BJPsych | The British Journal of Psychiatry (2018) 213, 498–501. doi: 10.1192/bjp.2018.127

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Edited by Kiriakos Xenitidis and Colin Campbell

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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 underdiagnosed 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.

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doi:10.1192/bjp.2018.126

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.

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doi:10.1192/bjp.2018.127

Personality disorder and suicide

The discussion about the association between personality disorder and suicide is important.[1] First, I want to present some information on the risk of suicide in patients with personality disorder with special reference to the subtype of personality disorder.

Coleman *et al.* conducted a cross-sectional study to understand the relationship between narcissistic personality disorder (NPD) and suicidal behaviour in 657 patients with mood disorders.[2] The adjusted odds ratio for suicide attempt in the participants with NPD was 0.41 (95% CI 0.19–0.88). In addition, being male, substance use disorder, aggression and hostility also presented a significant increase in odds ratio for suicide attempt. In contrast, the adjusted odds ratio for suicide attempt in those participants with borderline personality disorder (BPD) was 4.96 (95% CI 3.25–7.58). NPD in patients with mood disorders showed a protective effect for suicidal behaviour, which was different from that in participants with BPD. Sher reports that patients with NPD have a risk of suicide behaviour,[3] and I recommend stratified analysis by subtype of personality disorder for risk assessment of suicide.

Second, there is a difference between suicidal ideation and attempt.[4] In addition, mood disorder is a risk factor for suicidal behaviour.[5] Wang *et al.* conducted a prospective study to investigate the effect of stressful life events on subsequent suicidal behaviour in patients with major depressive disorder.[6] They clarified that financial stress was a strong predictor for suicide attempts after adjusting for sociodemographic variables, anxiety, substance use and personality disorder. As Liu also pointed out, comprehensive analysis is recommended for risk assessment of suicide.

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doi:10.1192/bjp.2018.133

A letter to Jim Crabb *et al*

Congratulations on your article,[1] which I have been thinking about since reading it some weeks ago. I fully agree with your aims (attracting doctors into the specialty) and many of your arguments, but also have some reservations, which I would like to share. I am also wondering what kind of reactions you have had from others, and whether you have heard anything similar to the following observations.

In this age of internet 'click-bait', it seems, when advertisements are designed 'to create an anxiety relieved by a purchase', people are often naturally suspicious of advertising, branding and marketing. It is seldom fully truthful, misleading by presenting opinion as facts, by being selective of data, and by concealing flaws and inadequacies. This is the hype, spin or propaganda designed to sell products and maximise financial profit, and arguably therefore unsuitable for persuading medical students and young doctors to think about psychiatry as a long-term career path.

In the cold light of day, for example, particularly in today's evidence-based, politically governed, underfunded and overstretched National Health Service, people might wonder how truthful are the statements comprising the mantra you propose for 'brand psychiatry'. The experience of a patient, or family members, might not be exactly as you describe. The rational, materialist, left-brain dominated 'scientific' approach – which tends to search out symptoms and diagnoses, and then to provide physical treatments (medication) and brief impersonal psychotherapies (such as cognitive–behavioural therapy), rather than seeking healing for the whole person, body, mind and soul – still prevails over a more holistic, intuitive, poetic, right-brain dependent, person-oriented approach, do you not think?

I am sure, however, that you are on the right track. It is a genuine ideal to be pursued, 'To understand the connection between the mind, the body and the soul', and 'To have the rare ability to treat the person, not the problem'. But might not other doctors, particularly general practitioners, want to make similar claims?

An approach that might work well could be to stress the equal values of biological, psychological, social *and* spiritual aspects of mental healthcare (see for example, regarding the latter Culliford[2,3] and Cook *et al*[4]). In other words, giving the message that there is a welcome in the specialty for people with a wide range of knowledge, skills and experience, enabling each to grow – through training and practice – in those areas and attributes perhaps previously less well developed.

There is an important place for those whose abilities and preferences lie within the biological domain, still the 'comfort-zone' for many psychiatrists; but the aim, I suggest, is both to encourage such folk to broaden their horizons out of their familiar orbit, and to encourage new people to enter the specialty whose inclinations are more towards (to paraphrase the mantra) 'feeling with one's mind' and 'thinking with one's soul'. Arguably, this means fostering awareness and familiarity with the spiritual dimension of mental healthcare. Some may be surprised to know that this valuable – and hitherto neglected – aspect of our discipline can be taught.[5]

An axiom for this new psychiatry would be that everyone is on some kind of self-improvement pathway towards a maturity that involves personal integration, with continuing growth in terms of wisdom, compassion and love, derived from a sense of belonging not to any faction but to the entirety of humanity, similarly connected seamlessly to nature, to the dynamic structure and energy of the cosmos that underpin all the natural laws known to science. To become a psychiatrist would thus offer an unparalleled opportunity for making progress along this (I would call it 'spiritual') path.

https://doi.org/10.1192/bjp.2018.127 Published online by Cambridge University Press