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The emerging evidence of a potentially autoimmune-mediated psychosis that is clinically indistinguishable from idiopathic schizophrenia[1] raises practical questions about whether this condition should be treated by neurologists or psychiatrists, as well as the applicability of mental health legislation should compulsory treatment with immunosuppressants or plasmapheresis be deemed necessary.

From an academic perspective, this development represents a nosological challenge to the present dichotomy between functional and organic psychoses, broadening the interface between psychiatry and neurology.[2]

Advances in neurobiological, genetic, and neuroimaging research might in future lead to ending the schism between the two medical specialities.[3] Meanwhile, the lack of integration between psychiatry and neurology training programmes does not serve patients well,[4] and is increasingly unjustified from a neuroscience viewpoint.

We declare no competing interests.

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Authors' reply

We thank Feras Mustafa, and Frank Leypoldt and colleagues for their comments on our study about the prevalence and clinical characteristics of serum neuronal cell surface antibodies in first-episode psychosis.[1]

We agree with Mustafa that the present divide between neurology and psychiatry services in Britain is unjustified and that training initiatives that bridge the divide are required. The Royal College of Psychiatrists' present initiative to review the neuroscience training curriculum for psychiatrists is welcome.[2]

Regarding the data analysis of our study, the statistical reviewer recommended using logistic regression with odds ratios reported, and likelihood ratios reported where odds ratios were not calculable. Analysis with Fisher's test is another option; however, it comes with its own controversies, such as conditioning on the margins and it being conservative in rejecting the null hypothesis. We acknowledge the low numbers of cases, and that statistical significance depends on the analysis method used. Our interpretation was appropriately cautious in stating that "Further work is required to establish the specificity and pathogenicity of antibodies in the context of psychosis".[1]

The threshold that we used for antibody positivity was not lower in this study than that used previously. We reported the "dilution of serum providing a score of 1",[1] with the lowest level being 1:30 (ie, the threshold is 1·5 at a dilution of 1:20), consistent with clinical practice and recent publications.[3]

We acknowledge there is disagreement regarding the sensitivity of the different antibody assays in detecting anti-NMDAR encephalitis. However, the study that Leypoldt and colleagues cite as demonstrating a higher sensitivity of the fixed-cell assay defined cases on the basis of positivity with that assay, rather than assessment of clinical relevance of the antibodies in the patients tested.[4] The discrepant findings between the two assays in serum testing in a proportion of patients could, therefore, reflect a higher specificity of the live assay, rather than a reduced sensitivity.

We did not intend to detect anti-NMDAR antibody encephalitis. We agree that it is important that further studies should include cerebrospinal fluid analysis and that lumbar punctures should be introduced into routine British psychiatric practice for the assessment of psychosis.

Finally, Leypoldt and colleagues quote a poster at the European Academy of Neurology[5] showing that immunohistochemistry was positive in 29 of 35 patients with the live cell-based assay compared with 30 of 35 patients with immunohistology in patients with clinically defined NMDAR-antibody encephalitis. Clearly, there is no statistical difference between the two methods based on those data.

We thank Dr Mei-Man Lee for her statistical advice.

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Schizophrenia polygenic risk score and psychotic risk detection

Lucy Riglin and colleagues[1] showed that children carrying schizophrenia-associated risk alleles with a population frequency higher than 1% are predisposed to have prepubertal developmental impairments. After controlling for social class and sex, schizophrenia polygenic risk scores remained associated with performance IQ, speech intelligibility and fluency, and headstrong behaviour at age 7–9 years, and with social difficulties and behaviour problems at age 4 years. These findings agree with familial high-risk studies, prospective cohort studies, and retrospective studies showing that schizophrenia is preceded by premorbid neurobehavioural alterations.[2]

The aim of the study by Riglin and colleagues[1] is to highlight that some of these heterogeneous phenotypic manifestations might index genetic liability for schizophrenia. However, the authors clearly noted that these impairments represent a genetic liability rather than an illness prodrome, and further studies are needed to distinguish early manifestations of liability that reflect pleiotropy from those that represent developmental impairments causally associated with schizophrenia.

Empirical knowledge on genetic risk of schizophrenia is rapidly expanding, but many gaps limit our ability to use genetic data to predict future psychosis. Several interacting individual and environmental risk or protective factors can affect the lifetime risk of developing schizophrenia, confounding the phenotypic expression of genetic liability. However, progress is also hindered by present strategic approaches to psychotic risk detection, which typically focus on attenuated psychotic symptoms in late-adolescents and young adults. Although genetic liability has an early developmental manifestation (with initial socio-behavioural deviations detectable by age 4 years),[1] child and adolescent mental health services are only marginally involved in psychotic risk detection, which remains substantially delegated to adult psychiatric services.

We propose that child and adolescent mental health services should be the primary setting for a multi-stage screening process for the timely detection of individuals at increased developmental risk for psychosis. Furthermore, as the risk of schizophrenia increases substantially within the first 5 years after the onset of any child and adolescent psychiatric disorder,[3] awareness of prepubertal developmental impairments associated with genetic liability[1] to schizophrenia could be important for clinical decision-making and early prognostic stratification.

Although early identification of children and adolescents at putative high risk for developing psychosis requires ad-hoc criteria, a heightened attention to those clinical features that could represent neurodevelopmental signs of psychosis proneness is essential.[4] This identification is achievable by integrating empirical findings from child, adolescent, and adult mental health within an overarching developmental framework. In this sense, we consider a neurodevelopmentally informed revision of the clinical staging model of psychosis[5] (eg, including prepubertal developmental impairments associated with genetic liability[1] and early atypical developmental impairments)[2,4] as the way forward. A developmentally oriented staging of early and broadly defined psychosis risk would catalyse a more comprehensive longitudinal understanding of the childhood neurobehavioural antecedents of psychosis, with positive effects for early differential diagnosis, etiopathogenetic research, and individualised care.

We declare no competing interests.

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Authors' reply

We thank Michele Poletti and colleagues for their interest in our recent population study[1] in which we investigated the association between schizophrenia risk alleles and neurodevelopmental outcomes in childhood. We agree that child and adolescent mental health services are a good place to detect individuals at increased risk for schizophrenia. We also agree that a developmentally informed framework for risk