

# From Brain to Insomnia: Can Neurotrophic Factors Unlock the Sleep Puzzle After Stroke? [Letter]

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## Dear editor

We have read the article titled

The Role of Mature Brain-Derived Neurotrophic Factor and Its Precursor in Predicting Early-Onset Insomnia in Stroke Patients Experiencing Early Neurological Deterioration<sup>1</sup>

published in your esteemed journal and highly appreciate the research work presented. The authors delved into the relationship between mature brain-derived neurotrophic factor (mBDNF) and its precursor (proBDNF) and early-onset insomnia (EOI) accompanying early neurological deterioration (END) in stroke patients, and proposed the mBDNF/proBDNF ratio as a potential biomarker for predicting EOI. This study has important clinical value and provides new insights into the biological mechanisms of insomnia after stroke. We highly appreciate the innovation and unique perspective presented in this study. Our intention is to further enhance the rigor of this already excellent piece of research, ensuring its robustness and contribution to the field.

First, patients with acute ischemic stroke (AIS) may exhibit symptoms of deepening impairment of consciousness, such as drowsiness and coma, when early neurological deterioration (END) occurs, especially when critical areas such as the brainstem and thalamus are damaged. Sleep at this time may not be a typical symptom of insomnia, but is more likely to be closely related to the acute pathophysiologic state and neurologic impairment.<sup>2</sup> In addition, the Pittsburgh Sleep Quality Index (PSQI) is a commonly used self-report tool, but in patients with early neurologic deterioration, this may affect the accuracy of their questionnaire completion. In this case, some more objective sleep monitoring tools may be more appropriate for assessing the sleep status of such patients.<sup>3</sup>

Second, in this study, the authors mentioned that the mBDNF/proBDNF ratio has better predictive ability in predicting EOI. It is well known that the ROC curve and AUC (area under the curve) are important tools for assessing the predictive ability of biomarkers. However, reporting AUC values alone does not adequately account for significant differences between the different metrics. Without the DeLong test, we could not determine whether the AUC differences between the three biomarkers were statistically significant.<sup>4</sup> This may affect the reliability and accuracy of the results.

Third, stroke patients are often associated with a variety of co-morbidities, such as depressive states, anxiety states, hypertension and diabetes. These common co-morbidities may also interfere with the correlation between EOI and neurotrophic factors by affecting levels of neurotrophic factors through mood regulation, altering neurologic function, or triggering other metabolic changes.<sup>5</sup> The authors did not perform subgroup analyses of these co-morbid states, which limits the study's ability to control for potential confounding factors.

In conclusion, we appreciate the authors' insight into the role of mBDNF and its precursor proBDNF in predicting early-onset insomnia. Future studies can reduce the influence of patient status on results and improve the accuracy of data by using more objective sleep monitoring tools. In addition, performing subgroup analyses of co-morbid states can help control for potential confounders, thereby improving the reliability of study results. The DeLong test can help more accurately assess the predictive power of biomarkers. As psychiatrists, this study provides us with valuable biomarkers to

help identify early onset insomnia after stroke and optimize treatment. Future treatment options may consider combining traditional treatments such as medications and cognitive behavioral therapy (CBT-I) with potential biomarkers to develop a more integrated treatment strategy.

## Data Sharing Statement

No new data was generated for this communication.

## Author Contributions

Hongrun Pan: Methodology, Formal analysis, Writing - Original Draft; Suqiong Yang and Peikun Hong: Conceptualization, Methodology, Supervision, Writing - Review & Editing. All authors agreed on the journal to which the article will be submitted, reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage and agreed to take responsibility and be accountable for the contents of the article.

## Funding

No funding obtained for this communication.

## Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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