Neuropsychiatric Disease and Treatment

Dovepress
Taylor & Francis Group

Open Access Full Text Article

LETTER

Inconsistent Cognitive Assessment Criteria in PD-MCI Research [Letter]

Jiawen Wang

Hanzhong People's Hospital, Hanzhong City, Shaanxi Province, 723000, People's Republic of China

Correspondence: Jiawen Wang, Hanzhong People's Hospital, 251 North Tuanjie Street, Hantai District, Hanzhong City, Shaanxi Province, 723000, People's Republic of China, Email 393632929@qq.com

Dear Editor

I read Yu et al's article "The Correlation Between RIN3 Gene Methylation and Cognitive Impairment in Parkinson's Disease" in Neuropsychiatric Disease and Treatment.[1] While their investigation into epigenetic mechanisms in Parkinson's disease is valuable, significant methodological concerns affect the reliability of their findings. I believe these results require cautious interpretation pending further methodological refinements.

The cognitive assessment criteria employed in the study present significant methodological limitations. First, the MMSE cut-off values used (>17 for illiterates, >20 for primary school education, >24 for secondary school and above) lack referenced justification and differ substantially from the systematically validated thresholds for Parkinson's disease patients established by Ji In Kim et al (MMSE < 19 for illiterate PD-MCI patients; MMSE < 29 for highly educated PD-MCI patients).[2] This discrepancy suggests that potentially inappropriate cut-off values, unvalidated in Parkinson's disease populations, were applied, likely resulting in inaccurate patient classification. Since patient stratification forms the foundation of the entire study, this methodological flaw directly compromises the reliability of the RIN3 gene methylation differential analysis and the validity of the conclusions. I recommend that researchers reanalyze their data using cognitive assessment criteria specifically validated in Parkinson's disease populations, adopting the multi-domain cognitive assessment and functional scale integration strategies.[3,4] Future research should strictly adopt disease-specific, education-adjusted cognitive assessment standards with clear rationale for their selection.

Additionally, the MoCA cut-off standard uniformly applied (<26 to define PD-MCI) represents another critical methodological flaw, as it fails to account for the significant impact of educational differences on cognitive assessment. Notably, in the authors' own cited references, Ji In Kim et al explicitly recommend education-adjusted standards (illiterate < 13, 0.5–3 years education <21, 4–6 years education <23, 7–9 years education <25, >10 years education <26), which the researchers did not follow.[2] This uniform approach likely resulted in the misclassification of many patients with lower educational levels as having PD-MCI, creating substantial false-positive bias. This directly affects the accuracy and reliability of the RIN3 gene methylation analysis results, rendering the study conclusions scientifically unsupported. I recommend that the authors thoroughly review their cited literature and strictly apply the cognitive assessment cut-off values recommended in these references, combining multi-domain cognitive assessment with education-adjusted MoCA thresholds for data reanalysis to establish a more accurate association pattern between PD-MCI and RIN3 gene methylation.

The study also overlooks the influence of nutrition and environmental exposures on DNA methylation. Yang et al (2024) demonstrated that insufficient folate supplementation reduces genome-wide methylation levels ($\beta = -0.48$, $P = 0.018$).[5] When assessing RIN3 methylation, uncontrolled dietary factors may introduce measurement bias. PD patients with cognitive impairment may experience dietary changes affecting methylation patterns, potentially serving as mediating variables in the RIN3-PD-MCI relationship. Future studies should include dietary information and food-related exposures as covariates to improve research reliability.

I believe these recommendations will substantially enhance future research in this important field.

Received: 11 March 2025
Accepted: 13 March 2025
Published: 19 March 2025

Funding

There is no funding to report.

Disclosure

The author reports no conflicts of interest in this communication.

References

1. Yu X, Zhu K, Wang T, et al. The correlation between RIN3 gene methylation and cognitive impairment in Parkinson's disease. *Neuropsychiatr Dis Treat*. 2025;21:511–524. doi:10.2147/NDT.S509510
2. Kim JI, Sunwoo MK, Sohn YH, Lee PH, Hong JY. The MMSE and MoCA for screening cognitive impairment in less educated patients with Parkinson's disease. *J Move Disord*. 2016;9(3):152–159. doi:10.14802/jmd.16020
3. Marinus J, Visser M, Verwey NA, et al. Assessment of cognition in Parkinson's disease. *Neurology*. 2003;61(9):1222–1228 doi:10.1212/01.wnl.0000091864.39702.1c.
4. Cao L, Kong W, Chan P, Zhang W, Morris M, Huang Y. Assessment tools for cognitive performance in Parkinson's disease and its genetic contributors. *Front Neurol*. 2024;15:1413187 doi:10.3389/fneur.2024.1413187.
5. Yang P, Wang X, Li H, et al. Maternal non-compliance with recommended folic acid supplement use alters global DNA methylation in cord blood of newborns: a cohort study. *Clin Nutr*. 2024;43(6):1191–1198. doi:10.1016/j.clnu.2024.04.007

https://doi.org/10.2147/NDT.S527716