis was based were accommodated primarily as a result of any type of parental illness.

As the survey involved no contact with the biological parents of participants and historical information about children who are looked after is notoriously scarce, we had no way of accurately assessing the mental health of the biological parents. Our paper refers to our frustration at the extremely limited amount of information available to the survey and in clinical practice, and we explicitly state that our analysis cannot be seen as covering all potential risk and resilience factors.

Even if we had access to data on the mental health of the biological parents, an excess of children with psychiatric disorder among parents with psychiatric disorder would not necessarily indicate a biological or genetic basis for this finding. The mean age that children participating in this survey entered the care system was between 7 and 8 years, and we know that mental illness can have an impact on parenting practices. Do the children of parents with mental illness have raised rates of psychiatric difficulties as a result of genetic vulnerability and/or exposure to maladaptive parenting, or perhaps both processes occur at the same time and/or moderate each other? The literature suggests that parenting is an important mediating variable, although other genetic and environmental factors also play a part in the familial aggregation of psychopathology (Ramachandani & Stein, 2003). Cross-sectional surveys are not able to disentangle such complex questions, as data about exposures and outcomes are gathered at the same time. Longitudinal designs would be needed to explore Dr Sekar's theory.

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T. Ford Institute of Psychiatry, King's College London, UK. Email: t.ford@iop.kcl.ac.uk

P.Vostanis Department of Health Sciences, Leicester University, UK

H. Meltzer, R. Goodman Institute of Psychiatry, King's College London, UK
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Lithium for prevention of Alzheimer's disease

Nunes *et al* (2007) reported that the prevalence of Alzheimer's disease in a group of elderly patients with bipolar disorder who were on continuous lithium treatment was significantly less than in a similar group without recent lithium therapy. After controlling for age, lithium use remained associated with a smaller risk of Alzheimer's disease (age-adjusted OR=0.079, 95% CI 0.020–0.321). Conversely, Dunn *et al* (2005) showed that patients who received lithium had a significantly higher risk of dementia than those who did not (age-adjusted OR=1.8, 95% CI 1.1–2.8).

Nunes *et al* (2007) found no differences between the lithium and the comparison group in neuropsychological performance after excluding patients with Alzheimer's disease. This is in accordance with our study using Mini-Mental State Examination (MMSE) scores (Terao *et al*, 2006). Our study, however, showed that patients with present and/or past history of lithium treatment had significantly better MMSE scores than patients without any history of lithium treatment (Terao *et al*, 2006). It is important to further investigate lithium in the prevention of Alzheimer's dementia with a large number of patients in prospective studies.

If lithium has a preventive effect for Alzheimer's disease, there may be two possible mechanisms. First, it might indirectly prevent dementia via its prophylactic effects on mood disorders, because the rate of dementia increased 13% with every episode leading to admission for patients with depressive disorder and 6% for patients with bipolar disorder, when adjusted for differences in age and gender (Kessing & Andersen, 2004). Second, lithium might

directly prevent dementia via its inhibition of glycogen synthase kinase 3 (GSK-3) alpha (Phiel *et al*, 2003) and GSK-3 beta (Phiel & Klein, 2001). Although Nunes *et al* (2007) found no significant differences in the number of previous depressive and manic episodes between the lithium and comparison groups, at present both possibilities should be borne in mind.

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T. Terao Oita University Faculty of Medicine, Oita, Japan. Email: terao@med.oita-u.ac.jp
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Authors' reply: Dunn *et al* (2005) identified from the General Practice Research Database in the UK all cases of dementia between 1992 and 2002 ($n=9954$) and compared the number of prescriptions of lithium for individuals with this diagnosis with a control group without dementia ($n=9374$). They found that more patients with dementia ($n=47$, 0.47%) than controls ($n=40$, 0.43%) were exposed to lithium. We feel that this finding does not allow conclusions to be drawn as to whether lithium protects against or confers a risk for dementia, because it has been shown that patients with dementia have an increased risk of developing mania and depression (Nilsson *et al*, 2002) and are thus more likely to receive treatment, including lithium. Conversely, affective disorders themselves seem to increase the risk for dementia.

In a series of studies based on data from the Danish psychiatric case register, Kessing *et al* found that 14% of elderly patients with bipolar disorder and 16% with