

Correspondence

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Schizophrenia and anxiety: yes, they are relatives not just neighbours

We are thrilled to see that the study of anxiety in people with psychotic spectrum disorders is gaining recognition. The paper published by Dr Hall provides a good insight about common grounds between the two disorders and highlights the advantages of studying anxiety in those with psychotic disorders.¹ One of the problems of studying anxiety is that it is often overshadowed when the diagnosis of schizophrenia is given to a patient. However, anxiety is often under-diagnosed and untreated regardless of the primary diagnosis, which represents a significant economic burden. One of the possible hypothesis for this diagnostic delay is the fact that current anxiety nosology is characterised by many subjective cognitive (anticipatory anxiety), behavioural (avoidance behaviour) and psychological (worry, fear) aspects of anxiety, but the often-comorbid somatic or physical conditions are neglected.

Our group found that anxiety disorders are indeed very common among patients with schizophrenia, with estimated prevalences of 30%.² We also found that those with comorbid anxiety disorders were more likely to display positive symptoms and greater fears, suggesting that those patients with comorbid anxiety had a specific profile of symptoms.³ Interestingly, patients with this phenotype experienced greater joint hypermobility syndrome, which has been associated with anxiety in clinical and non-clinical populations. Our group initially described this associated in 1988 in a letter to the *Lancet*⁴ and this field has expanded significantly during past years. This phenotype is rich in somatic and bodily complaints that seems to be mediated by an autonomic nervous system dysfunction, and many of these patients experience stress-related illnesses such as chronic pain, irritable bowel syndrome or dysautonomia. Other hypothesised underlying mechanisms behind this association include genetic risks, atypical body perception profiles, increased interoception and exteroception, and decreased proprioception.⁵ Neuroimaging studies showed that joint hypermobility is associated with the expression of anxiety through autonomic hyper-reactivity linked to aberrant engagement of the amygdala and insula.⁶

Taking into account that heightened anxiety may be important in both the development of psychosis and psychosis relapses as described by Dr Hall, it is imperative to ensure a proper anxiety assessment. Joint hypermobility syndrome can be a helpful marker for identifying somatic and bodily complaints, and it is particular significant in schizophrenia because it is associated with greater fears and anxiety severity and higher frequency of positive

symptoms. In addition, this phenotype may open opportunities for new therapeutic interventions that should be further studied in subsequent studies.

References

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Author reply

I thank Drs Bulbena-Cabre & Bulbena for their comments on my editorial ‘Schizophrenia – an anxiety disorder?’¹ In it they raise a number of interesting points.

The first is that there is likely a subgroup of patients with schizophrenia in whom high levels of anxiety are a particularly prominent feature. This is important as these individuals are those who are most likely to benefit from interventions to decrease anxiety as a potential secondary prevention measure for psychosis. Future possible trials aimed at testing whether anti-anxiety measures in psychosis targeted at decreasing anxiety could be effective would benefit from stratifying patients according to their pre-existing anxiety symptoms.

The second point they raise concerns the prevalence of anxiety and psychosis in joint hypermobility syndrome. They have themselves previously reviewed the literature showing an association between joint hypermobility syndrome and a range of psychiatric presentations including anxiety, psychosis and autism.² Indeed, this association is one that many clinicians have noted in their own practice. Although the exact mechanism underlying this association is not known, it is notable that connective tissue proteins (mutations in which cause joint hypermobility syndrome) are present in the brain.^{3,4} Furthermore, many are localised to the region of synapses, which are a key site of mutations related to psychiatric disorders.⁴ Although genes encoding connective tissue proteins have not, as a class, been identified as associated with risk for disorders such as schizophrenia and autism, the present results suggest that they may alter synaptic function in susceptible populations and increase risk for disease. This is clearly an interesting area worthy of further investigation.

Overall the letter of Drs Bulbena-Cabre & Bulbena reinforces the point that anxiety contributes to pathology in patients with schizophrenia and related disorders, and may represent a treatment target in appropriate subgroups.