# **Hierarchical Clustering Analysis and Comparison with Clinical Diagnosis**

## 1. Objective

The goal of this analysis was to explore whether structural brain measures alone can automatically differentiate subjects in a way that reflects the clinical diagnosis of Alzheimer’s Disease (AD). To this end, we applied unsupervised hierarchical clustering (using Ward’s method) to standardized volumetric data of key brain regions (e.g., hippocampus, thalamus, insula, etc.).

## 2. Hierarchical Clustering Results

The resulting dendrogram was cut into 2 clusters, after evaluating that a cut at 3 clusters did not correspond meaningfully with the clinical diagnosis groups (Normal, MCI, AD). A two-cluster solution was therefore adopted for clearer interpretability and clinical relevance.

The cophenetic correlation coefficient confirmed good preservation of the distance structure by the hierarchical model.

A Multivariate Analysis of Variance (MANOVA) comparing the brain features across the two clusters showed statistically significant multivariate differences (Pillai = 0.486, F = 29.327, p < 2.2e-16), indicating that the clusters differ meaningfully along the brain measures.

Immagine che contiene diagramma, Disegno tecnico, Piano, schizzo

Descrizione generata automaticamente

Figure 1: Dendrogram from hierarchical clustering (Ward's method).

Immagine che contiene testo, modello

Descrizione generata automaticamente

Figure 2: Pairwise scatterplot of standardized brain features colored by cluster.

## 3. Comparison with Clinical Diagnosis

The clinical diagnosis variable (DIAGNOSIS) was grouped into two categories:  
- Non-Alzheimer’s: combining Normal and Mild Cognitive Impairment (MCI) subjects.  
- Alzheimer’s: including only AD-diagnosed subjects.

Boxplots of selected brain features (e.g., Hippocampus\_Total) showed similar trends across both the clustered groups and clinical diagnosis groups. In both cases, lower hippocampal volume was associated with Alzheimer’s and with the more impaired cluster (cluster 1).

Immagine che contiene testo, schermata, diagramma, linea

Descrizione generata automaticamente

Figure 3: Distribution of Hippocampus\_Total by identified clusters.

Immagine che contiene testo, diagramma, schermata, linea

Descrizione generata automaticamente

Figure 4: Distribution of Hippocampus\_Total by grouped clinical diagnosis.

## 4. Conclusions

This analysis highlights that an unsupervised hierarchical clustering based solely on brain volumetric measures can partially replicate the clinical classification of Alzheimer’s Disease