The effects of sleep-disordered breathing on neuroimaging biomarkers of Alzheimer's disease

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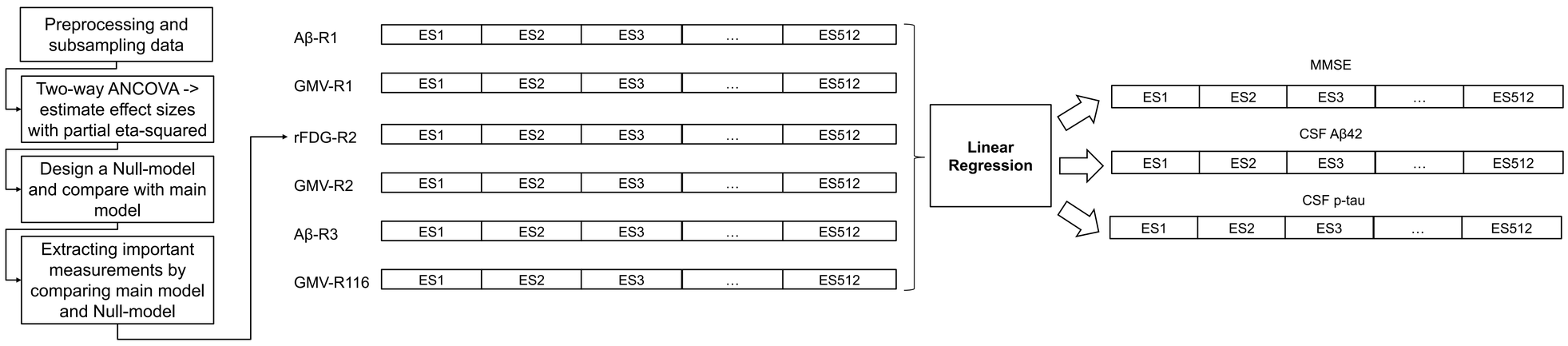
INTRODUCTION

- Unclear neurobiological mechanism of the association of SDB with AD progression [1, 2]: Higher cortical Aβ accumulation in middle-aged patients with severe SDB [3], decreased Cerebrospinal Fluid (CSF) Aβ, and increased CSF phosphorylated tau (p-tau) in healthy and MCI groups, particularly in subjects with SDB [4].
- SDB may interact with AD pathophysiology in preclinical stages to increase the risk of developing AD and finally exacerbate the development of AD-related cognitive impairments.
- Developing biomarkers, including amyloid-beta Positron Emission Tomography (Aβ-PET), 18F-Fluorodeoxyglucose PET (FDG-PET), and structural Magnetic Resonance Imaging (sMRI) [5], as well as Aβ and tau assessment in CSF, advanced our understanding of pathophysiological mechanisms, early detection, and monitoring of the progress and treatment of AD [6].

How Aβ-PET, FDG-PET, and sMRI biomarkers may help to understand the underlying neurobiological mechanisms of the association between SDB and AD progression.

METHODS

- **ADNI dataset:**
  CU, SDB- (n=265)
  CU, SDB+ (n=28)
  MCI, SDB- (n=276)
  MCI, SDB+ (n=58)
  AD, SDB- (=114)
  AD, SDB+ (n=16)
- **Subjects' cognitive status:**
  MMSE score
- **Sleep status:**
  self-reported
- **Brain measurements:**
  Aβ, rFDG, GMV
- **Covariates:**
  Age, sex, APOE Ɛ4, BMI



RESULTS

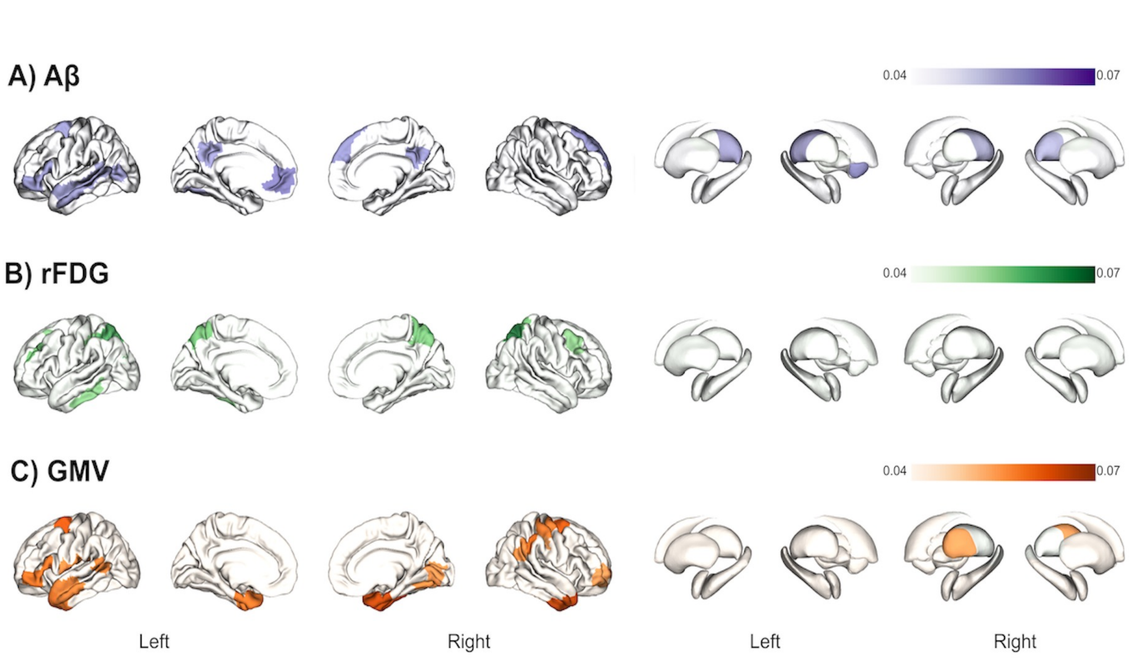


Fig. 1 Cognitive status-SDB interaction medium effect sizes on AD biomarkers. The brain regions that have medium effect sizes of the interaction between cognitive status (Alzheimer's disease, mild cognitive impairment and cognitively unimpaired) and SDB condition (with and without sleep-disordered breathing) for different biomarkers: A) amyloid-plaque burden (Aβ), B) regional fluorodeoxyglucose (rFDG), C) grey matter volume (GMV).

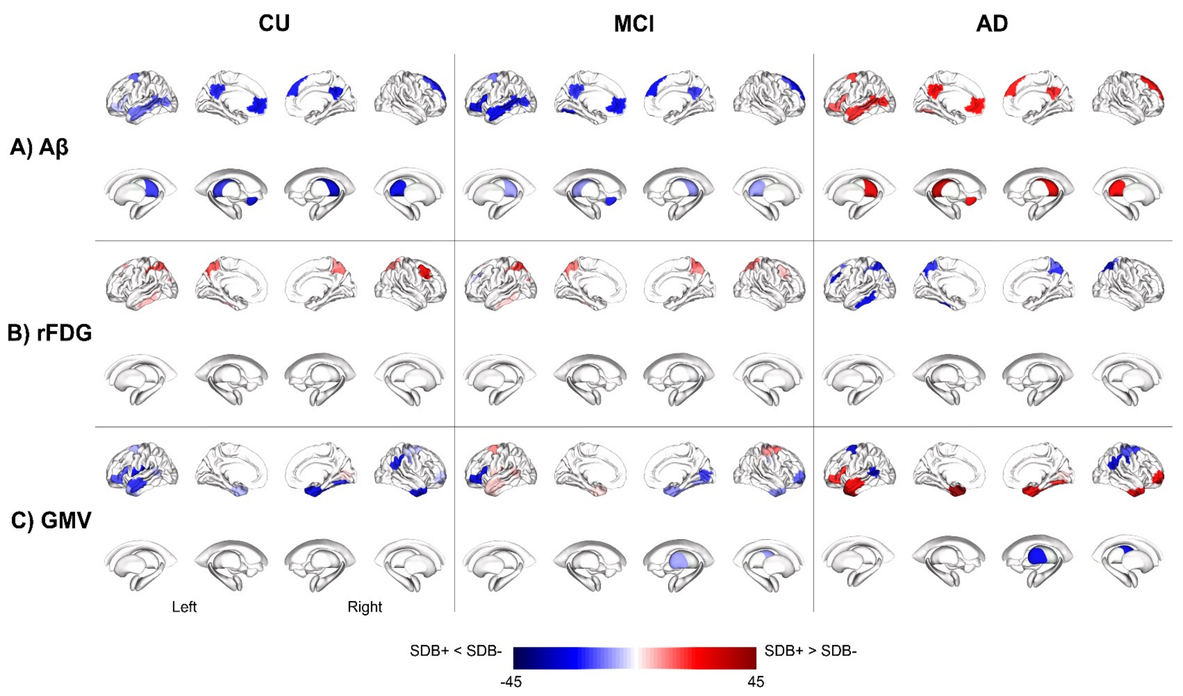


Fig. 2 AD biomarkers alteration in different groups. Differences in each biomarker value in different states of SDB condition (with and without SDB) through different disease groups (Alzheimer's disease, mild cognitive impairment, and cognitively unimpaired).

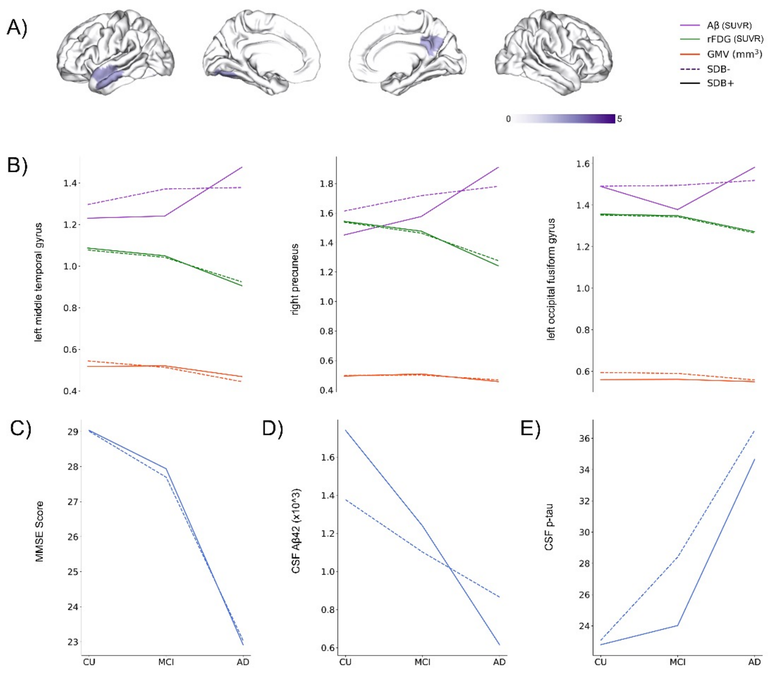


Fig. 3 Association between cognitive status-SDB interaction and cognitive score and pattern of biomarker's changes. A) Interaction between cognitive status and SDB condition has a medium effect size on highlighted regions. Furthermore, the highlighted regions are significantly associated with cognitive status-SDB interaction effect size on MMSE. B) changes pattern (Aβ, rFDG, and GMV) through different cognitive status in the highlighted regions from A. C) MMSE score changes through different cognitive status. D) CSF Aβ42 changes through different cognitive status. E) CSF p-tau changes through different cognitive status.

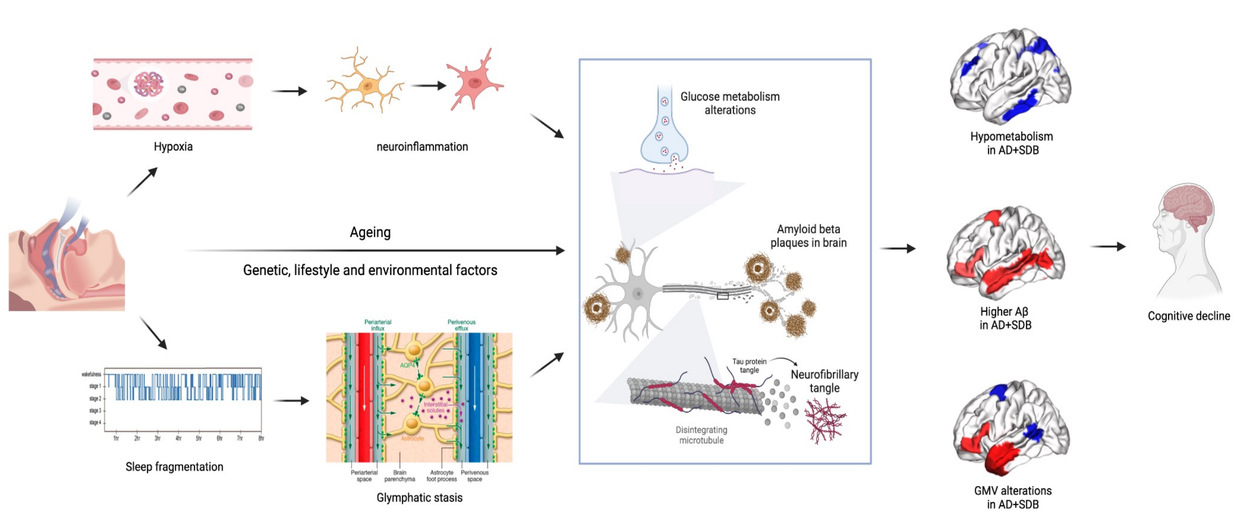


Fig. 4 The neurobiological interaction between SDB and AD. SDB induces hypoxia and sleep fragmentation, which leads to neuroinflammation and glymphatic stasis. These changes, together with genetic, environmental, and lifestyle factors, exacerbate aging effects on the accumulation of amyloid-beta, and insoluble tau protein, which results in brain metabolic and structural alterations and precedes AD pathology. * Glymphatic system illustration obtained from [8].

CONCLUSION

SDB moderately affects AD-related neuroimaging biomarkers (Aβ, rFDG, GMV). Individuals with SDB had lower Aβ levels in CU and MCI groups but higher in AD, suggesting SDB may accelerate AD-related changes. SDB was linked to hypermetabolism in CU/MCI and hypometabolism in AD. AD patients with SDB showed altered GMV. Aβ levels in specific brain regions are strongly related to cognitive scores. These findings suggest that SDB may hasten cognitive decline and susceptibility to AD pathology.

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