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INF 2178 -Assignment 4

Introduction

This study investigates the impact of dementia on brain volume changes over time, using MRI data from the "INF2178_A4_data.csv" dataset. The dataset includes longitudinal MRI results from subjects categorized as 'Nondemented', 'Demented', and 'Converted'—those transitioning from nondemented to demented status. Our analysis applies mixed-effects ANOVA to explore the effects of dementia status, gender, and visit on normalized whole brain volume (nWBV), along with statistical power analysis to determine sample size adequacy.

Research Question: How does dementia status influence brain atrophy progression, as reflected in nWBV changes across two visits?
Research Question 2: Does gender play a role in the relationship between dementia status and brain volume changes over two visits?

Data cleaning and feature engineering

The dataset includes 294 rows and 16 columns, and merges demographic, clinical, and MRI measures to examine dementia's impact on brain structure. Key features include Subject ID, MRI ID, demographic information (gender, age, education, and socio-economic status), clinical measures (MMSE, CDR), and MRI measures (eTIV, nWBV, ASF). Initial assessment identified missing values in 'SES' and 'MMSE', addressed by replacing them with the mode and median, respectively. Data cleaning involved dropping the 'Hand' column, encoding gender ('M/F') numerically, and adjusting the 'Visit' to be treated as a categorical variable for plotting later analysis.

Exploratory Data Analysis

Firstly, the side-by-side histograms were made to display the normalized whole brain volume (nWBV) distributions for Nondemented, Demented, and Converted groups across two visits.

For the Nondemented group, the distributions of nWBV for the first and second visits mostly overlap, suggesting stability in brain volume over two visits. In the Demented group, there is a more noticeable decrease in nWBV from the first to the second visit. The peak of the distribution for the second visit is shifted leftward more than in the Nondemented group. In the Converted group, the shift in nWBV between visits is less apparent but noticeable, indicating a brain volume loss that accompanies the clinical change in dementia status.

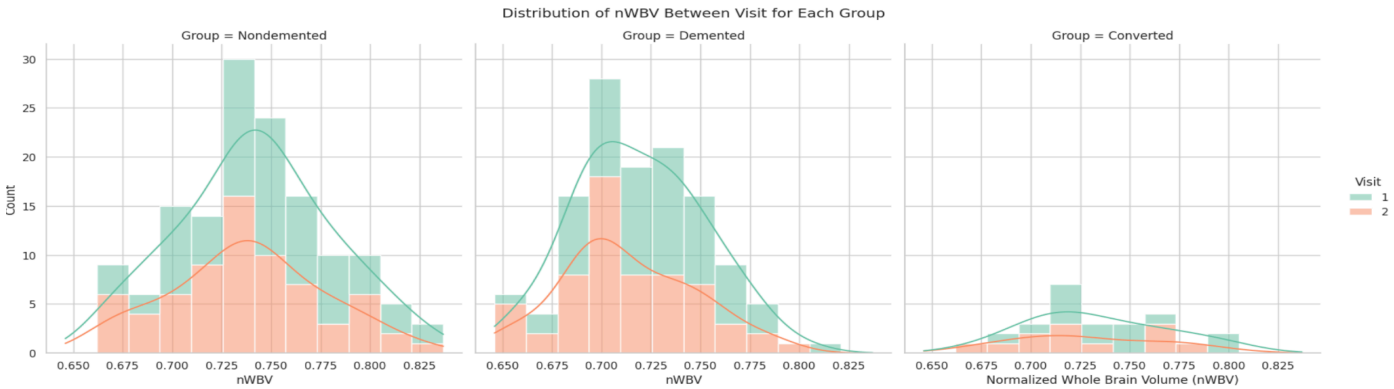

Figure 1 Histogram of nWBV Cross Visit for Each Group

Then, we constructed box and swarm plots, which reveal more insights into the progression of brain volume changes. The overlay of individual data points on the box plots clarifies the variability and distribution patterns

within each dementia status group. For the Nondemented group, while the overall range remains similar, the individual data points indicate a subtle spread toward lower nWBV values over the two visits. The Demented group's distribution demonstrates a more apparent spread of individual nWBV measures, particularly toward the lower end, from the first to the second visit. This suggests a broader brain volume loss than initially perceived. The Converted group shows increased variability and a transition with individual points in the second visit dispersing toward lower nWBV, reinforcing the notion of a shift in brain volume that could be linked to the onset of dementia symptoms.

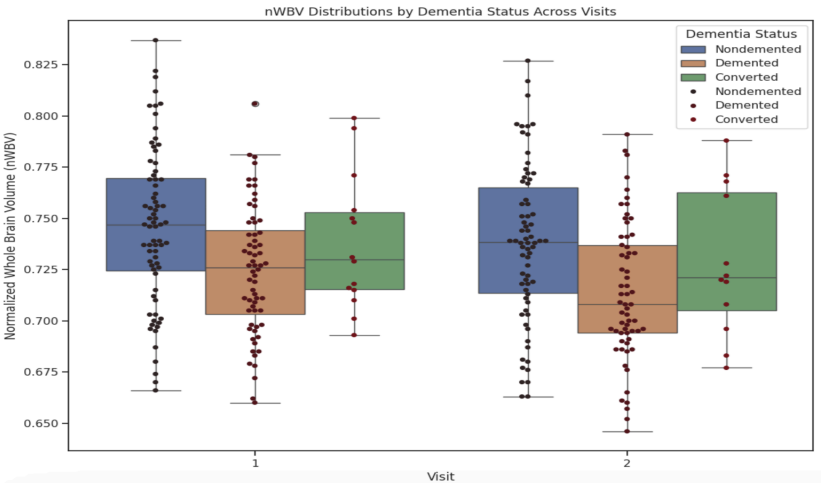

Figure 2 Box and Swarm plots of nWBV Cross Visit for Each Group

To explore the second research question, analyzing the pointplot for gender-specific trends in nWBV across different groups, we find that females begin with a higher nWBV in the non-demented group. As we move to the demented group, both males and females show a reduction in nWBV, with females experiencing a more pronounced reduction. This suggests that while both genders are affected by dementia, the impact on nWBV is more significant in males at this stage. Notably, in the 'Converted' group, female nWBV increases, contrasting with the progressive decline observed in males. Moreover, the error bars for the converted group, particularly for females, are more prominent, suggesting a high degree of variability or uncertainty about the average nWBV in this group.

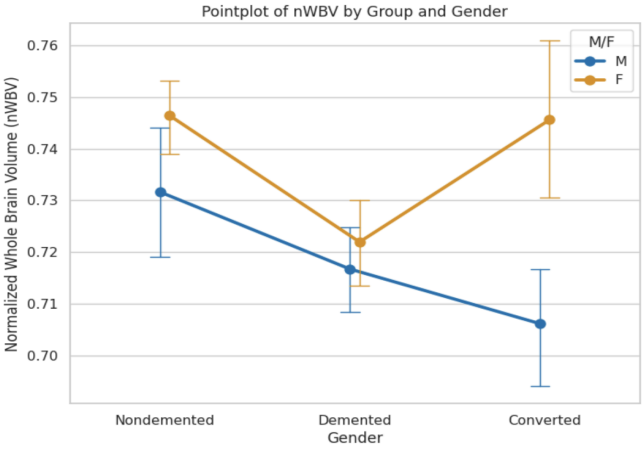

Figure 3 Pointplot of nWBV by Gender for Each Group

Following our earlier trend analysis through a pointplot in Figure 3, this box and swarm plot in Figure 4 reveals more insights on nWBV distributions by gender across visits. Remarkably, females display higher median nWBV values than males, a pattern consistent in both visits and suggests intrinsic gender differences in brain volume metrics. The box and swarm plot indicates a modest decrease in median nWBV for females across visits, while males show a marked decline, highlighting a significant gender disparity in the

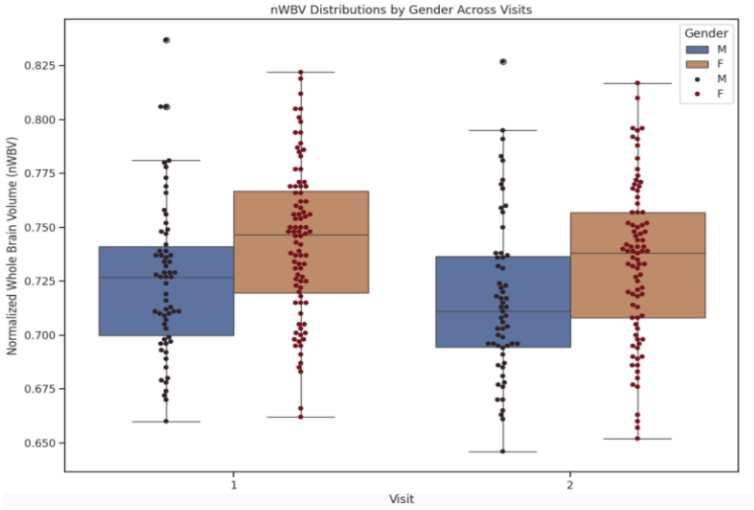

Figure 4 Box and Swarm Plot by Gender across Visits

progression of brain volume changes over time. Outliers, more prominent in the male subset, accentuate this variability. Taken together with the earlier findings, these observations contribute to a layered picture of nWBV changes over two visits between gender, underlining not just the influence of dementia status but also the potential moderating role of gender.

Mixed-Effects ANOVA Analysis

Research Question 1

To explore the research question "Does dementia status affect brain volume changes over successive visits?" we conducted a mixed ANOVA using 'Group' as the between-subjects factor and 'Visit' as the within-subjects factor. Our analysis found a significant main effect of 'Group' on nWBV, with an F-value of 6.712 and a p-value of 0.002, indicating that different dementia status groups exhibit distinct nWBV measures. The 'Visit' factor also had a highly significant main effect on nWBV, evidenced by an F-value of 94.251 and a p-value of 0.000, which confirms that brain volume significantly changes over time across all subjects. However, the interaction effect between 'Group' and 'Visit' was not statistically significant (F-value of 1.534, p-value of 0.219), suggesting that the rate of brain volume change does not significantly differ among the dementia groups across the visits.

	SS	DF1	DF2	MS	F	p-unc	NP2
Group	0.034	2	141	0.017	6.712	0.002	0.087
Visit	0.007	1	141	0.007	94.251	0.000	0.401
Interaction	0.000	2	141	0	1.534	0.219	0.021

Figure 4 ANOVA Summary I

Post-Hoc Analysis: Using pairwise t-tests with Bonferroni corrections, we identified a statistically significant ($p < 0.001$) decrease in nWBV between the first and second visits. Specifically, when comparing dementia groups, the Demented group showed a significantly lower brain volume than the Nondemented group at both time points ($p < 0.001$). Moreover, significant interactions between visits and dementia status were observed, indicating the extent of brain volume reduction differed between Demented and Nondemented groups across visits ($p \leq 0.005$).

Research Question 2

To address the second research question "Does gender play a role in the relationship between dementia status and brain volume changes over successive visits?" we modified our mixed ANOVA approach. Due to the limitations in the pingouin library, which does not support multiple between-subjects factors in a mixed ANOVA, we created a new variable, 'Group_Gender', which combines dementia status ('Group') with the biological sex of the participants ('Gender'), allowing us to analyze the effects of both factors simultaneously on nWBV.

The mixed ANOVA results revealed significant differences in nWBV among the combined categories of dementia status and gender, as evidenced by an F-value of 4.149 and a p-value of 0.002. A highly significant main effect of 'Visit' on nWBV (F-value of 93.980, p-value < 0.001) was also observed, confirming that brain volume significantly changes over time. However, the interaction between 'Group_Gender' and 'Visit' did not show a significant difference (F-value of 1.130, p-value of 0.347), indicating that while both dementia status and gender individually affect nWBV, their combined effect does not significantly alter the trajectory of brain volume change across visits. This results underlines the complexity of the factors influencing nWBV, particularly the importance of gender in the context of dementia.

	SS	DF1	DF2	MS	F	p-unc	NP2
Group_Gender	0.051	5	138	0.010	4.149	0.002	0.131
Visit	0.007	1	138	0.007	93.980	0.000	0.405
Interaction	0.000	5	138	0.000	1.130	0.347	0.039

Figure 5 ANOVA Summary II

Post-Hoc Analysis: Following a mixed ANOVA, our pairwise t-tests with Bonferroni corrections identified lower nWBV in Demented females compared to Nondemented females ($p = 0.003$), and between Demented males and Nondemented females ($p < 0.004$), indicating gender differences in the impact of dementia. Notably, at the first visit, Converted males differed significantly from Nondemented females ($p = 0.005$), and at the second visit, Demented females also showed a significant decline from their Nondemented counterparts ($p = 0.001$). These findings point to a complex interplay between gender and dementia status in brain volume changes over successive visits.

Statistical power analysis

The power analysis plot for t-tests demonstrates the relationship between sample size and the ability to detect an effect of size 0.7 at a significance level of 0.05. The curve illustrates how power increases with the number of observations. For our specific parameters, a sample size of approximately 45.451 participants per group is required to achieve a desired power of 0.91, meaning there's a 91% probability of correctly rejecting the null hypothesis for the given effect size and alpha level. The horizontal dashed red line marks the target power level, while the vertical dashed blue line indicates the minimum sample size needed to reach this power, serving as a practical reference for ensuring our study is designed with adequate statistical power. This ensures our study's findings will be both valid and reliable.

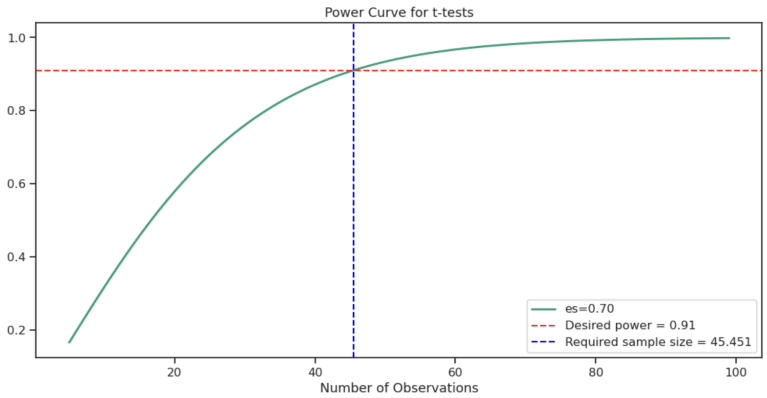

Figure 6 Statistical Power Analysis Plot for t-test

Conclusion

To Summarize findings and address our research questions, from the above analyses, we found that dementia status significantly impacts brain volume reduction across visits, and gender differences notably influence this relationship. The 'Demented' group experienced a significant decrease in brain volume compared to the 'Nondemented' group, while the 'Converted' group displayed intermediate effects. Additionally, gender differences notably affect this progression, with female participants showing more pronounced brain volume reduction as dementia advances. Despite the robustness of our analyses, the limitations should be acknowledged, including the potential impact of a limited sample size on the generalizability of our results and constraints of the Pingouin statistical library used for the analysis.

Reflecting on our study, it is evident that while dementia uniformly exacerbates brain atrophy, the interplay with gender presents a nuanced dynamic, with females experiencing more pronounced brain volume reduction as dementia progresses. This insight warrants further investigation into gender-specific therapeutic interventions and underscores the importance of personalized approaches in treatment and care planning.