Sheng Zhang
eily.zhang@mail.utoronto.ca

# An Investigation of an MRI results Longitudinal Study

## 1. Introduction

A longitudinal study on MRI results of patients with/without dementia was taken. Based on the investigation of the dataset "INF2178_A4_data.xlsx," the report employs exploratory data analysis (EDA) and mixed-effect ANOVA to address the following research questions:

1. Does the estimated Total Intracranial Volume (eTIV) vary significantly among different groups and over different visit times, and is there an interaction effect between group membership and visit time?
2. Does the normalised Whole Brain Volume (nWBV) vary significantly among different groups and over different visit times, and is there an interaction effect between group membership and visit time?
3. Does the Atlas Scaling Factor (ASF) vary significantly among different groups and over different visit times, and is there an interaction effect between group membership and visit time?

## 2. Data Cleaning and Data Wrangling

The initial dataset has 16 columns and 294 rows. After checking the column definitions, we would like to work on the columns:

- id: the unique id representing the patient (this is extracted as the unique integer at the end of "Subject ID")
- Group: the status of patients, including Nondemented, Demented, and Converted
- Visit: the sequential identifier for the number of the visits of a patient
- eTIV: estimated Total Intracranial Volume
- nWBV: normalised Whole Brain Volume
- ASF: Atlas Scaling Factor

## 3. Exploratory Data Analysis(EDA)

First we construct a summary table to check the statistics of the dataset [Figure 1].

| | id | eTIV | nWBV | ASF |
|---|---|---|---|---|
| **count** | 294 | 294 | 294 | 294 |
| **mean** | 93.08163265 | 1478.853741 | 0.7313809524 | 1.203108844 |
| **std** | 52.82058113 | 176.5597551 | 0.03737346494 | 0.1393648503 |
| **min** | 1 | 1106 | 0.646 | 0.876 |
| **25%** | 48.25 | 1347.25 | 0.703 | 1.11825 |
| **50%** | 93 | 1461.5 | 0.732 | 1.201 |
| **75%** | 138.75 | 1569 | 0.756 | 1.30275 |
| **max** | 186 | 2004 | 0.837 | 1.587 |

Figure 1: Summary statistics for the data frame

We can also check the stacked bar graph that counts the number of patients for each group and each visit time. [Figure 2]

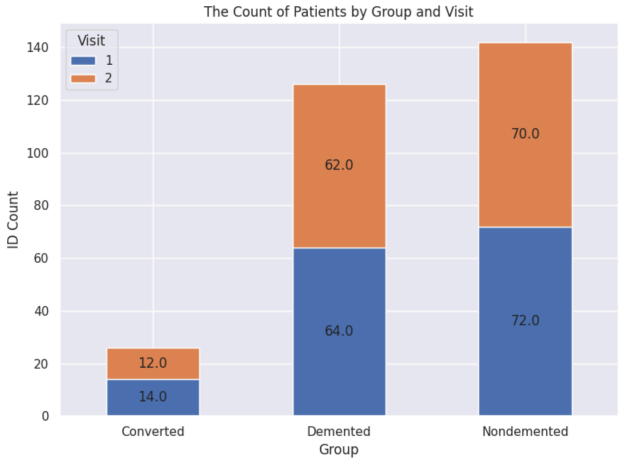
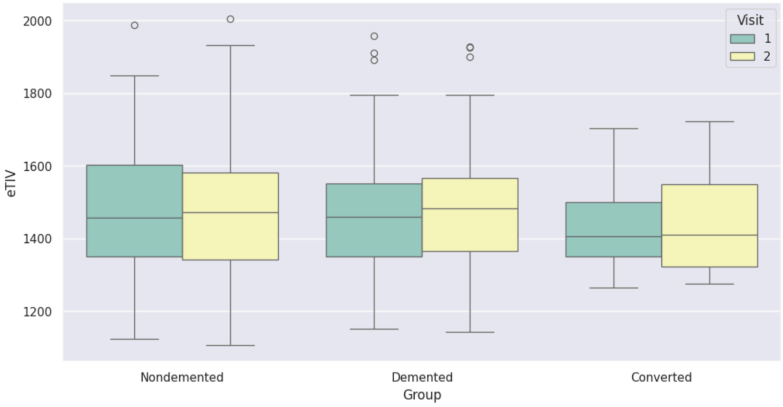
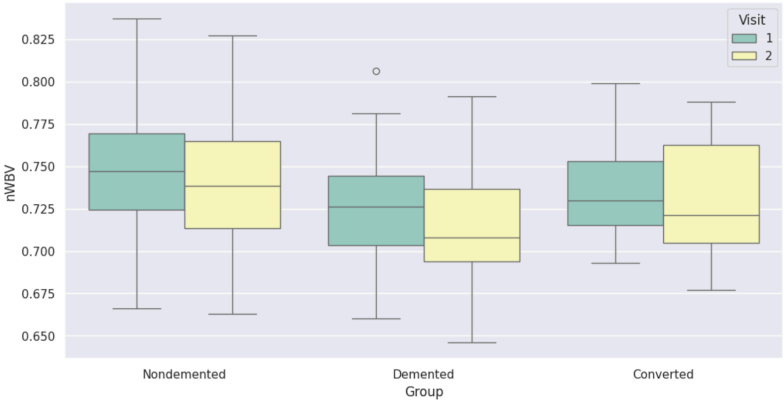



Figure 2: Bar graph for the number of patients by group and visit

Now, we can further check the box plots for eTIV, nMBV, and ASF for each group and visit time to find out whether there is an interesting intuitive pattern. [Figure 3, 4, 5]



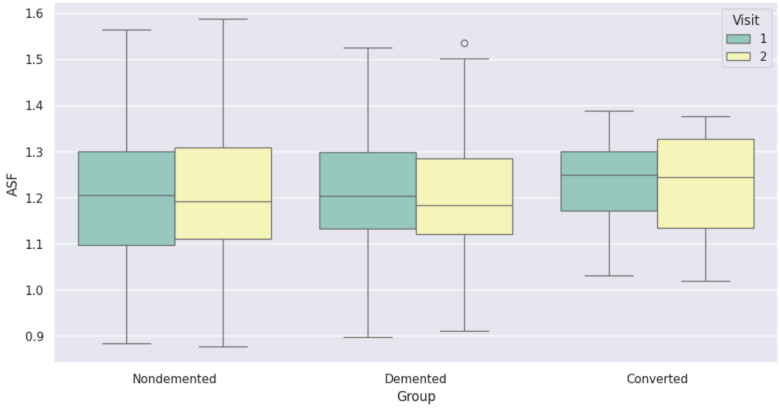




Figure 3 (Top Left): Box plot for eTIV for each group and each visit time

Figure 4 (Top Right): Box plot for nWBV for each group and each visit time

Figure 5(Bottom Left): Box plot for ASF for each group and each visit time

We observe that there are not many extremely obvious patterns here. But we can roughly guess that these data might be normal, and the means for each box plot are similar. So there might be similar conclusions for mixed-effect ANOVA, which needs us to further analyse.

## 4. eTIV across different groups and visit times

Research Question 1: Does the estimated Total Intracranial Volume (eTIV) vary significantly among different groups and over different visit times, and is there an interaction effect between group membership and visit time?

The null hypothesis is that there is no significant difference in the estimated Total Intracranial Volume (eTIV) among different groups and over different visit times, and there is no interaction effect between group membership and visit time and the chosen alpha-level is 0.05.

We perform the output plot in Figure 6, and the ANOVA table in Figure 7.

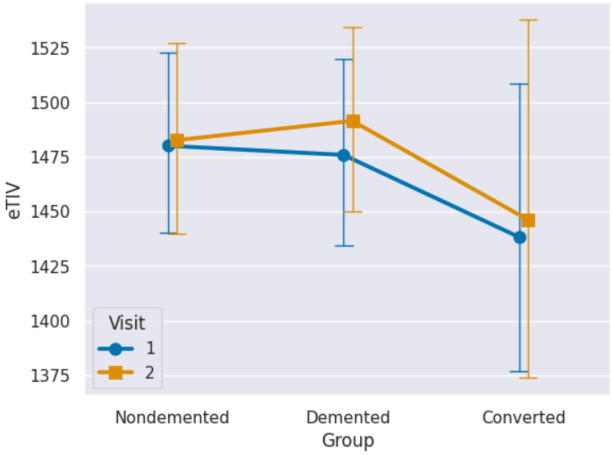



Figure 6 (Left): Output plot for research question 1

Figure 7 (Down): Mixed-effect ANOVA table for research question 1

| | Source | SS | DF1 | DF2 | MS | F | p-unc | np2 | eps |
|---|---|---|---|---|---|---|---|---|---|
| **0** | Group | 37,424.7084 | 2.0000 | 141.0000 | 18,712.3542 | 0.2973 | 0.7433 | 0.0042 | NaN |
| **1** | Visit | 5,573.9201 | 1.0000 | 141.0000 | 5,573.9201 | 9.2249 | 0.0028 | 0.0614 | 1 |
| **2** | Interaction | 1,004.7832 | 2.0000 | 141.0000 | 502.3916 | 0.8315 | 0.4375 | 0.0117 | NaN |

The mixed-effects ANOVA results indicate that there is no significant main effect of the Group on the estimated Total Intracranial Volume (eTIV), with the F-value below the critical threshold and the p-value exceeding 0.05. Similarly, the interaction effect between Group and Visit is not significant, suggesting that the difference in eTIV between the groups does not vary significantly across different visit times. However, a significant main effect of Visit on eTIV is observed, indicating that eTIV varies significantly over different visit times. Nevertheless, the effect size of this main effect is relatively small. Overall, while visit time influences eTIV, neither group membership nor the interaction between group membership and visit time significantly impacts eTIV in this analysis.

Let us also check the assumptions:

- Assumption 1: Spericity
  By Mauchly's test of sphericity, we have a result of p-value of 1>0.05. So the assumption of sphericity is met.
- Assumption 2: Normality
  By the Shapiro-Wilk test, all combinations of factors are normal (p>0.05). So the assumption of normality is met.
- Assumption 3: Homogeneity
  By Levene's test, we have p>0.05 for both within groups. So the assumption of homogeneity is met.

## 5. nWBV across different groups and visit times

Research Question 2: Does the normalised Whole Brain Volume (nWBV) vary significantly among different groups and over different visit times, and is there an interaction effect between group membership and visit time?

The null hypothesis is that there is no significant difference in the normalised Whole Brain Volume (nWBV) among different groups and over different visit times, and there is no interaction effect between group membership and visit time and the chosen alpha-level is 0.05.We perform the output plot in Figure 8, and the ANOVA table in Figure 9.

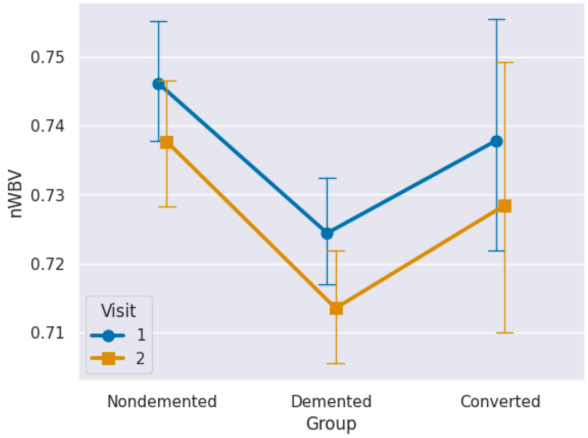



Figure 8 (Left): Output plot for research question 2

Figure 9 (Down): Mixed-effect ANOVA table for research question 2

| | Source | SS | DF1 | DF2 | MS | F | p-unc | np2 | eps |
|---|---|---|---|---|---|---|---|---|---|
| **0** | Group | 0.0336 | 2.0000 | 141.0000 | 0.0168 | 6.7124 | 0.0016 | 0.0869 | NaN |
| **1** | Visit | 0.0065 | 1.0000 | 141.0000 | 0.0065 | 94.2512 | <0.05 | 0.4006 | 1 |
| **2** | Interaction | 0.0002 | 2.0000 | 141.0000 | 0.0001 | 1.5335 | 0.2194 | 0.0213 | NaN |

The mixed-effects ANOVA results reveal significant main effects of Group and Visit (different visit times) on the normalised Whole Brain Volume (nWBV), indicating differences in nWBV among the groups and across visit times. Specifically, both Group and Visit significantly influence nWBV, with the former demonstrating a small but significant effect and the latter showing a substantial effect size. However, there is no significant interaction effect between Group and Visit, suggesting that the difference in nWBV between the groups remains consistent across different visit times. Consequently, while nWBV varies significantly among different groups and over different visit times, the variation in nWBV is not dependent on the interaction between group membership and visit time.

Let us also check the assumptions:

- Assumption 1: Spericity
  By Mauchly's test of sphericity, we have a result of p-value of 1>0.05. So the assumption of sphericity is met.
- Assumption 2: Normality
  By the Shapiro-Wilk test, all combinations of factors are normal (p>0.05). So the assumption of normality is met.
- Assumption 3: Homogeneity
  By Levene's test, we have p>0.05 for both within groups. So the assumption of homogeneity is met.

## 6. ASF across different groups and visit times

Research Question 3: Does the Atlas Scaling Factor (ASF) vary significantly among different groups and over different visit times, and is there an interaction effect between group membership and visit time?

The null hypothesis is that there is no significant difference in the Atlas Scaling Factor (ASF) among different groups and over different visit times, and there is no interaction effect between group membership and visit time and the chosen alpha-level is 0.05.We perform the output plot in Figure 10, and the ANOVA table in Figure 11.

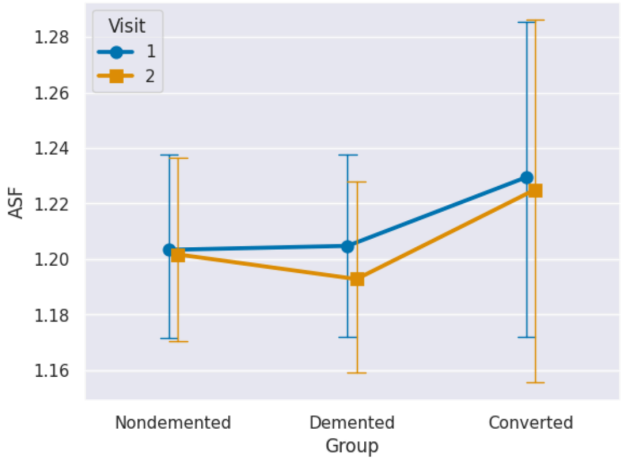



Figure 10 (Left): Output plot for research question 3

Figure 11 (Down): Mixed-effect ANOVA table for research question 3

| index | Source | SS | DF1 | DF2 | MS | F | p-unc | np2 | eps |
|---|---|---|---|---|---|---|---|---|---|
| **2** | Interaction | 0.0007 | 2.0000 | 141.0000 | 0.0004 | 1.0276 | 0.3605 | 0.0144 | NaN |
| **1** | Visit | 0.0032 | 1.0000 | 141.0000 | 0.0032 | 8.7543 | 0.0036 | 0.0585 | 1 |
| **0** | Group | 0.0184 | 2.0000 | 141.0000 | 0.0092 | 0.2337 | 0.7919 | 0.0033 | NaN |

The mixed-effects ANOVA results for Research Question 3 reveal that the Atlas Scaling Factor (ASF) varies significantly over different visit times, as evidenced by a significant main effect of Visit. However, there are no significant effects observed for Group or the interaction between Group and Visit. Specifically, there is no significant difference in ASF among the groups, and the difference in ASF between these groups does not significantly vary across different visit times. Consequently, while visit time influences ASF, group membership and the interaction between group membership and visit time do not significantly impact ASF in this analysis.

Let us also check the assumptions:

- Assumption 1: Spericity
  By Mauchly's test of sphericity, we have a result of p-value of 1>0.05. So the assumption of sphericity is met.
- Assumption 2: Normality
  By the Shapiro-Wilk test, all combinations of factors are normal (p>0.05). So the assumption of normality is met.
- Assumption 3: Homogeneity
  By Levene's test, we have p>0.05 for both within groups. So the assumption of homogeneity is met.

## 7. Sample Size Computation

Given the effect size of 0.7, power of 0.91, and the alpha level of 0.05, by using the statistical power analysis, we compute that the sample size satisfying these conditions is about 45.45, which rounds up to 46 as sample size must be integer.

## 8. Conclusion

Overall, while visit time significantly influences the measured brain metrics (eTIV, nWBV, ASF), group membership and its interaction with visit time do not significantly contribute to these variations.