



# Letter to Editor: Atrophy asymmetry in hippocampal subfields in patients with Alzheimer's disease and mild cognitive impairment

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Dear Editor

We thoroughly read with interest, the research article entitled “Atrophy asymmetry in hippocampal subfields in patients with Alzheimer's disease and mild cognitive impairment” (Jahanshahi et al. 2023). The authors investigated the volumes of hippocampal subfields, as well as the asymmetry index (AI) and laterality ( $\Delta RL$ ), in a sample of 20 healthy controls (HC), 20 mild cognitive impairment (MCI), and 20 Alzheimer's disease (AD) patients. Based on their findings, the authors suggest that the asymmetry index (AI) and laterality ( $\Delta RL$ ) of hippocampal subfields could serve as valuable biomarkers for both AD and MCI.

The conclusion drawn regarding laterality as a biomarker in AD and MCI is not supported due to contradictory findings in the laterality graphs. The observed patterns of laterality differ among various hippocampal subfields across the three groups. Additionally, the presence of several typographical errors is also present, such as inaccuracies in the formulae for AI and  $\Delta RL$ , the repeated mention of a significant difference between AD and HC instead of MCI, etc. The justification for selecting 20 random samples for each of the three study groups in a cross-sectional design is insufficient. In the methods section, the authors state that the age range for all study participants is 60–65 years, but in the discussion section, they provide a reason for the lack of significant differences in hippocampal subfield volumes between HC and MCI, suggesting that most patients

with cognitive impairment in this age range (50–60 years) may represent a subset of early MCI, which contradicts the earlier statement. The author mentioned FAQ in the legend for Table 1, but fails to explain it in the methods section. Moreover, if there are no significant differences in age and gender among HC, MCI and AD, the rationale for conducting an analysis of covariance (ANCOVA) with age and gender as covariates is unclear. Finally, the authors discussed the ‘progression’ of MCI and AD from HC, even though they employed a cross-sectional design. To address the research question regarding the ‘progression’ of MCI/AD, a prospective longitudinal study would have been more appropriate. The interpretation of the results appears to be misinterpreted and misleading.

The current state of the paper lacks information sufficient enough to support the author's conclusion that laterality ( $\Delta RL$ ) can serve as a valuable biomarker in AD and MCI. Therefore, we raise concerns regarding the study design and statistical analysis, which appear to be non-corroborative and not entirely suitable for drawing any definitive conclusions. The reported findings appear to exhibit limited reproducibility and generalizability, thereby inadequately supporting the study's overall conclusion.

## Declarations

**Conflict of interest** The authors declare that they have no financial or personal associations with individuals or organizations that could inappropriately influence their work.

## Reference

Jahanshahi AR, Naghdi Sadeh R, Khezerloo D (2023) Atrophy asymmetry in hippocampal subfields in patients with Alzheimer's disease and mild cognitive impairment. *Exp Brain Res* 241(2):495–504. <https://doi.org/10.1007/s00221-022-06543-z>

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