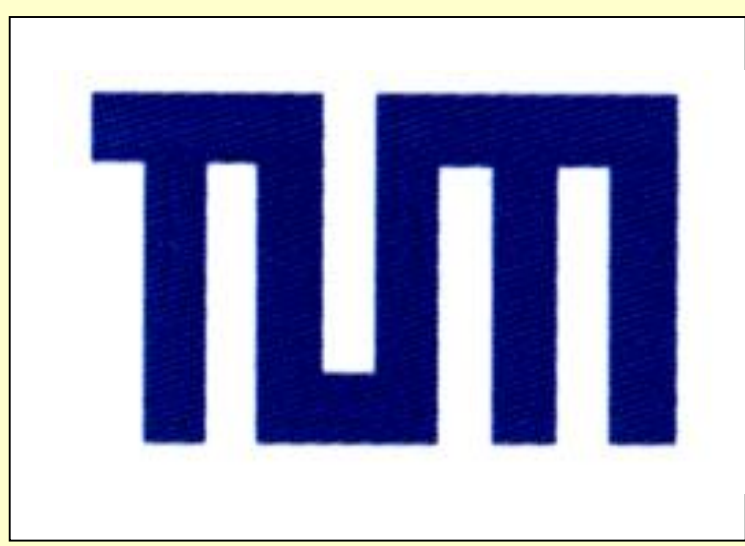




Nasal Secretions As A Non-invasive Biomarker Matrix For Alzheimer's Disease: A Feasibility Study

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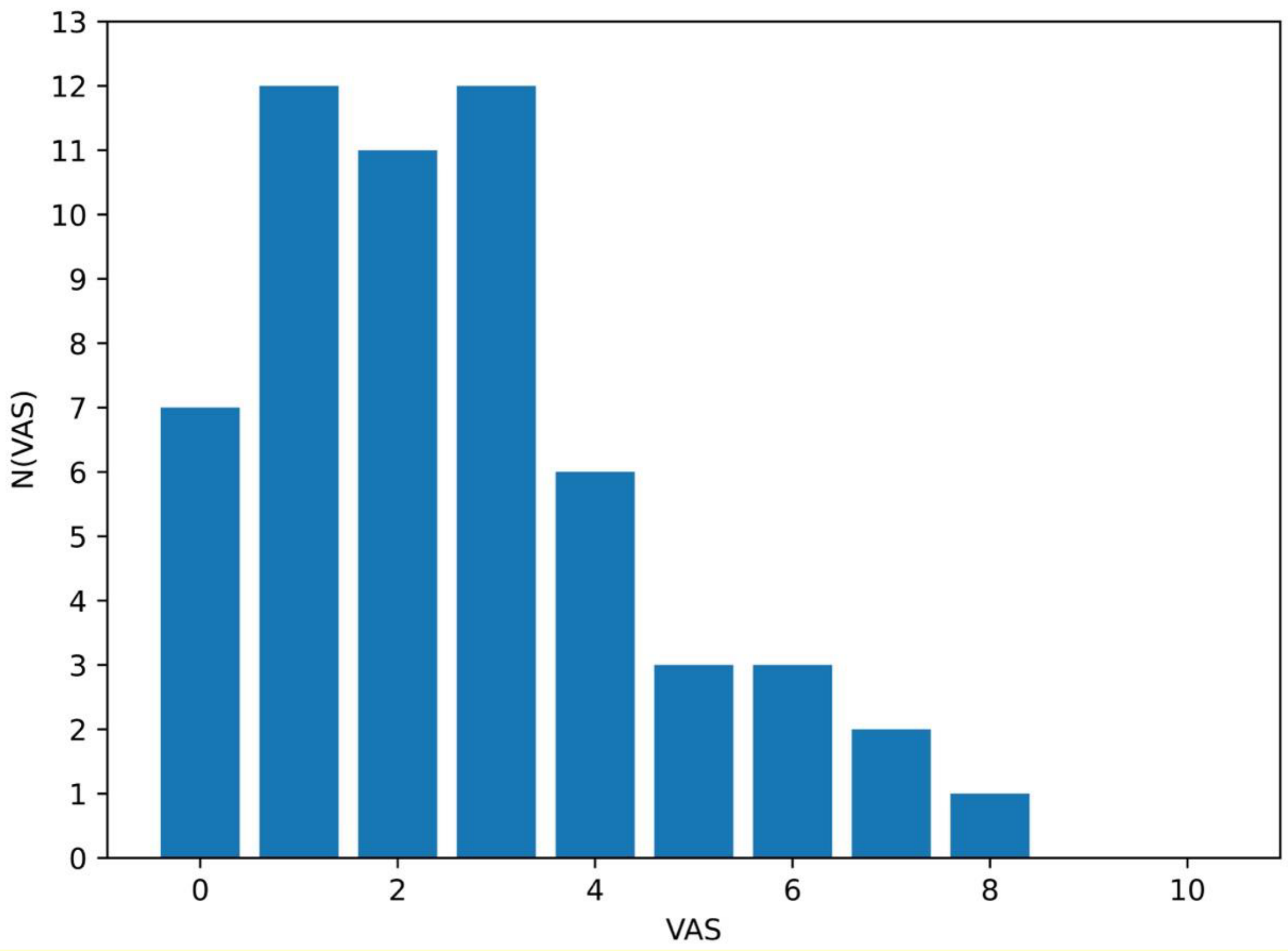
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Background

Emerging evidence demonstrates CSF drainage through the brain-nose interface (BNI), suggesting nasal secretions may provide non-invasive access to AD biomarkers. This feasibility study evaluated biomarker detection in nasal secretion, biomarker pattern preservation between nasal secretion and CSF, inter-matrix correlations, and diagnostic potential in nasal secretions.

Methods

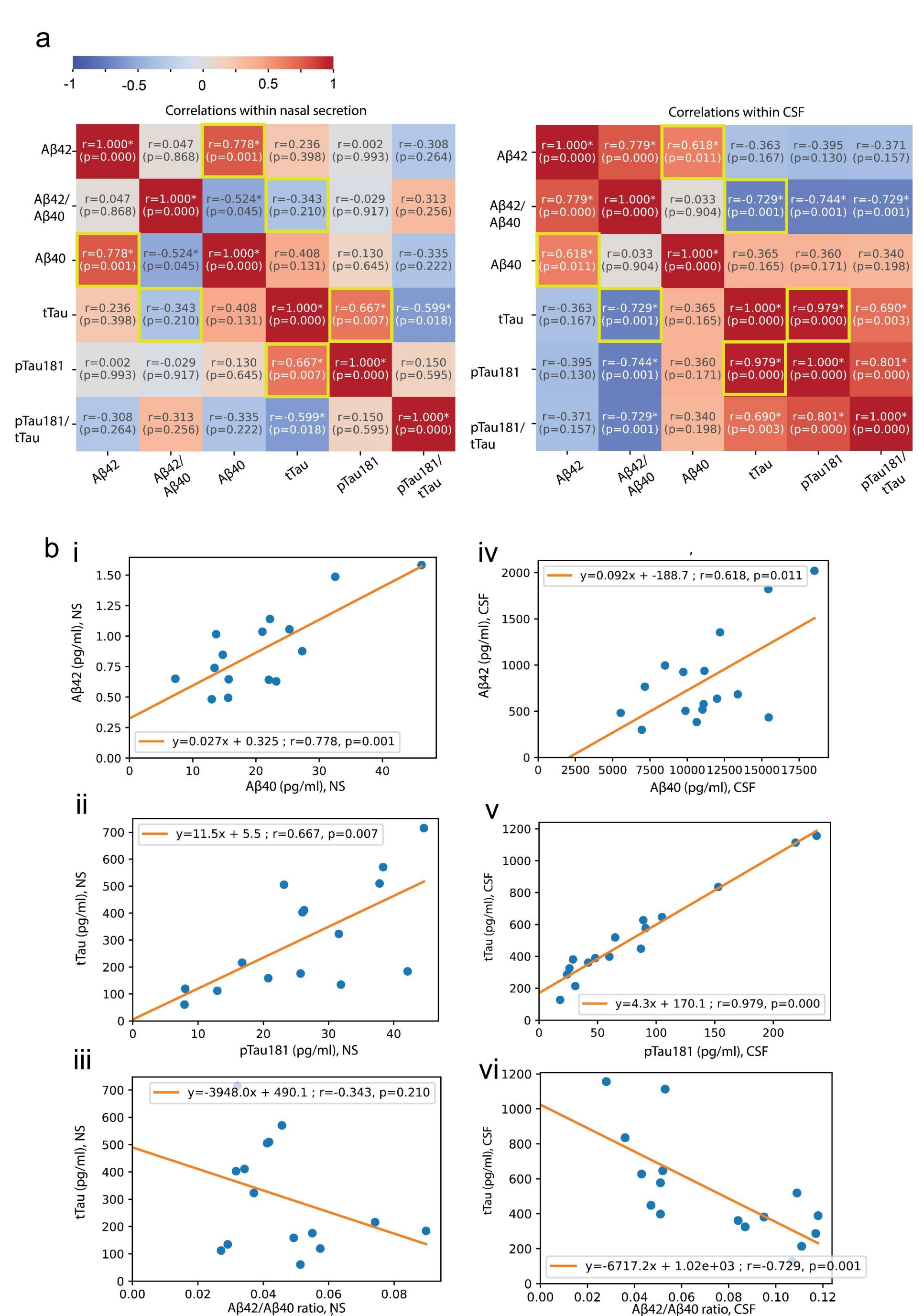
Nasal secretions from 57 cognitively impaired patients were collected using standardized BNI sampling protocol. AD diagnosis was established through CSF analysis (A β 42/40, pTau181, total tau) along with clinical assessment. Nasal samples were analyzed using SIMOA Quanterix technology with systematic CSF comparison.



Patient comfort assessment during standardized nasal secretion collection.

Distribution of visual analog scale (VAS) scores for discomfort during BNI sampling using specialized absorbent material. x-axis represents the VAS values while y- axis shows the number of patients (n(VAS)).

A total of 84% of participants reported VAS scores ≤ 4 , indicating minimal discomfort with the non-invasive collection procedure. VAS scale: 0 = no discomfort, 10 = severe discomfort. These findings support the clinical feasibility and patient acceptability of standardized nasal secretion collection for biomarker analysis.

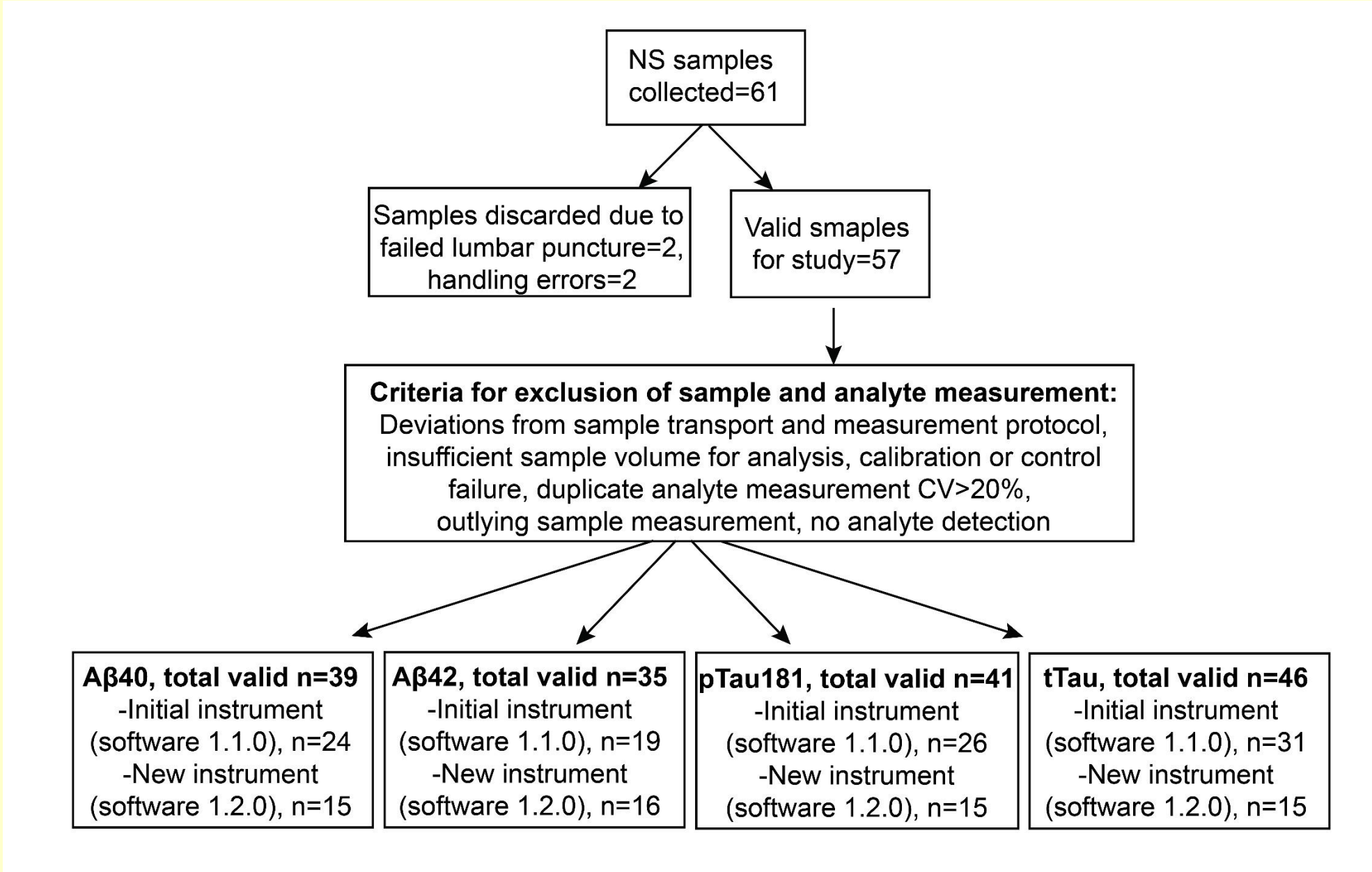


Intra-matrix Correlation of AD Biomarkers in nasal Secretion and CSF

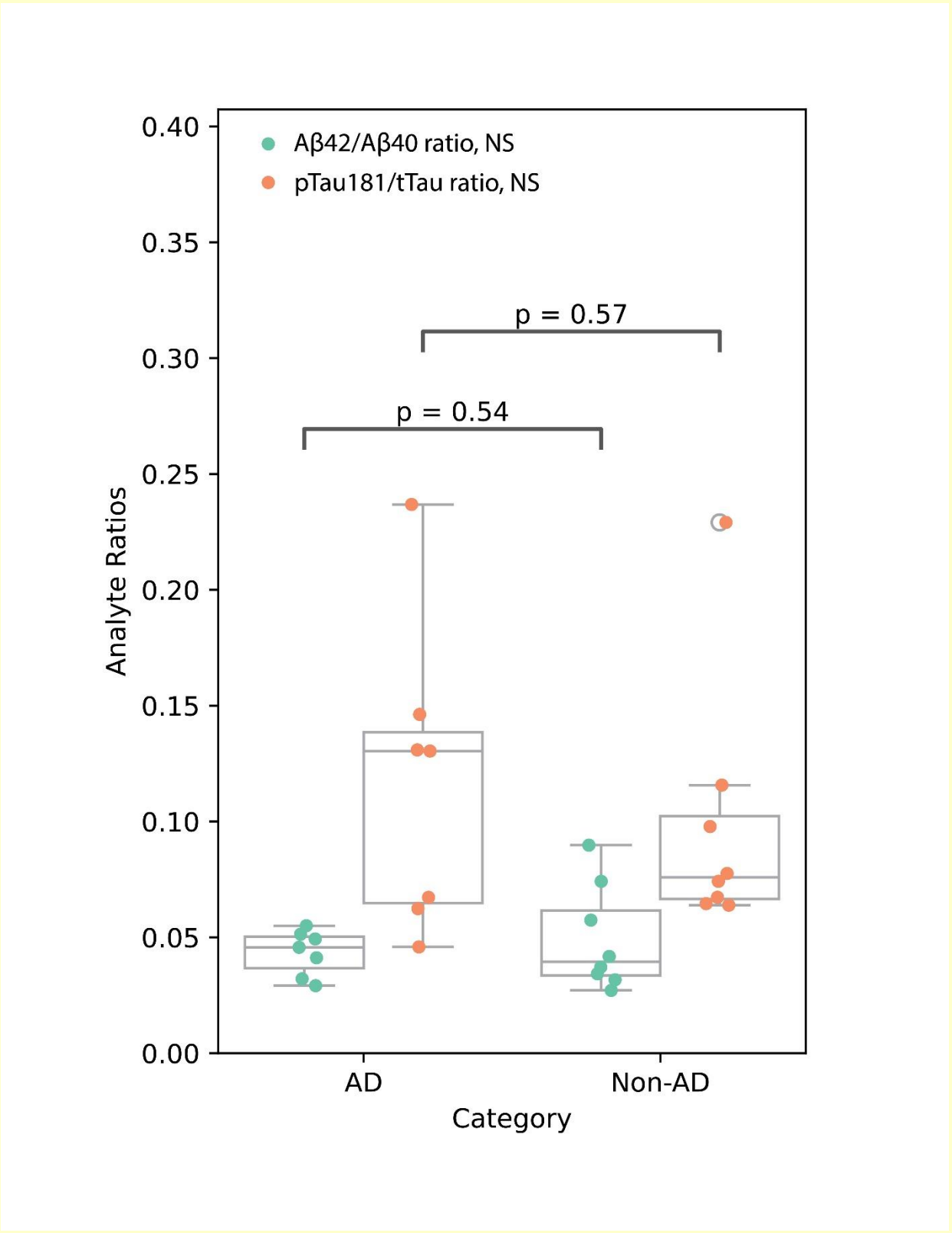
a. Heatmap displaying intra-matrix Pearson correlation coefficients(r) and p value for AD biomarkers within nasal secretion(left) and CSF (right). These heatmaps provide a comprehensive overview of the relationships among A β 42, A β 40, pTau181, tTau, and their derived ratios within each biofluid, allowing direct visual comparison of molecular interplay in the two compartments. Notably, both matrices exhibited strong positive correlations between A β 42 and A β 40, as well as between pTau181 and tTau. Additionally, a negative correlation between tTau and the A β 42/A β 40 ratio was observed in both CSF and nasal secretions, though it reached statistical significance only in CSF. Aforementioned correlations are highlighted in the heatmap with a yellow box. These shared patterns indicate that key molecular relationships characteristic of AD pathology in CSF are also present in nasal secretions.

b. Scatter plots illustrating the following intra-matrix correlations.

Nasal secretion is denoted as NS in the correlation plots. Biomarker levels in nasal secretion and CSF are represented in picogram/millilitres (pg/ml)



Cohort characteristics	Number
Total number enrolled in study	61
Final analysis	57
Male, n (%)	35 (61.4 %)
Female, n (%)	22 (38.6 %)
Mean age $\pm$ SD, years (range)	67.9 $\pm$ 9.2 (45 – 85)
Diagnosis	
AD - Dementia due to AD	20 (35.1 %)
AD - MCI due to AD	11 (19.3 %)
Non AD - CI with ND, no AD	19 (33.3 %)
Non AD - CI without ND, no AD	7 (12.3 %)



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Results

All four AD biomarkers were quantified in nasal secretions. Tau levels as well as ratios of A β 42/A β 40 and pTau181/tTau were comparable across fluids. Critical biomarker pattern preservation was significant in both fluids between A β 42 and A β 40 as well as pTau181 and tTau. Diagnostic discrimination was not achieved in this single-center study comparing cognitively impaired populations.

Conclusion

Nasal secretions represent analytically robust biomarker matrix with preserved AD specific relationships. Reliable quantification and maintained correlation patterns strongly suggest biological coherence with CSF profiles.

Comparison of A β 42/A β 40 and pTau181/tTau ratios in nasal secretions between AD and non-AD groups:

Comparison of biomarker ratios in nasal secretions between participants classified as AD (n=7) and non-AD (n=8). A β 42/A β 40 ratios (green) showed no statistically significant difference between groups (AD: 0.043 $\pm$ 0.009 vs. non-AD: 0.049 $\pm$ 0.022; p=0.54, student t-test). pTau181/tTau ratios (green) similarly demonstrated no significant group discrimination (AD: 0.117 $\pm$ 0.06 vs. non-AD: 0.09 $\pm$ 0.05, p=0.57, student t-test). Both ratios exhibited directional trends consistent with expected AD pathophysiology, with the AD group showing numerically lower A β 42/A β 40 ratios and higher pTau181/tTau ratios. The data points are shown in a box plot: the box represents the interquartile range, the horizontal line inside the box indicates median, and whiskers show the range excluding outliers; points outside indicate outliers.