Brazilian Journal of Psychiatry
bjp
Revista Brasileira de Psiquiatria

Braz J Psychiatry. 2025;47:e20254121
Brazilian Psychiatric Association

CC BY

LETTER TO THE EDITORS

It is unlikely that major depression severity correlates with white matter lesion volume

Braz J Psychiatry. 2025;47:e20254121
doi:10.47626/1516-4446-2025-4121

CC BY

We read with interest the article by Baudouin et al. describing a cross-sectional ancillary study on the association between major depressive disorder (MDD) and periventricular and deep white matter lesions (WML) in 69 patients and >30 controls.[1] Depression severity was assessed using the Hamilton Depression Rating Scale and WML volume was calculated by summing the number of 1 mm^3 voxels after MRI images were registered to 1 mm^3 Montreal Neurological Institute space using the Advanced Normalization Tools algorithm.[1] No significant association was found between WML volume and MDD severity, but it was concluded that WML volume may contribute to more severe depression later in life.[1] The study is noteworthy, but several points should be discussed.

The first problem is that alternative causes of depression have not been adequately ruled out.[1] MDD could be due to life events, stressful events, a personality with low self-esteem or excessive self-criticism, a positive family history for depression, pregnancy and childbirth, menopause, loneliness, alcohol/drug abuse, or serious illness.[2] Different causes of depression may correlate to varying degrees with WML volume.

The second point is that, according to the methodology, the 69 patients were compared with 32 healthy controls in terms of age and sex.[1] Since the number of MDD patients and the number of healthy controls were very unequal, how can these two groups be matched in terms of age and sex?

The third point is that medical history in addition to MDD was not or only partially included in the analysis. Of particular interest is whether the individual medical history was positive for diseases associated with WML in addition to ischemic heart disease, arterial hypertension, diabetes, hyperlipidemia or tobacco use, such as cerebrovascular disease, infectious and immunologic encephalitis, dementia, traumatic brain injury, rheumatologic disease, malignancies, autoimmune disease, and various hereditary diseases.

The fourth point is that there is a discrepancy between the number of healthy controls included in the methods section and the results section.[1] According to the abstract and the methods section, 32 healthy controls were included, but according to the results, only 31 healthy controls were included. This discrepancy should be corrected.

The fifth point is that the study did not differentiate between the two main subgroups of WML, periventricular and deep WML. In order to assess whether one or the other subtype affects depression scores more than the other subtype, it would have been essential to analyze these two subgroups separately.

To summarize, this interesting study has limitations that call the results and their interpretation into question. Addressing these limitations could strengthen the conclusions and reinforce the study's message. All unanswered questions should be clarified to prevent readers from uncritically accepting the study's conclusions. Before it can be ruled out that MDD is associated with WML volume, studies with an appropriate design should be conducted and the various causes of MDD should be considered.

Josef **Finsterer**,[1] Joao **Gama Marques**[2,3]
[1]*Neurology Department, Neurology & Neurophysiology Center, Vienna, Austria.* [2]*Consulta de Esquizofrenia Resistente, Hospital Júlio de Matos, Unidade Local de Saúde de São José, Centro Clínico Académico de Lisboa, Lisboa, Portugal.* [3]*Clínica Universitária de Psiquiatria e Psicologia Médica, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisboa, Portugal.*

Submitted Jan 13 2025, accepted Feb 06 2025.

Disclosure

The authors report no conflicts of interest.

Data availability statement

All data are available from the corresponding author.

Author contributions

JF: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing.
JGM: Investigation, Writing – review & editing
Both authors have read and approved of the final version to be published.

How to cite this article: Finsterer J, Gama Marques J. It is unlikely that major depression severity correlates with white matter lesion volume. Braz J Psychiatry. 2025;47:e20254121. http://doi.org/10.47626/1516-4446-2025-4121

References

1 Baudouin E, Corruble E, Gori P, Bloch I, Becquemont L, Duron E, et al. White matter hyperintensities and their role in major depressive episodes: A cross-sectional study in adults under 65. Braz J Psychiatry. 2024 Dec 28. doi: 10.47626/1516-4446-2024-3921. Epub ahead of print.
2 National Research Council (US) and Institute of Medicine (US) Committee on Depression, Parenting Practices, and the Healthy Development of Children [Internet]. The Etiology of Depression. In: England MJ, Sim LJ, editors. Depression in parents, parenting, and children: Opportunities to improve identification, treatment, and prevention. Washington, DC: National Academies Press (US); 2009 [cited 2025 Feb 24]. https://www.ncbi.nlm.nih.gov/books/NBK215119/