

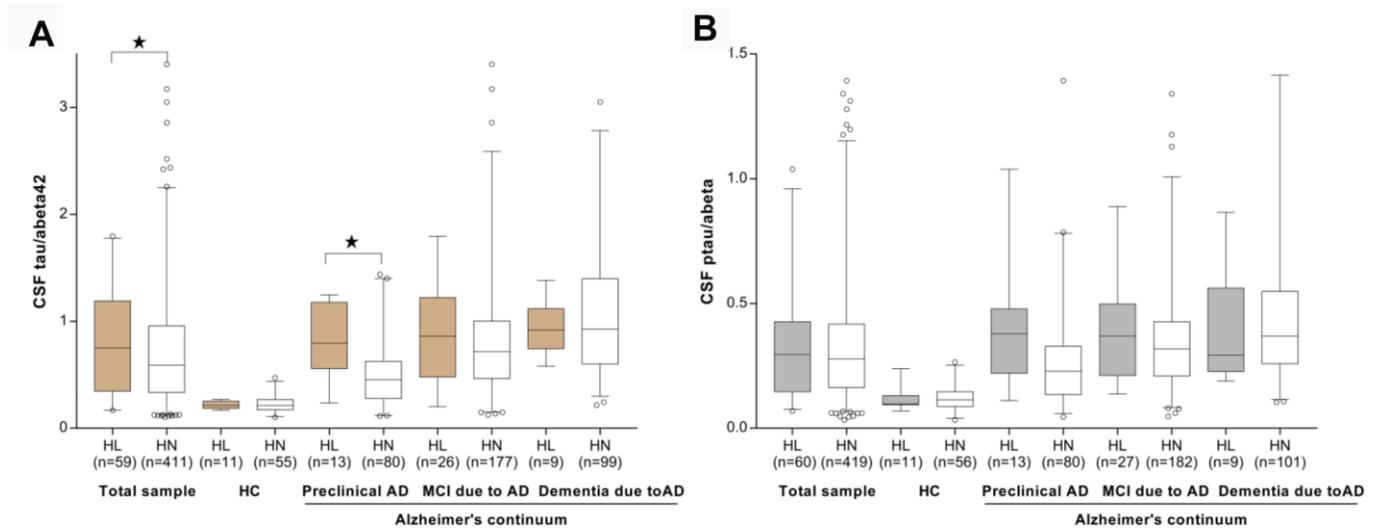
SUPPLEMENTARY MATERIALS

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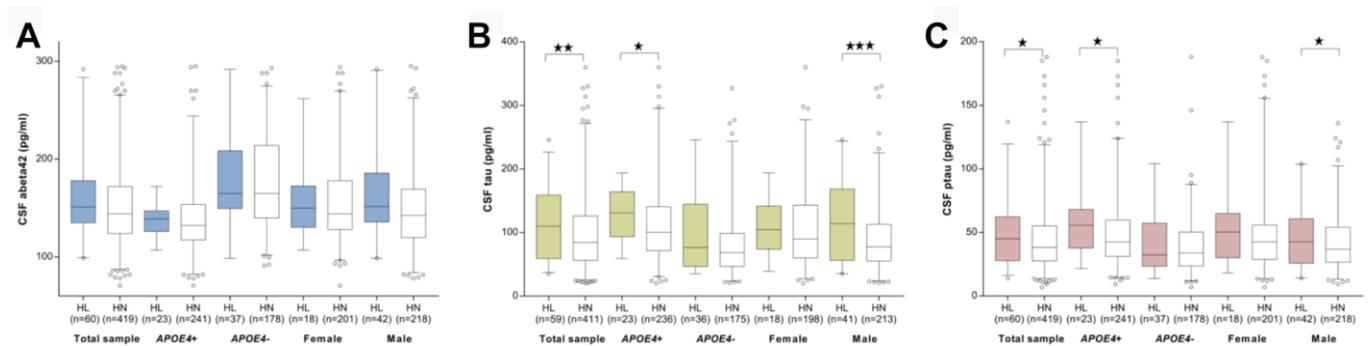
Supplementary Table 1. The records of ARHL definition in ADNI database (for CSF biomarker analyses, n = 60)

Supplementary Table 2. The records of ARHL definition in ADNI database (for hippocampus analyses, n = 131)

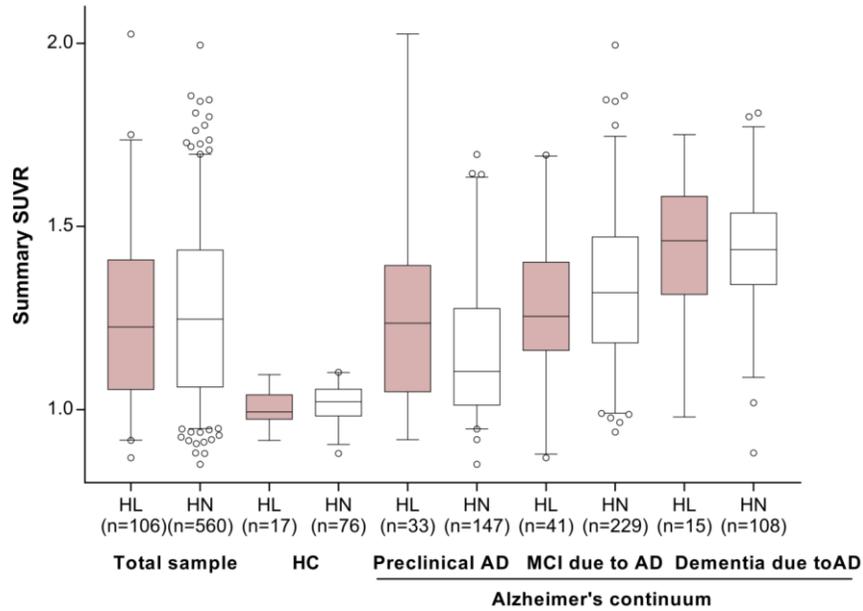
Supplementary Table 3. The records of ARHL definition in ADNI database (for other ROIs, n = 74)



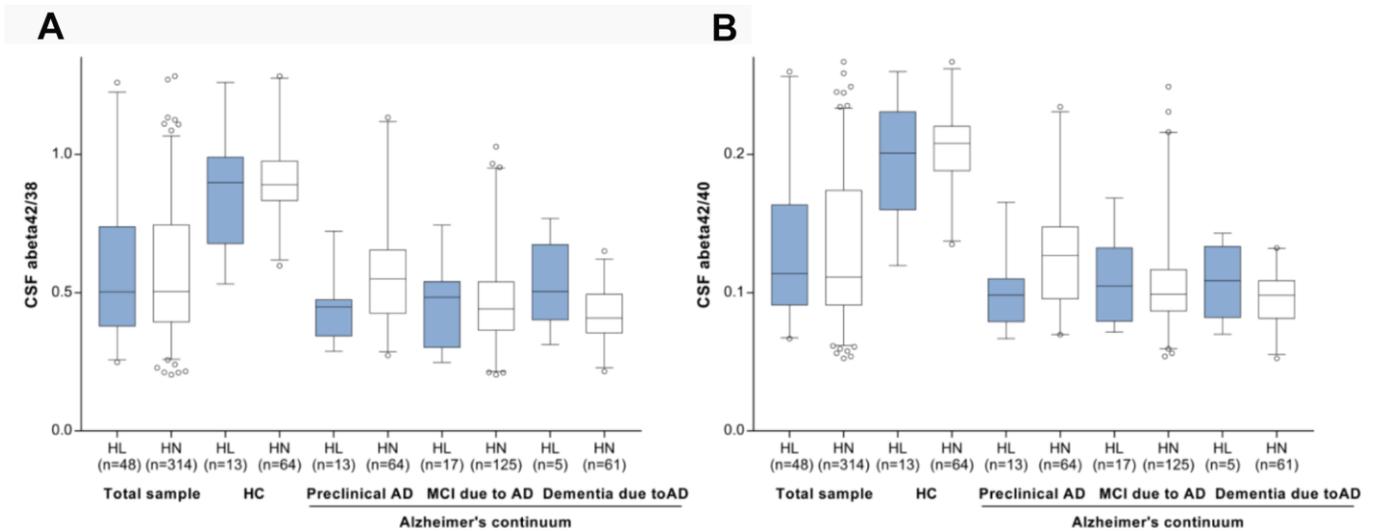
Supplementary Figure 1. The cross-sectional association of ARHL with CSF tau/Aβ₄₂ and ptau₁₈₁/Aβ₄₂ ratio. ARHL was associated with higher CSF total tau/Aβ₄₂ ratio (A), but not with ptau₁₈₁/Aβ₄₂ ratio (B).



Supplementary Figure 2. Subgroup analyses according to gender and APOE₄. Subgroup analyses showed no association of ARHL with CSF Aβ₄₂ (A) and that ARHL was associated with greater CSF tau (B) or ptau₁₈₁ (C) only among APOE₄ carrier (β = 0.24, p = 0.03 for tau; β = 0.25, p = 0.03 for ptau₁₈₁) and male (β = 0.30, p = 0.001 for tau; β = 0.19, p = 0.03 for ptau₁₈₁) group.



Supplementary Figure 3. The cross-sectional association of ARHL with brain amyloid deposition. No significant associations between ARHL and SUVR were found when adjusting for age, gender, education, *APOE4* status, AD continuum group, DM2, hypertension, hyperlipidemia, and BMI.



Supplementary Figure 4. The cross-sectional association of ARHL with CSF $\text{A}\beta_{42}/\text{A}\beta_{38}$ and $\text{A}\beta_{42}/\text{A}\beta_{40}$ ratio. No significant association was revealed with either $\text{A}\beta_{42}/\text{A}\beta_{38}$ (A) or $\text{A}\beta_{42}/\text{A}\beta_{40}$ ratio (B). In ADNI, CSF $\text{A}\beta_{1-42}$, $\text{A}\beta_{1-40}$, and $\text{A}\beta_{1-38}$ were measured by 2D-UPLC-tandem mass spectrometry. The overall performance of quality control is finely acceptable, with the coefficient of variation <15% (6.5-12.8% for $\text{A}\beta_{1-42}$, 2.2-7.0% for $\text{A}\beta_{1-40}$, and 5.7-8.0% for $\text{A}\beta_{1-38}$, respectively). Data was downloaded from ADNI. (HL = 48, HN = 314)