BJPsych | The British Journal of Psychiatry (2024)
225, 341–342. doi: 10.1192/bjp.2024.74

Commentary

Towards a unified theory of the aetiology of schizophrenia†: commentary, Kumari

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Keywords
Schizophrenia; heterogeneity; neuroimaging; biomarkers; hippocampus.

Response

Schizophrenia is a complex illness with marked heterogeneity in genetics, environmental risk factors, age at onset, symptoms, neurocognitive profiles, illness progression, treatment outcomes and long-term prognosis. This heterogeneity, which undoubtably has implications for our conceptual understanding of the 'schizophrenia' syndrome, as well as for developing effective prevention and treatment approaches, has motivated 'big data' studies (e.g.[1,2]) to identify patient groups with distinct neurobiological profiles. Recently, Jiang et al[2] employed a pioneering approach, combining phenotypic heterogeneity and illness stage, to identify neuroimaging biomarkers of schizophrenia. Based on the findings of this research, in their editorial in the *BJPsych* Jiang, Chang & Feng propose two neurophysiological subtypes in schizophrenia, marked by different brain regions of initial grey matter loss (for subtype 1, in Broca's area; for subtype 2, in the hippocampus). Their seemingly uncomplicated yet potentially game-changing model deserves further study taking population-level and individual patient characteristics into account.

The model, in its current form, appears to be based mainly on the findings from a sample of predominantly Asian/Han Chinese patients and therefore needs to be confirmed in other populations. It may or may not be fully applicable, like some genetic findings,[3] in certain populations. Concerning patient characteristics, in addition to the positive and negative symptom profiles, illness stage and treatment outcomes that were considered by Jiang and colleagues in their innovative work,[2] prodromal functioning, duration of untreated psychosis and age at illness onset also need to be carefully considered in further testing of this model, given previous data linking these factors to patterns of brain alteration and/or treatment outcomes. Another important factor to consider in this context is the presence (or absence) of environmental stress and trauma and, where relevant, the age at which individual patients might have been exposed to stress or trauma, given possible differences in developmental trajectories of the brain areas[4,5] implicated in the two schizophrenia subtypes, as well as their differential sensitivity to early environmental stressors such as childhood abuse.[6] It would be very useful to know, both from prevention and intervention perspectives, why some people with schizophrenia may fall under 'subtype 1' or 'subtype 2'. Are there distinct genetic or environmental risk factors at play and, if so, how?

If the model does survive rigorous empirical scrutiny, to maximise its utility in the context of personalised patient care, especially where routine brain scanning of people with schizophrenia is not a real option, it would be worthwhile to establish any alterations or deficits in 'specific' cognitive processes (for example, in language production and comprehension, the primary functions of Broca's area; or in forming and retrieving memories, where the hippocampus plays a key role) which might be present over and above any generalised cognitive impairment in the two schizophrenia subtypes. There will also be a strong case for looking into how to precisely map existing or new animal or experimental models of psychosis onto these two subtypes for a more targeted drug development, the development of other (non-drug) therapy approaches and identification of points of intervention for optimal outcomes.

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First received 9 Mar 2024, accepted 13 Mar 2024

Data availability

Data availability is not applicable to this article as no new data were created or analysed in this work.

Funding

This work received no specific grant from any funding agency, commercial or not-for-profit sectors.

Declaration of interest

None.

References

1 Xiao Y, Liao W, Long Z, Tao B, Zhao Q, Luo C, et al. Subtyping schizophrenia patients based on patterns of structural brain alterations. *Schizo Bull* 2022; **48**: 241–50.

2 Jiang Y, Wang J, Zhou E, Palaniyappan L, Luo C, Ji G, et al. Neuroimaging biomarkers define neurophysiological subtypes with distinct trajectories in schizophrenia. *Nature Mental Health* 2023; **1**(3): 186–99.

3 Prasad S, Bhatia T, Kukshal P, Nimgaonkar VL, Deshpande SN, Thelma BK. Attempts to replicate genetic associations with schizophrenia in a cohort from north India. *NPJ Schizophr* 2017; **3**(1): 28.

† See editorial, pp. 299–301, this issue.

4 Amunts K, Schleicher A, Ditterich A, Zilles K. Broca's region: cytoarchitectonic asymmetry and developmental changes. *J Comp Neurol* 2003; **465**: 72–89.

5 Lee JK, Johnson EG, Ghetti S. Hippocampal development: structure, function and implications. In *The Hippocampus from Cells to Systems: Structure, Connectivity, and Functional Contributions to Memory and Flexible Cognition* (eds DE Hannula, MC Duff): 141–66. Springer International Publishing AG, 2017.

6 Teicher MH, Samson JA. Annual research review: enduring neurobiological effects of childhood abuse and neglect. *J Child Psychol Psychiatry* 2016; **57**: 241–66.

Poem

Walking grief

Temitope Ogundare

You learned of walking pneumonia
In medical school,
An indolent invasion of the lungs,
A kind of slow death.

And now, you acquaint myself with
Walking grief:
A slow-cooked, simmering sorrow,
Reluctant to claim you swiftly.

It makes you gasp for air,
Choke on a sob, and ache
With each breath,
But it won't leave you prostrate.

You wear a mask of normalcy,
Smile, sleep, eat, and appear healthy;
Its heat meticulously roasts
Your heart, layer by singed layer.

Your heart throbs achingly,
But not overwhelmingly so –
this strain of grief is not virulent.

At times, you may forget
That your body is a battleground,
Until you wake, crying inconsolably,

Or find yourself sobbing
Midway through an America's Got Talent
YouTube video,
Tears cascading like confetti
On the golden-buzzered contestant.

Your tears lack joy,
Unlike the man's tears
Upon the realization of his dreams,
Urged by the crowd's chant.

Your tears carry death –
Your father's.
Yours was not a close bond,
But his absence opened your body
To invasion by a different strain of grief;

Your body convalescing from mourning
Your mother's passing – a near-fatal invasion
That left you incapacitated, fighting for survival.

This grief is indolent, slow-growing,
Unhurried in its quest to annihilate you.

The British Journal of Psychiatry (2024) 225, 342. doi: 10.1192/bjp.2024.28

https://doi.org/10.1192/bjp.2024.74 Published online by Cambridge University Press