Effects of Different Pain Relievers and Dosages on Cognitive Retention

Exploratory Data Analysis (EDA)

Navya Hooda Mohammed Yusuf Shaikh Shivank Goel
Vanshika Vanshika Jena Shah

March 21, 2025

Painkillers are commonly used to manage pain, and their effects are often associated with physical relief. While they provide immediate physical comfort, their impact on cognitive performance is often overlooked. This study explores how different painkillers and dosages influence cognitive function. Using simulated testing from a virtual population, participants were randomly assigned a treatment (drug type and dosage) while controlling for variables such as age. Our findings indicate no significant relationship between drug type, dosage, and overall cognitive performance post-treatment. However, we observed some correlation between certain drug-dosage combinations and memory improvement, suggesting a potential area for further research. While the results were not statistically significant, this study contributes to a deeper understanding of the cognitive effects of painkillers and highlights the need for further investigation into their potential impact on memory and cognition.

Table of contents

1 Acknowledgements **2**

2 Introduction **2**
2.1 Research Questions 3
2.2 Study Design 3
2.3 Confounding Variable: Age 4
2.4 Quantitative and Qualitative Variables 4
2.5 Data Analysis Method 4

3 Summary Statistics **4**
3.1 Summary of quantitative variables 4
3.2 Summary of counts and percentage for qualitative variables 5
3.3 Confounding Variable 6

4 Plots **9**
4.1 Game Score Distribution Before and After Treatment 9
4.2 Memory Card Score Distribution Before and After Treatment 9

5 Assumptions **9**
5.1 Model 9

6 Analysis **10**

7 Discussion **13**
7.1 Interpretation of Results 13
7.1.1 Exploratory Observations 13

8 Limitations **14**

9 Conclusion **14**

10 References **14**

11 Appendix **15**

1 Acknowledgements

We extend our gratitude to the academic community for their contributions to this research.No auto-complete tools such as co-pilot were used in the course of this project, however, Language Learning Model ChatGPT was used while writing this paper. It was used for the purpose of code debugging, understanding models, and knowledge of certain topics, which we were not aware of. The chat with the AI bot is also attached as a reference under Section 11

2 Introduction

Pain can make everyday tasks harder, particularly when mental focus and clarity are required. Study has shown that individuals with pain tend to have cognitive dysfunction symptoms (Hu, 2010). Common pain relievers like Aspirin, Paracetamol, and Tramadol are often used to reduce physical discomfort, but their impact on cognitive functions are not well understood. Memory retention is a process that requires mental effort – which becomes more difficult

when we're in pain. This study investigates how different pain relievers (Aspirin, Paracetamol, and Tramadol) at standard dosages affect memory performance. We will also look at how the interaction between drug type and dosage level influence memory function. Since the ability to recall information is a basis for optimized human function, understanding how pain relief might impact cognitive performance is important for managing pain without affecting productivity.

2.1 Research Questions

1. *How does the type of pain reliever (Aspirin 500 mg, Paracetamol 500 mg, Tramadol 50 mg, and Placebo) affect cognitive task performance?*

- Null Hypothesis: All pain relievers at normal dosages act the same for cognitive retention game performances.
- Alternative Hypothesis: There exists at least one pair of distinct pain relievers at normal dosages which act differently for cognitive retention game performances.

2. *How does the dosage (low vs. high) of each drug affect cognitive retention, while accounting for confounding factors like age?*

- Null Hypothesis: There is no interaction effect between the type of pain reliever and dosage level on the improvement in memory task performance.
- Alternative Hypothesis: There is an interaction effect between at least one of the types of pain reliever and dosage level on the improvement in memory task performance.

2.2 Study Design

This study involves 2 factors, pain reliever type (4 levels) and dosage(2 levels). Crossing them provides us with *8 treatment groups*, with **30 participants** assigned to each. The groups are as follows:

1. Aspirin 500 mg (Low)
2. Aspirin 1000 mg (High)
3. Paracetamol 500 mg (Low)
4. Paracetamol 1000 mg (High)
5. Tramadol 50 mg (Low)
6. Tramadol 100 mg (High)
7. Placebo (Low)
8. Placebo (High)

This results in **240 total observations** ($8 \times 30 = 240$).

2.3 Confounding Variable: Age

To reduce bias, we consider to control the experiment by controlling participant ages to be 18+. Hence in this study **age** acts as a **confounding variable**. Participants will be categorized into three groups evenly to prevent bias created through age. The groups are as follows:

1. 18–34 years
2. 35–50 years
3. 50+ years

2.4 Quantitative and Qualitative Variables

In our study the quantitative and qualitative variables are as follows:

1. Quantitative variables: Memory Game Scores, Memory Test Cards Scores
2. Qualitative variables: Type of pain reliever, dosage level (low/high)

2.5 Data Analysis Method

We will use **one-way ANOVA** to analyze the effects of different pain relievers on memory performance. Similarly, we will use **two-way ANOVA** to analyze the effects of different dosage levels per drug type on memory performance and cognitive retention.

The structure of the paper is as follows: Section 2 outlines our data and methodology. Section 3 presents our quantitative analysis. In Section 4, we discuss the results and address our findings from the analysis. Section 5 covers the limitations of our study, and Section 6 presents a conclusion to our analysis. After that, we have the bibliography in Section 7. Lastly, we attached the code for our study into the Appendix at Section 8.

3 Summary Statistics

3.1 Summary of quantitative variables

Table 1 shows the summary statistics of memory game scores before and after the treatment. The mean is similar across all groups, however, the standard deviation (SD) is relatively high. The median game scores remain close to the mean, and the IQR (Interquartile Range) is smaller than the SD. The cards memory task shows little change before and after treatment, suggesting that pain relievers may not have a major effect on this specific task.

Evident through the results, Paracetamol is the drug that has the greatest mean & median improvement in the game scores after administering the drug (without dosage taken into

Table 1: Summary Statistics for Quantitative Variables

Statistic	Memory Game Score	Memory Cards Score
Mean	62.57583	7.945833
Median	61.50000	9.000000
SD	15.63703	1.960164
IQR	23.35000	2.000000

Table 2: Summary of Drug Types

Drug	Count	Percentage
Aspirin	60	25
Paracetamol	60	25
Placebo	60	25
Tramadol	60	25

account). Aspirin appears to negatively impact the results of the game after being given to people, this was seen through the mean and median improvements.

Table 3: Summary of Dosage Levels

Dosage	Count	Percentage
High	120	50
Low	120	50

Table 4: Summary of Age Groups

Age_Group	Count	Percentage
18-34	80	33.33
35-50	80	33.33
50+	80	33.33

3.2 Summary of counts and percentage for qualitative variables

Table 2 shows the distribution of participants across drug types. Aspirin, Paracetamol, and Tramadol, and Placebo each have 60 participants (25%), ensuring balance.

Table 3 shows the dosage levels assigned to participants. There is an equal split between high-dose (120 participants, 50%) and low-dose (120 participants, 50%) conditions.

3.3 Confounding Variable

Table 4 shows the breakdown of age groups, which is a confounding variable in this study. The three age groups: 18–34, 35–50, and 50+ each have 80 participants (33.33%).

Figure 1: Interaction Plot: Drug Type vs. Dosage Level

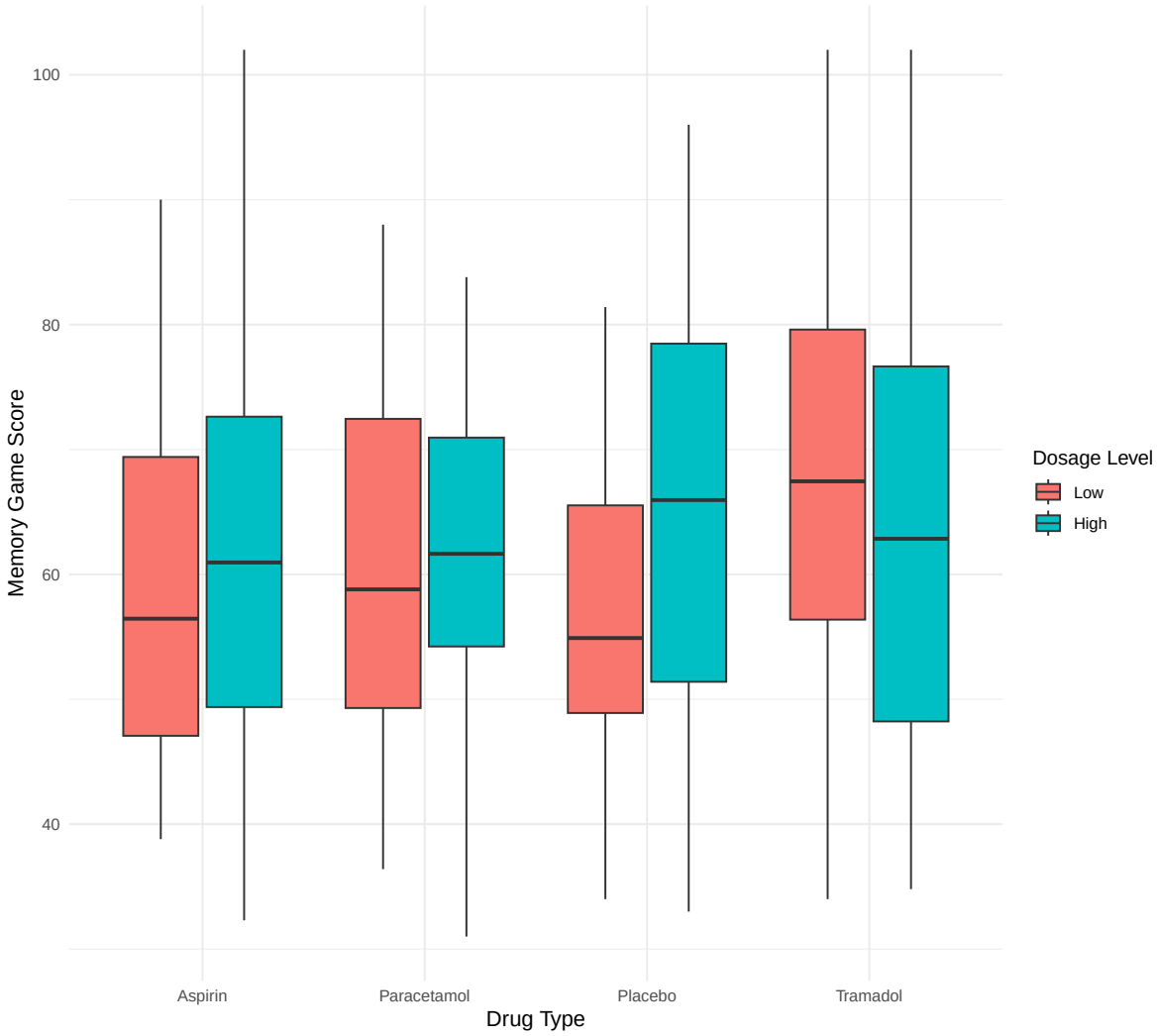


Figure 2: Memory Game Scores by Drug Type and Dosage Level

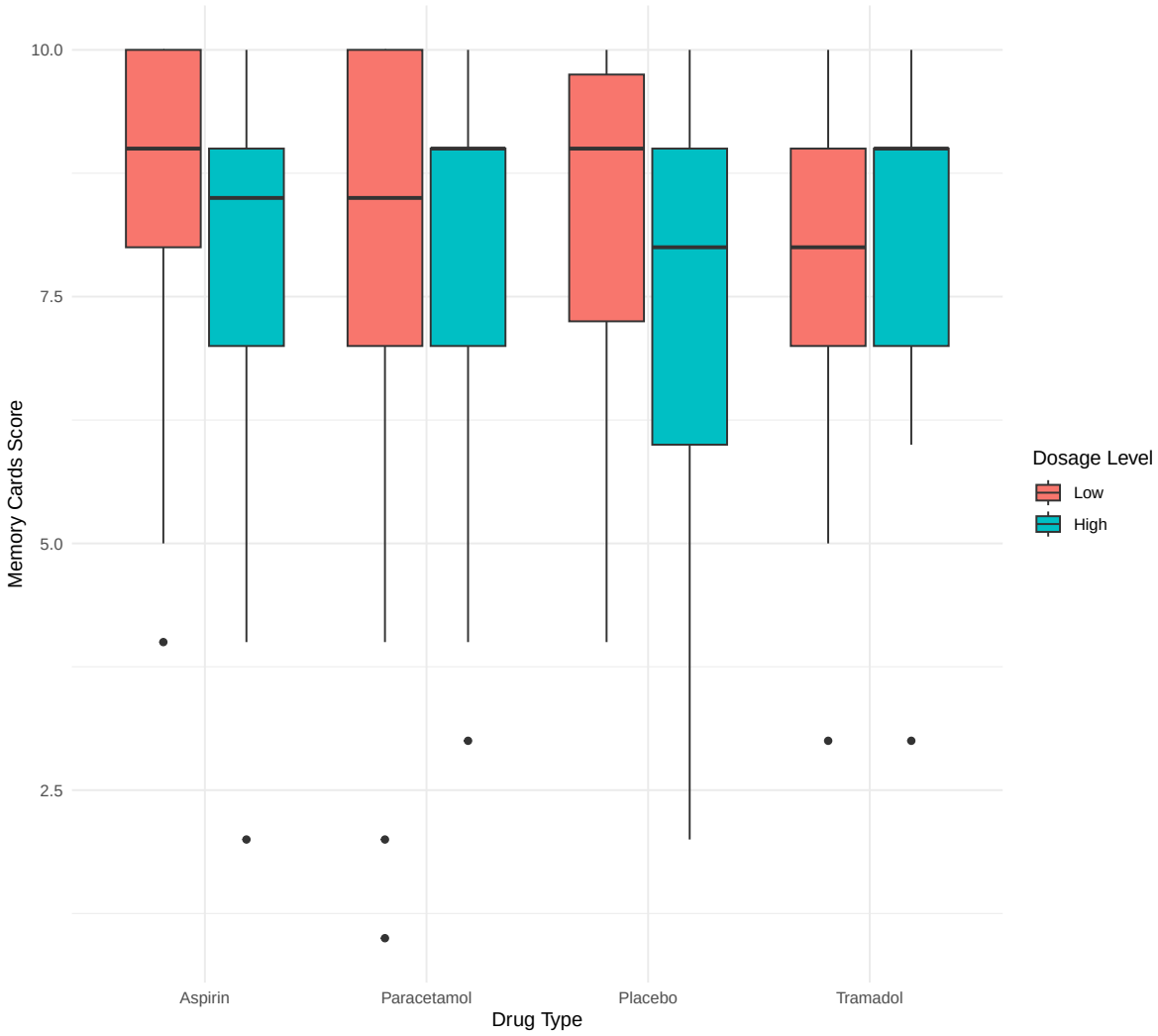


Figure 3: Memory Game Scores by Drug Type and Dosage Level

4 Plots

4.1 Game Score Distribution Before and After Treatment

Figure 2 shows the distribution of memory game scores before and after treatment across different drug types using box plots.

1. The median scores for all drugs appear similar before treatment.
2. Tramadol has a higher median than other drugs both before and after treatment.
3. The Placebo group has a slightly lower median score compared to other drugs.
4. There is one outlier in the Tramadol group before treatment.
5. The (IQR) is **similar across all drug types**, though Tramadol sees a decrease in its IQR in the memory game scores after treatment.

These boxplots provide an initial comparison of cognitive performance changes before and after drug administration.

4.2 Memory Card Score Distribution Before and After Treatment

Figure 3 shows the distribution of **memory card scores before and after treatment** across drug types.

1. Before treatment, the scores are relatively high across all groups, with Paracetamol and Placebo showing slightly higher medians than the others.
2. After treatment, the distributions remain similar, though there is a slight increase in spread for Aspirin, Paracetamol, and Placebo.
3. There is a slight decrease in the IQR of Tramadol.
4. Outliers are present in all groups, indicating some variability in memory card performance across individuals.

5 Assumptions

5.1 Model

$$\text{memory\_game\_score}_i = \beta_0 + \beta_1 \cdot \text{drug}_i + \beta_2 \cdot \text{dosage\_level}_i + \beta_3 \cdot (\text{drug}_i \times \text{dosage\_level}_i) + \varepsilon_i$$

Where:

- β_0 is the intercept.
- β_1, β_2, and β_3 are coefficients for the predictors and interaction term.

Table 5: Regression Results for Memory Game Score

term	estimate	std.error	statistic	p.value
(Intercept)	60.020000	2.839371	21.1384816	0.0000000
drugParacetamol	1.326667	4.015478	0.3303883	0.7414048
drugPlacebo	-3.053333	4.015478	-0.7603911	0.4477929
drugTramadol	7.416667	4.015478	1.8470198	0.0660176
dosage_levelHigh	2.180000	4.015478	0.5428993	0.5877203
drugParacetamol:dosage_levelHigh	-1.290000	5.678743	-0.2271630	0.8204971
drugPlacebo:dosage_levelHigh	6.516667	5.678743	1.1475545	0.2523345
drugTramadol:dosage_levelHigh	-4.880000	5.678743	-0.8593451	0.3910372

Table 6: Model Fit Statistics for Memory Game Score

r.squared	adj.r.squared	sigma	statistic	p.value	df	logLik	AIC	BIC	deviance	df.residual	nobs
0.0398318	0.0108612	15.55188	1.374906	0.216744	7	-995.0806	2008.161	2039.487	56111.73	232	240

- ε_i is the random error term.

$$Y_{ijk} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + \varepsilon_{ijk}$$

Where:

- Y_{ijk}: Memory score
- μ: Overall mean
- α_i: Effect of the i^{th} drug
- β_j: Effect of the j^{th} dosage level
- $(\alpha\beta)_{ij}$: Interaction effect between drug and dosage
- $\varepsilon_{ijk} \sim \mathcal{N}(0, \sigma^2)$: Random error

6 Analysis

The method of two-way ANOVA is used to estimate the mean of a memory game score changes according to the levels of two categorical variables that is drug and dosage level. The research question explores if there is an interaction effect between at least one of the types of pain

Table 7: Two-Way ANOVA Results for Memory Game Score

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
drug	3	1000.7542	333.5847	1.379242	0.2498211
dosage_level	1	308.2667	308.2667	1.274562	0.2600786
drug:dosage_level	3	1018.7310	339.5770	1.404018	0.2423452
Residuals	232	56111.7280	241.8609	NA	NA

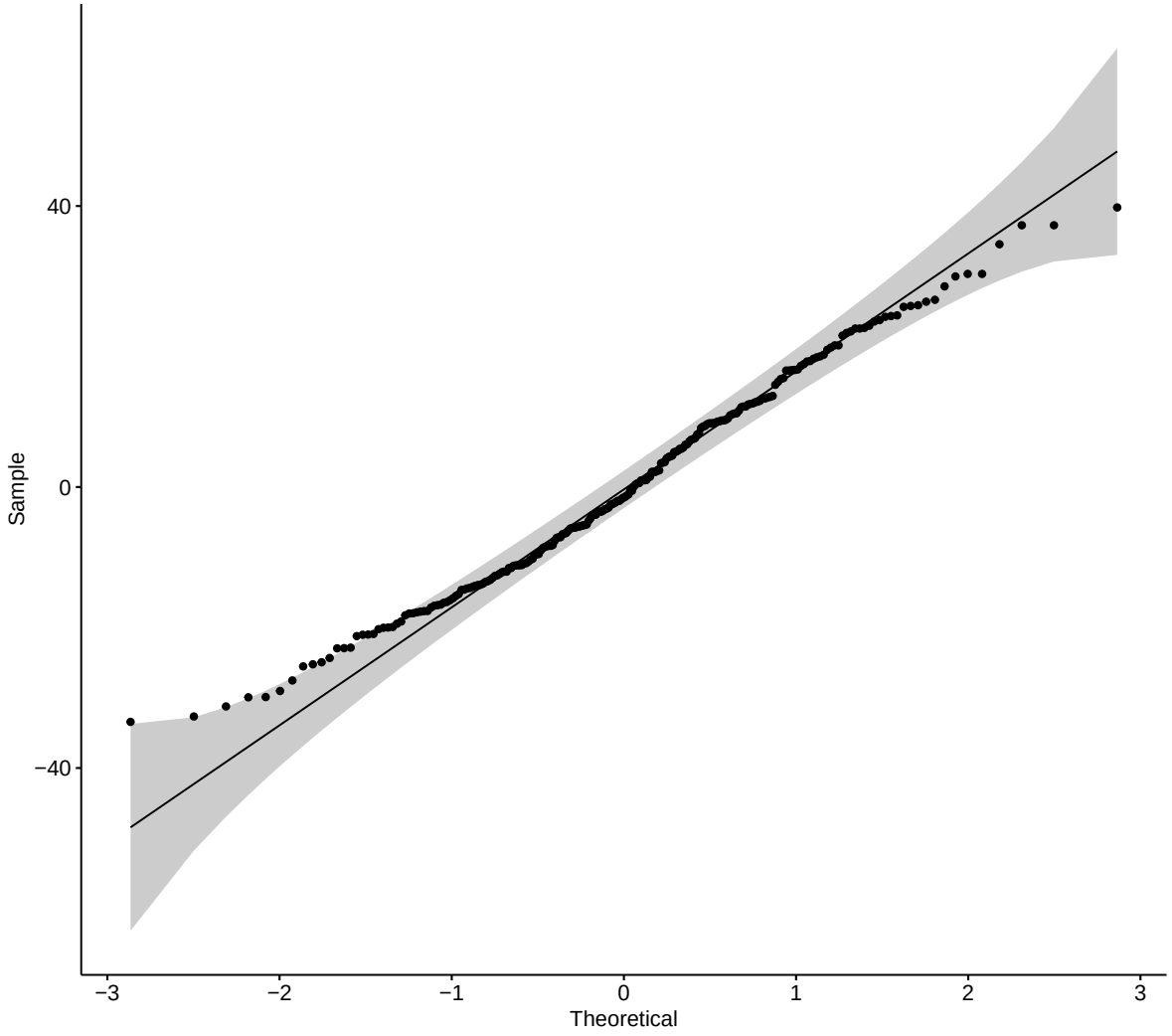


Figure 4: Q-Q Plot of Residuals

Table 8: Shapiro-Wilk Test for Normality

	Statistic	P_Value	Method
W	0.9886	0.0555	Shapiro-Wilk normality test

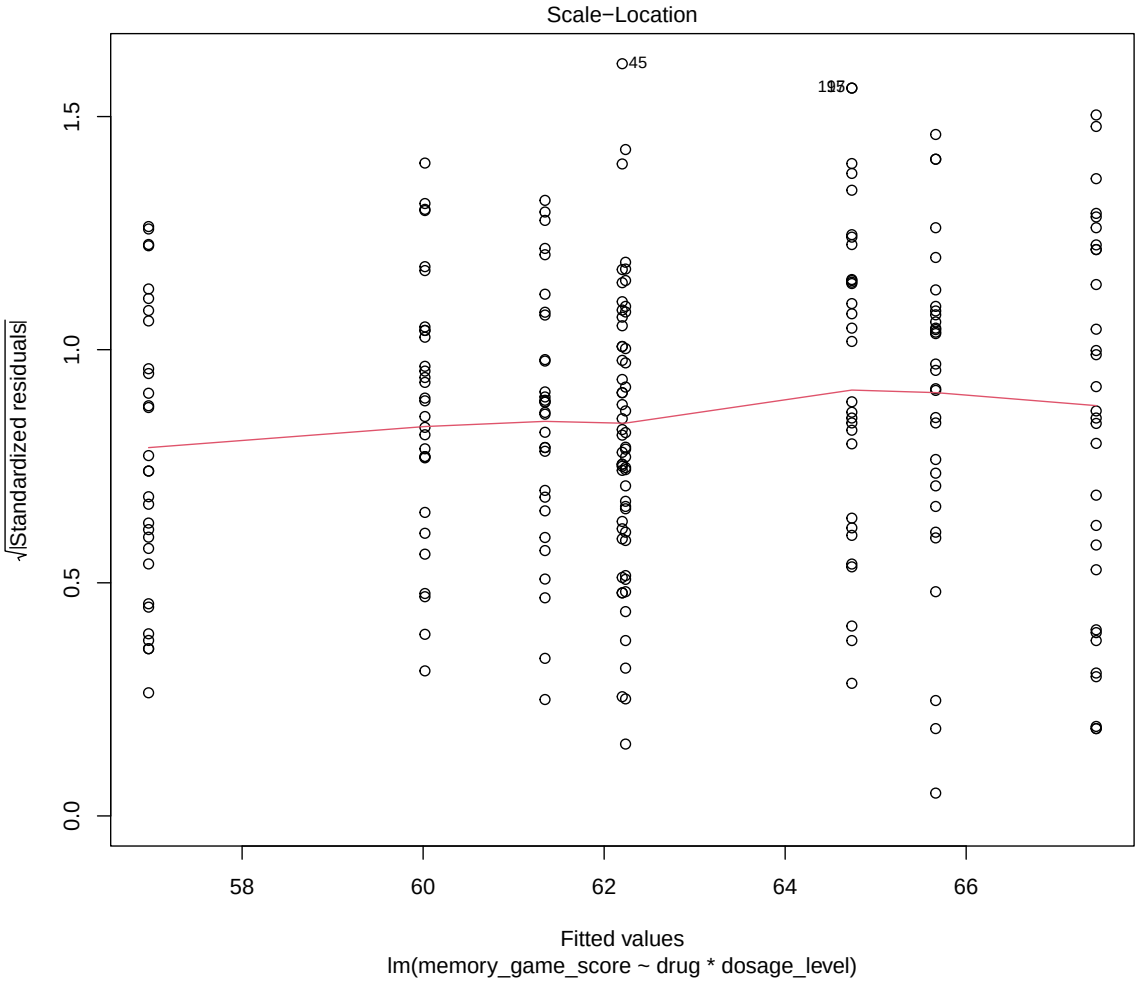


Figure 5: Q-Q Plot of Residuals

Table 9: Bartlett's Test for Homogeneity of Variance

	Statistic	DF	P_Value	Method
Bartlett's K-squared	7.9776	7	0.3346	Bartlett test of homogeneity of variances

reliever and dosage level on the improvement in memory task performance. We verified the assumption of the two-way ANOVA model as seen from graph normality, using Q-Q plot. The Shapiro-Wilk Test confirms a p-value = 0.05553, so we fail to reject the null hypothesis and the result confirms that the dataset is normally distributed.
Our second assumption of Homogeneity of Variance is verified by the p-value = 0.3346 from the Bartlett test, which is greater than 0.05. Due to this, we fail to reject the null hypothesis. Thirdly, for our two-way ANOVA model, the different combinations of pain reliever type and dosage levels were randomly assigned to all participants, in random order. The two-way ANOVA factorial design involves the linear regression model followed by the ANOVA model. The model uses the reference (baseline) group which is Aspirin (Drug) & High (Dosage level). The regression model from the 'table' shows the intercept(beta_0) which represents the predicted mean of memory game score for participants receiving high dosage of aspirin is 62.20 and the p-value = 0.00000 indicates the intercept is statistically significant. The variance explained by the model is R^2 = 0.03983, approximately 4% of the response variable. And the p-value = 0.2167 of the model can be interpreted as not statistically significant

7 Discussion

7.1 Interpretation of Results

The two-way ANOVA analysis revealed no statistically significant main effects of drug type ($p = 0.25$) or dosage level ($p = 0.26$) on memory game scores. Similarly, the interaction effect between drug type and dosage level was not significant ($p = 0.24$). These results suggest that neither the type of pain reliever (Aspirin, Paracetamol, Tramadol, or Placebo) nor its dosage (low vs. high) had a meaningful impact on cognitive retention in this study. The lack of significance persisted even after accounting for age as a confounding variable, which was controlled through participant stratification into three balanced groups (18–34, 35–50, and 50+ years).

7.1.1 Exploratory Observations

Despite the absence of statistical significance, exploratory insights emerged:
1. **Paracetamol** showed the largest mean improvement in memory game scores (+1.33 points, Table 5), though this effect was not robust enough to reject the null hypothesis ($p = 0.74$).
2. **Tramadol** exhibited higher median memory scores both before and after treatment compared to other drugs (Figure 1). However, its high-dosage group saw a slight decline in mean scores (−4.88 points), hinting at a potential dosage-dependent response that warrants further investigation.
3. The **Placebo** group consistently underperformed relative to active drugs in median scores (Figure 1), though this difference was not statistically significant.

8 Limitations

Our study is overall focused on memory, which may have links to one's education and IQ level as they are all related to mental function and cognition. In the future, we could test everyone for IQ scores and their highest level of education – these two nuisance variables can be taken care of by using the four principles of experimental design. Additionally, we used 30 observations for each treatment group which may not be large enough. We can increase this number for future studies. To add on, not all participants were in pain, so the efficacy of the improvement of pain killers may be biased and using a virtual population may not ensure whether this aspect could be captured. Lastly, cognitive retention was measured immediately post-treatment – the long term impacts are not yet explored. To improve our study, we can only consider individuals of equal pain levels before the study to ensure a reduction of bias. Additionally, carrying the experiment out in the long-term would help with understanding the effects of painkillers and dosages on memory.

9 Conclusion

This study found no conclusive evidence that pain relievers or their dosages significantly affect cognitive retention. However, the exploratory trends observed, particularly with Paracetamol and Tramadol, highlight the need for larger-scale studies to investigate subtle or context-dependent effects. Future research could incorporate longitudinal designs, broader age-specific analyses, and alternative cognitive metrics to deepen understanding of painkillers' cognitive implications.

10 References

(Ha, 2010) https://journals.lww.com/ejanaesthesiology/FullText/2010/02000/Amitriptyline_rather_than_lorn

11 Appendix

```
library(tidyverse)
library(janitor)
library(here)
library(lubridate)
library(patchwork)
library(arrow)
library(dplyr)
library(knitr)
library(performance)
library(modelsummary)
library(kableExtra)
library(performance)
library(ggpubr)


clean_data <- read.csv(here("data", "analysis_data", "clean_data.csv"))
```

```
# Compute statistics for Memory Game Score
mean_game <- mean(clean_data$memory_game_score, na.rm = TRUE)
median_game <- median(clean_data$memory_game_score, na.rm = TRUE)
sd_game <- sd(clean_data$memory_game_score, na.rm = TRUE)
iqr_game <- IQR(clean_data$memory_game_score, na.rm = TRUE)

# Compute statistics for Memory Cards Score
mean_cards <- mean(clean_data$memory_cards_score, na.rm = TRUE)
median_cards <- median(clean_data$memory_cards_score, na.rm = TRUE)
sd_cards <- sd(clean_data$memory_cards_score, na.rm = TRUE)
iqr_cards <- IQR(clean_data$memory_cards_score, na.rm = TRUE)

# Combine into a summary table
summary_table <- data.frame(
  Statistic = c("Mean", "Median", "SD", "IQR"),
  `Memory Game Score` = c(mean_game, median_game, sd_game, iqr_game),
  `Memory Cards Score` = c(mean_cards, median_cards, sd_cards, iqr_cards)
)

colnames(summary_table) <- c("Statistic", "Memory Game Score", "Memory Cards Score")
```

```r
# Display table

kable(summary_table, format = "latex", booktabs = TRUE)
```

Statistic	Memory Game Score	Memory Cards Score
Mean	62.57583	7.945833
Median	61.50000	9.000000
SD	15.63703	1.960164
IQR	23.35000	2.000000

```r
drug_counts <- table(clean_data$drug)

# percentages
drug_percentages <- prop.table(drug_counts) * 100

#  summary dataframe
drug_summary <- data.frame(
  Drug = names(drug_counts),
  Count = as.numeric(drug_counts),
  Percentage = round(as.numeric(drug_percentages), 2)
)

# Display table
kable(drug_summary, format = "latex", booktabs = TRUE)
```

Drug	Count	Percentage
Aspirin	60	25
Paracetamol	60	25
Placebo	60	25
Tramadol	60	25

```r
dosage_counts <- table(clean_data$dosage_level)

# percentage for each dosage level
dosage_percentages <- prop.table(dosage_counts) * 100

# summary dataframe
dosage_summary <- data.frame(
  Dosage = names(dosage_counts),
```

```
  Count = as.numeric(dosage_counts),
  Percentage = round(as.numeric(dosage_percentages), 2)
)


# Display table
kable(dosage_summary, booktabs = TRUE, row.names = FALSE)
```

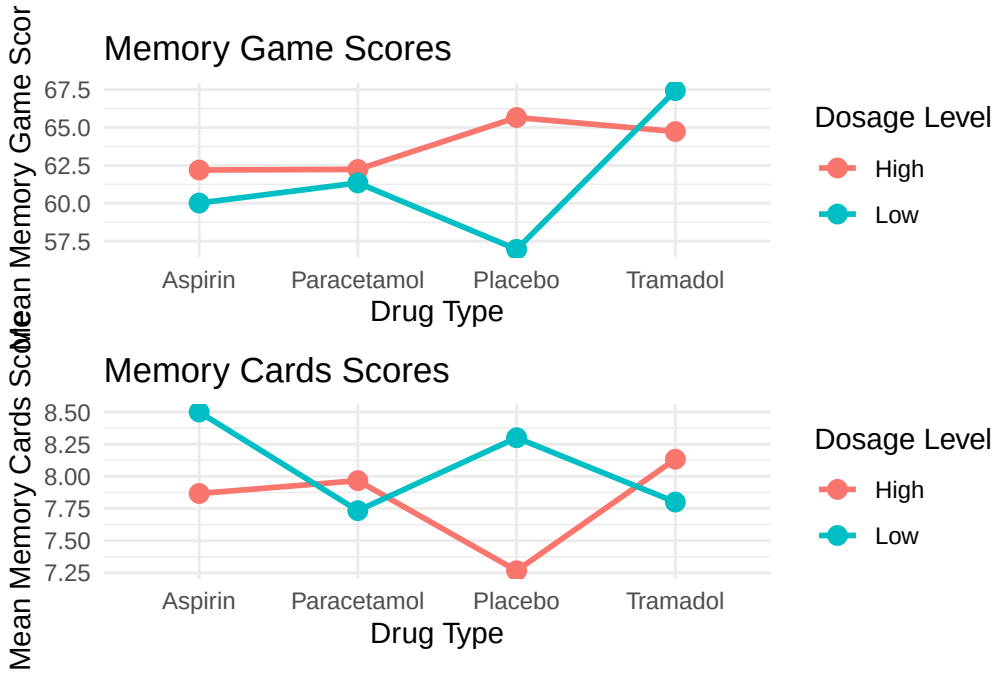
Dosage	Count	Percentage
High	120	50
Low	120	50

```
age_counts <- table(clean_data$age_group)

# percentages for each age group
age_percentages <- prop.table(age_counts) * 100

# summary dataframe
age_summary <- data.frame(
  Age_Group = names(age_counts),
  Count = as.numeric(age_counts),
  Percentage = round(as.numeric(age_percentages), 2)
)

# Display table
kable(age_summary, booktabs = TRUE, row.names = FALSE)
```

Age_Group	Count	Percentage
18-34	80	33.33
35-50	80	33.33
50+	80	33.33

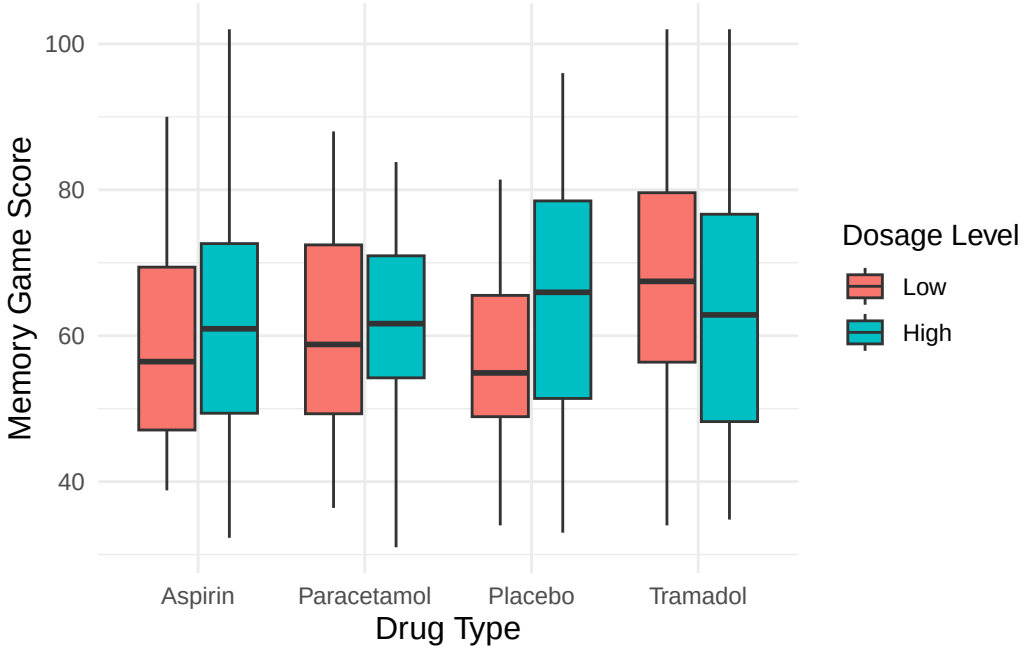
```
p1 <- ggplot(clean_data, aes(x = drug, y = memory_game_score, color = dosage_level, group
  stat_summary(fun = mean, geom = "point", size = 3) +
  stat_summary(fun = mean, geom = "line", size = 1) +
  labs(title = "Memory Game Scores",
       x = "Drug Type",
       y = "Mean Memory Game Score",
```

```
       color = "Dosage Level") +
  theme_minimal()

# Interaction plot for Memory Cards Scores
p2 <- ggplot(clean_data, aes(x = drug, y = memory_cards_score, color = dosage_level, group
  stat_summary(fun = mean, geom = "point", size = 3) +
  stat_summary(fun = mean, geom = "line", size = 1) +
  labs(title = "Memory Cards Scores",
       x = "Drug Type",
       y = "Mean Memory Cards Score",
       color = "Dosage Level") +
  theme_minimal()

# Combine the two plots vertically
combined_plot <- p1 / p2
combined_plot
```

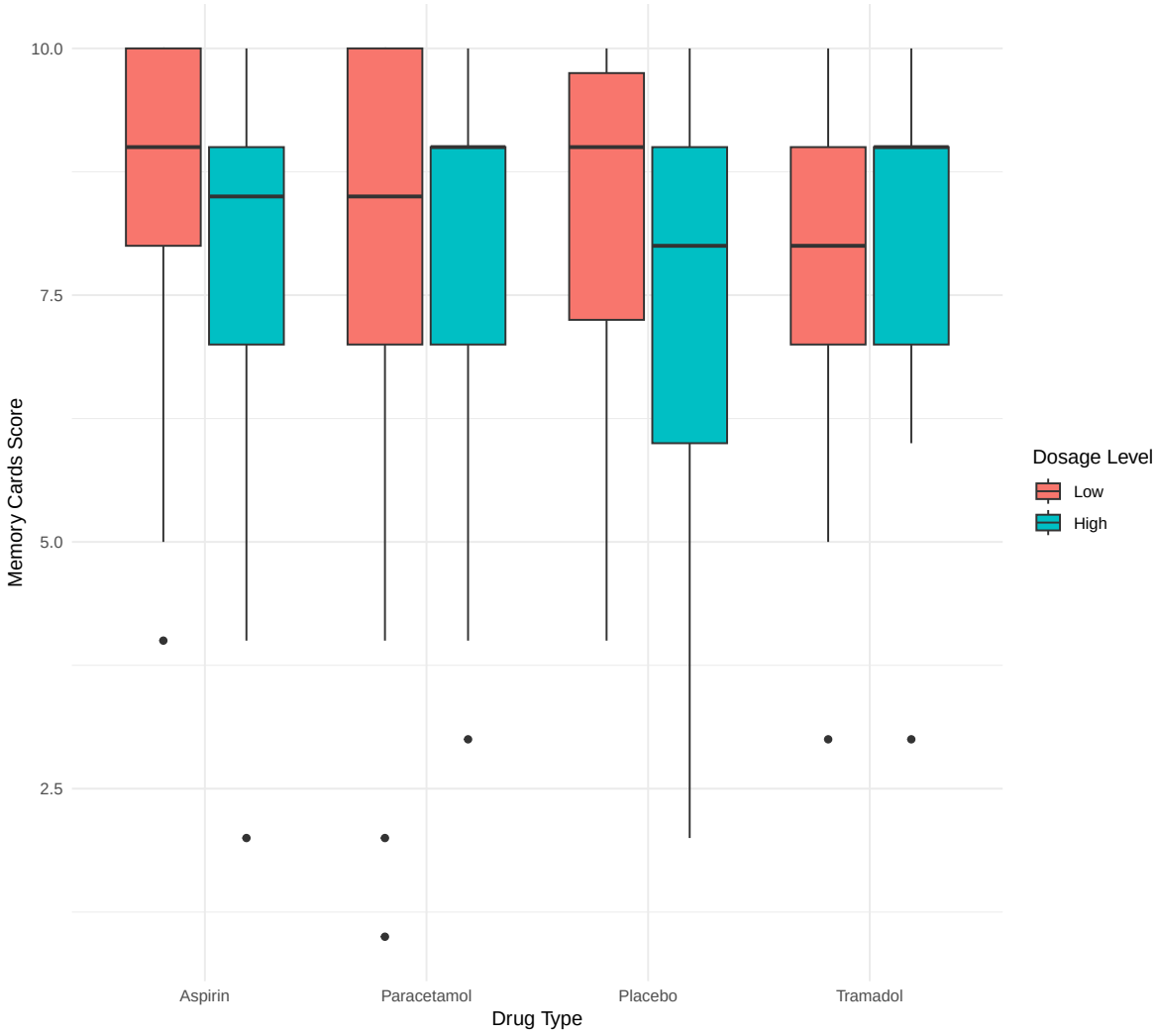



```
clean_data$dosage_level <- factor(clean_data$dosage_level, levels = c("Low", "High"))

# Boxplot of Memory Game Scores by Drug, colored by Dosage Level
ggplot(clean_data, aes(x = drug, y = memory_game_score, fill = dosage_level)) +
```

```
  geom_boxplot() +
  labs(
    x = "Drug Type",
    y = "Memory Game Score",
    fill = "Dosage Level"
  ) +
  theme_minimal() +
  theme(
    plot.title = element_text(size = 14, face = "bold"),
    axis.title = element_text(size = 12)
  )
```




```
ggplot(clean_data, aes(x = drug, y = memory_cards_score, fill = dosage_level)) +
  geom_boxplot() +
  labs(
    x = "Drug Type",
    y = "Memory Cards Score",
    fill = "Dosage Level"
  ) +
  theme_minimal()
```




```r
# References: https://cran.r-project.org/web/packages/broom/vignettes/broom.html

library(broom)

# Regression Model results
anova_model <- lm(memory_game_score ~ drug * dosage_level, data = clean_data)

model_tidy <- tidy(anova_model)

kable(model_tidy, format = "latex", booktabs = TRUE)
```

r.squared	adj.r.squared	sigma	statistic	p.value	df	logLik	AIC	BIC	deviance	df.residual	nobs
0.0398318	0.0108612	15.55188	1.374906	0.216744	7	-995.0806	2008.161	2039.487	56111.73	232	240

term	estimate	std.error	statistic	p.value
(Intercept)	60.020000	2.839371	21.1384816	0.0000000
drugParacetamol	1.326667	4.015478	0.3303883	0.7414048
drugPlacebo	-3.053333	4.015478	-0.7603911	0.4477929
drugTramadol	7.416667	4.015478	1.8470198	0.0660176
dosage_levelHigh	2.180000	4.015478	0.5428993	0.5877203
drugParacetamol:dosage_levelHigh	-1.290000	5.678743	-0.2271630	0.8204971
drugPlacebo:dosage_levelHigh	6.516667	5.678743	1.1475545	0.2523345
drugTramadol:dosage_levelHigh	-4.880000	5.678743	-0.8593451	0.3910372

```
model_glance <- glance(anova_model)
kable(model_glance, format = "latex", booktabs = TRUE) %>%
   kable_styling(latex_options = "scale_down")
```

```
# Two way ANOVA result
anova_result <- anova(anova_model)

anova_table_df <- as.data.frame(anova_result)

kable(anova_table_df, format = "latex", booktabs = TRUE)
```

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
drug	3	1000.7542	333.5847	1.379242	0.2498211
dosage_level	1	308.2667	308.2667	1.274562	0.2600786
drug:dosage_level	3	1018.7310	339.5770	1.404018	0.2423452
Residuals	232	56111.7280	241.8609	NA	NA

```
# Normality Check
ggqqplot(residuals(anova_model))
```

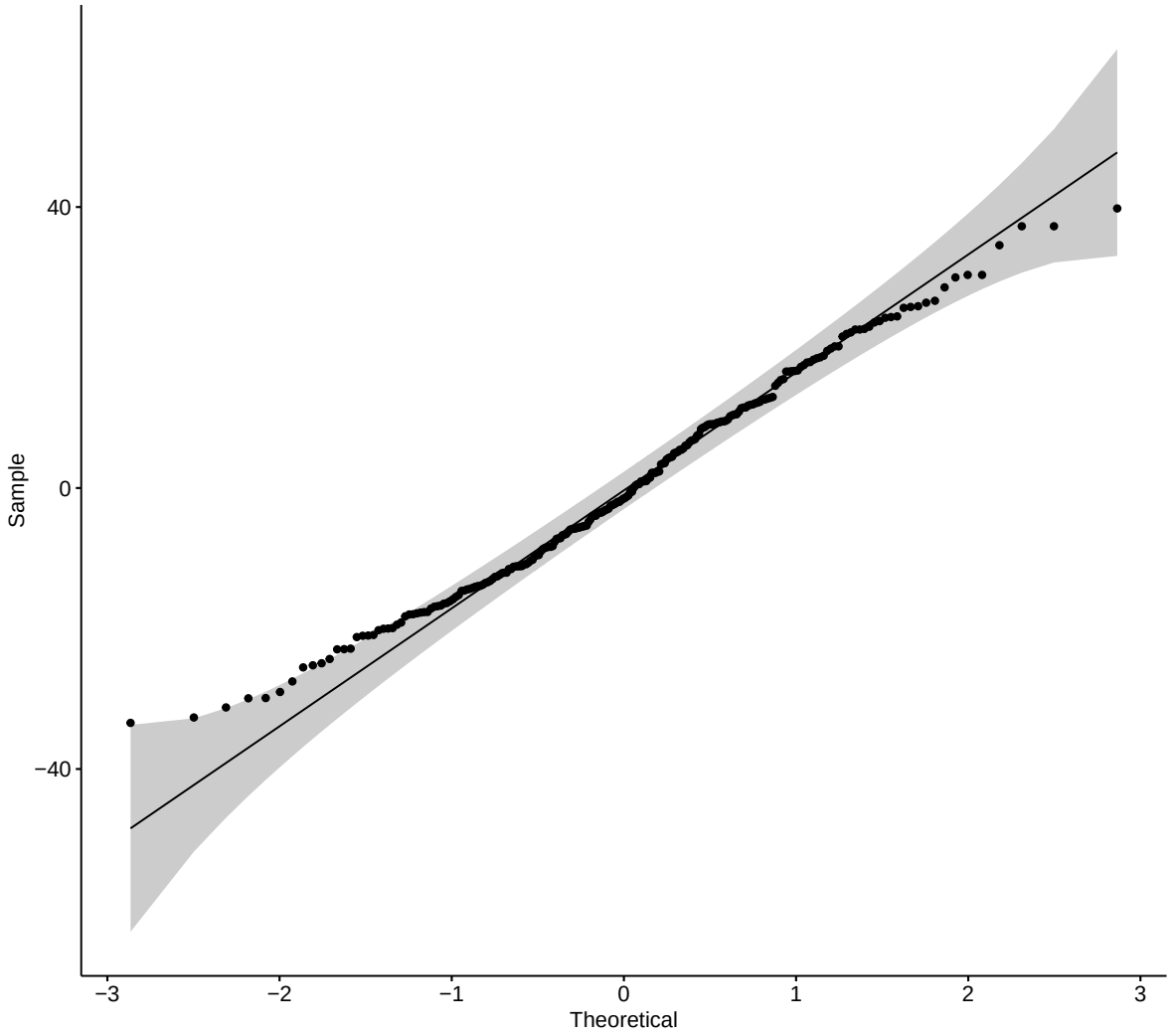


Figure 6: Q-Q Plot of Residuals

```r
# Shapiro-Wilk Normality Test
shapiro_test <- shapiro.test(residuals(anova_model))
shapiro_table <- data.frame(
  Statistic = round(shapiro_test$statistic, 4),
  P_Value = round(shapiro_test$p.value, 4),
  Method = shapiro_test$method
)

kable(shapiro_table, format = "latex", booktabs = TRUE)
```

	Statistic	P_Value	Method
W	0.9886	0.0555	Shapiro-Wilk normality test

```
plot(anova_model, which = 3)
```