Synergistic Neural Circuits for Novelty and Goal-Directed Behavior in the Human Brain

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Methods

See Elliott et al., 2024 (doi: https://doi.org/10.1101/2024.12.16.628816) https://www.biorxiv.org/content/10.1101/2024.12.16.628816v1.abstract

##Participants Participants were recruited for this experiment as healthy control subjects in a larger study examining psychosis risk. The final sample with usable task data and structural scans included 77 healthy, right handed participants. Informed consent was obtained from each participant in a manner approved by Temple University's Institutional Review Board. Procedure The protocol and materials used in this experiment were based on previously published work (Murty et al., 2013, 2017). In brief, the task involved two phases: a familiarization phase and a novelty exposure phase (Figure 2). Before scanning, participants completed the familiarization phase in which 120 outdoor scene images were shown one at a time while participants completed a continuous recognition task. 80 of the scene images were repeated 6 times ("familiar"), while 40 were presented just once (foils), with the repetition aimed at familiarizing participants with these 80 stimuli. Approximately 20 minutes later, participants entered the MRI scanner for the novelty exposure phase. During this phase participants viewed a sequence of outdoor scene images, including novel images that had never been seen before, as well as the familiar images seen previously during the familiarization phase (Figure 2). In the novelty exposure phase, participants completed a target detection task in which they were instructed to press a button every time a specific outdoor scene image ("target") was presented. The target scene image was repeated 40 times, intermixed with the 80 novel scene images and 80 familiar scene images. All trials were presented in a randomized order.

fMRI Data Analysis

Detailed procedures and analysis methods for the fMRI data were employed to ensure rigorous and reproducible results. fMRI data were analyzed using AFNI version 24.0.06. Univariate Analysis During Novelty Exposure Task To measure BOLD response during the novelty exposure phase of the task, we computed a GLM with regressors for each condition (novel, familiar, target) for each block (40 of each). A block was defined as the trials preceding a target (Figure 2). Individual events were convolved with a double-gamma hemodynamic response (HDR) function. Noise-related measures were also added as additional nuisance regressors. Noise-related measures were computed for average signal in CSF and white matter masks (generated using FSL's FAST segmentation tool), time points of excessive head motion (identified using FSL's motion outliers tool), as well as the six head motion parameters and their first derivatives. The resulting contrasts were registered to standard MNI space, from which we then extracted the b parameters from each condition, (e.g., novel, familiar, target greater than baseline) for each block, for each participant. We examined univariate responses across our ROIs of interest, in the hippocampus, VTA, and limbic striatum, and dlPFC regions.

```r
require(lmerTest)
```

```
## Loading required package: lmerTest
```

```
##
## Attaching package: 'lmerTest'
```

```
## The following object is masked from 'package:lme4':
##
##     lmer
```

```
## The following object is masked from 'package:stats':
##
##     step
```

```r
MAP_Data <- read.csv("/Users/tup45568/Library/CloudStorage/OneDrive-TempleUniversity/0.Experiments/Map_

# Create a new dataframe by selecting columns that start with "Novel"
novel_columns <- grep("^Novel", names(MAP_Data), value = TRUE)

# Drop rows with NA in these columns
MAP_Data_NoNA <- MAP_Data[complete.cases(MAP_Data[ , novel_columns]), ]

#Analysis 1: Novelty_Ant_HPC predict Target VTA, Novelty_dlPFC predicting Target VTA
basemodel <- lmer(Target_VTA ~ 1 + (1 | Subject), data = MAP_Data_NoNA)
HPC_regression <- lmer(Target_VTA ~  Novel_HPC + (1 | Subject), data = MAP_Data_NoNA)
summary(HPC_regression)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Novel_HPC + (1 | Subject)
##    Data: MAP_Data_NoNA
##
## REML criterion at convergence: -1979.6
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.7180 -0.6557 -0.0092  0.6152  4.1239
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0003666 0.01915
##  Residual             0.0200796 0.14170
## Number of obs: 1889, groups:  Subject, 77
##
## Fixed effects:
##              Estimate Std. Error        df t value Pr(>|t|)
## (Intercept) 2.765e-02  3.928e-03 7.674e+01   7.038 7.16e-10 ***
## Novel_HPC   5.076e-02  1.787e-02 1.862e+03   2.840  0.00456 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## Correlation of Fixed Effects:
##           (Intr)
## Novel_HPC -0.050
```

```
anova(basemodel, HPC_regression)
```

```
## refitting model(s) with ML (instead of REML)
```

```
## Data: MAP_Data_NoNA
## Models:
## basemodel: Target_VTA ~ 1 + (1 | Subject)
## HPC_regression: Target_VTA ~ Novel_HPC + (1 | Subject)
##                npar     AIC     BIC logLik deviance Chisq Df Pr(>Chisq)
## basemodel         3 -1981.0 -1964.4 993.50  -1987.0
## HPC_regression    4 -1987.1 -1964.9 997.54  -1995.1 8.062  1    0.00452 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

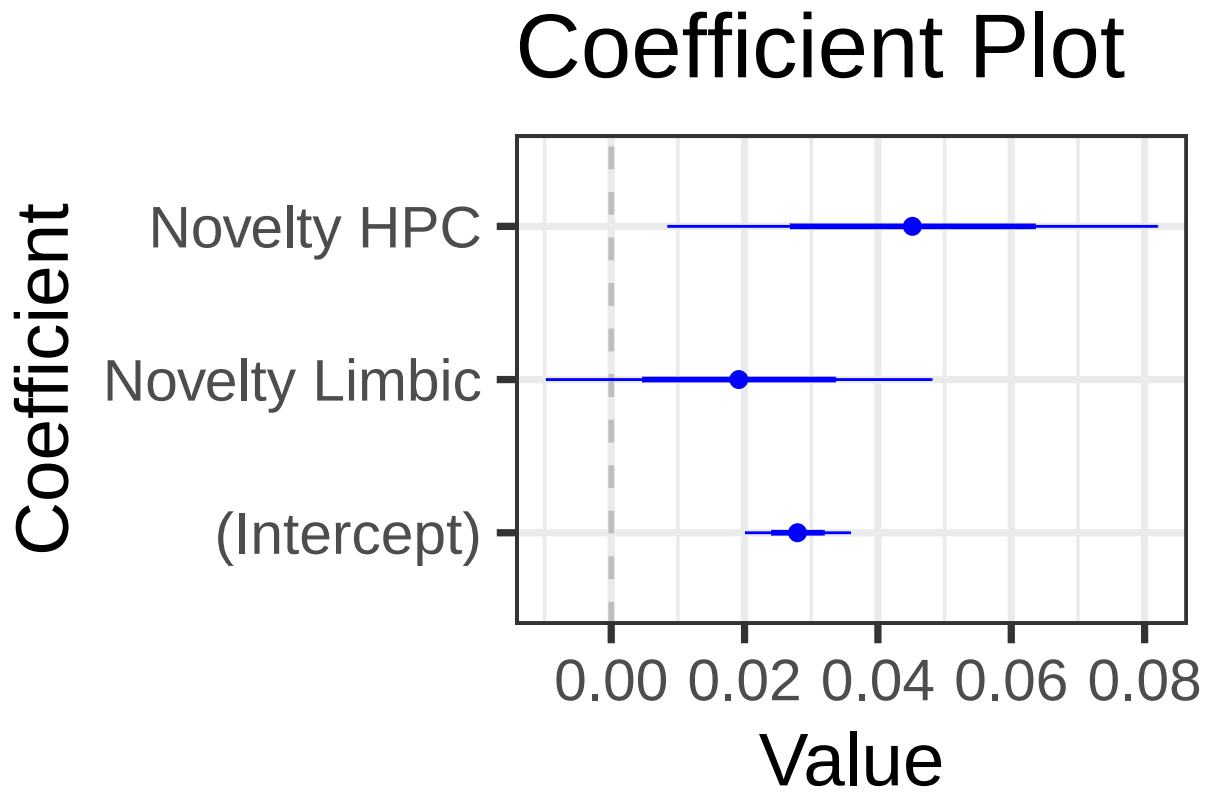
```
#Analysis 2: Effect of Adding NAc
HPC_Limbic_fullregression <- lmer(Target_VTA ~ Novel_Limbic + Novel_HPC +(1 | Subject), data = MAP_Data_
summary(HPC_Limbic_fullregression)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Novel_Limbic + Novel_HPC + (1 | Subject)
##    Data: MAP_Data_NoNA
##
## REML criterion at convergence: -1974.7
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.7166 -0.6635 -0.0116  0.6168  4.1627
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0003661 0.01913
##  Residual             0.0200719 0.14168
## Number of obs: 1889, groups:  Subject, 77
##
## Fixed effects:
##               Estimate Std. Error        df t value Pr(>|t|)
## (Intercept)  2.794e-02  3.933e-03 7.718e+01   7.104 5.22e-10 ***
## Novel_Limbic 1.913e-02  1.446e-02 1.871e+03   1.323    0.186
## Novel_HPC    4.517e-02  1.836e-02 1.862e+03   2.461    0.014 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Nvl_Lm
## Novel_Limbc  0.057
## Novel_HPC   -0.062 -0.230
```

```r
anova(HPC_regression, HPC_Limbic_fullregression)
```

```
## refitting model(s) with ML (instead of REML)

## Data: MAP_Data_NoNA
## Models:
## HPC_regression: Target_VTA ~ Novel_HPC + (1 | Subject)
## HPC_Limbic_fullregression: Target_VTA ~ Novel_Limbic + Novel_HPC + (1 | Subject)
##                           npar     AIC     BIC logLik deviance  Chisq Df
## HPC_regression               4 -1987.1 -1964.9 997.54  -1995.1
## HPC_Limbic_fullregression    5 -1986.8 -1959.1 998.41  -1996.8 1.7526  1
##                           Pr(>Chisq)
## HPC_regression
## HPC_Limbic_fullregression     0.1856
```

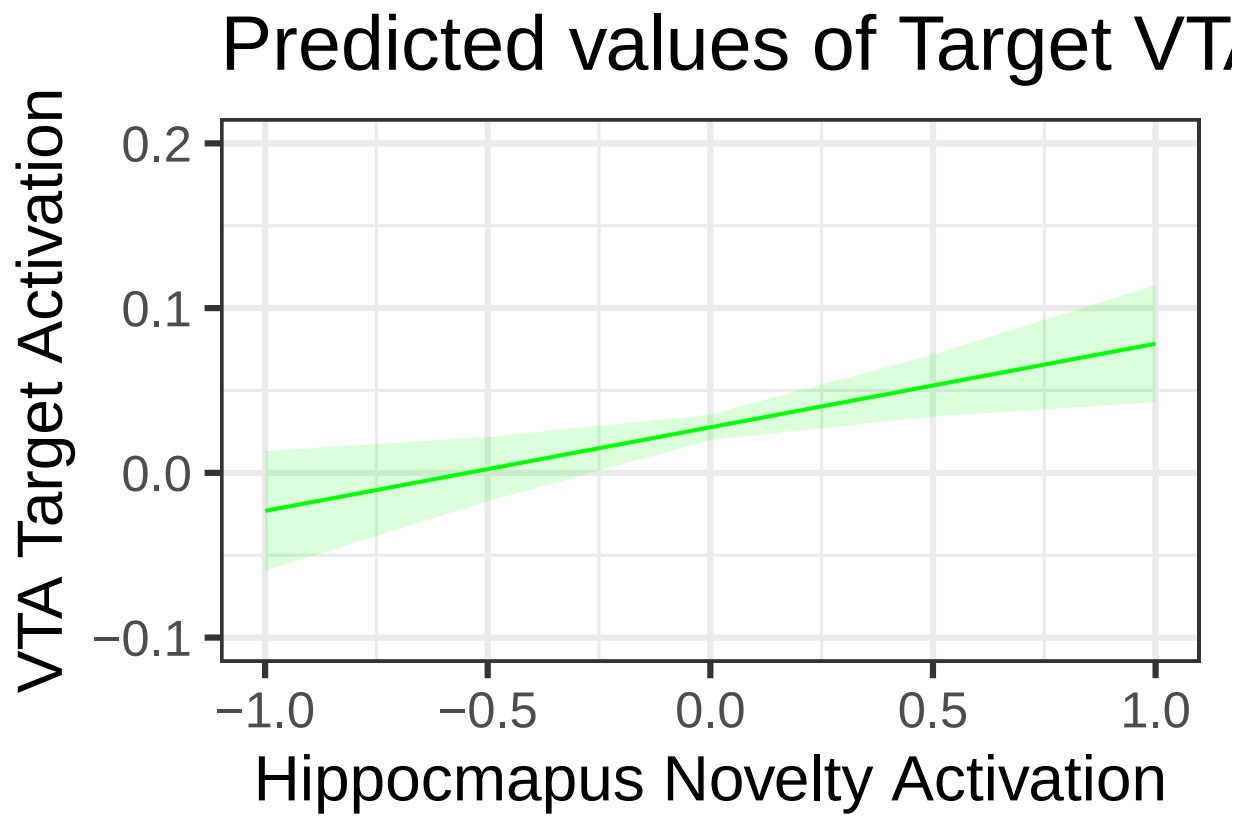
```r
plot_ALL_HPC_Novelty <- coefplot(HPC_Limbic_fullregression)
# Modify y-axis labels
plot_ALL_HPC_Novelty <- plot_ALL_HPC_Novelty +
  scale_y_discrete(labels = c("(Intercept)", "Novelty Limbic", "Novelty HPC")) +
  theme(text = element_text(size = 28)) +
  theme_bw(base_size = 28) +
  scale_x_continuous(labels = scales::number_format(accuracy = 0.01))

print(plot_ALL_HPC_Novelty)
```



```r
coefs <- data.frame(coef(summary(HPC_regression)))

fm1 <- lmer("Target_VTA ~ Novel_HPC + (1 | Subject)", data = MAP_Data_NoNA)

x = sjPlot::plot_model(fm1, type="eff", xlim =-1, ylim(-0.5, 0.5), colors = "green") + theme_bw(base_si
  labs(x = "Hippocmapus Novelty Activation", y = "VTA Target Activation")
x = x + ylim(-0.1, 0.2)
```

```
## Scale for y is already present.
## Adding another scale for y, which will replace the existing scale.
```

```r
print(x)
```




```r
#Analysis 3: dlPFC Target Activation Predicting VTA Target Activation

# Identify columns that start with "Target"
target_columns <- grep("^Target", names(MAP_Data), value = TRUE)

# Drop rows with NA in these columns only
MAP_Data_NoNA_Target <- MAP_Data[complete.cases(MAP_Data[ , target_columns]), ]


#dlPFC regression
basemodel <- lmer(Target_VTA ~ 1 + (1 | Subject), data = MAP_Data_NoNA_Target)
```

```
dlPFC_regression <- lmer(Target_VTA ~  Target_dlPFC + (1 | Subject), data = MAP_Data_NoNA_Target)
summary(dlPFC_regression)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Target_dlPFC + (1 | Subject)
##    Data: MAP_Data_NoNA_Target
##
## REML criterion at convergence: -3259.7
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.9653 -0.6469 -0.0137  0.5904  4.3454
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0001667 0.01291
##  Residual             0.0200748 0.14169
## Number of obs: 3080, groups:  Subject, 77
##
## Fixed effects:
##               Estimate Std. Error        df t value Pr(>|t|)
## (Intercept)  1.982e-02  2.950e-03 7.628e+01   6.718 2.93e-09 ***
## Target_dlPFC 5.690e-02  1.028e-02 3.061e+03   5.533 3.42e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr)
## Targt_dlPFC -0.049
```

```
anova(basemodel, dlPFC_regression)
```

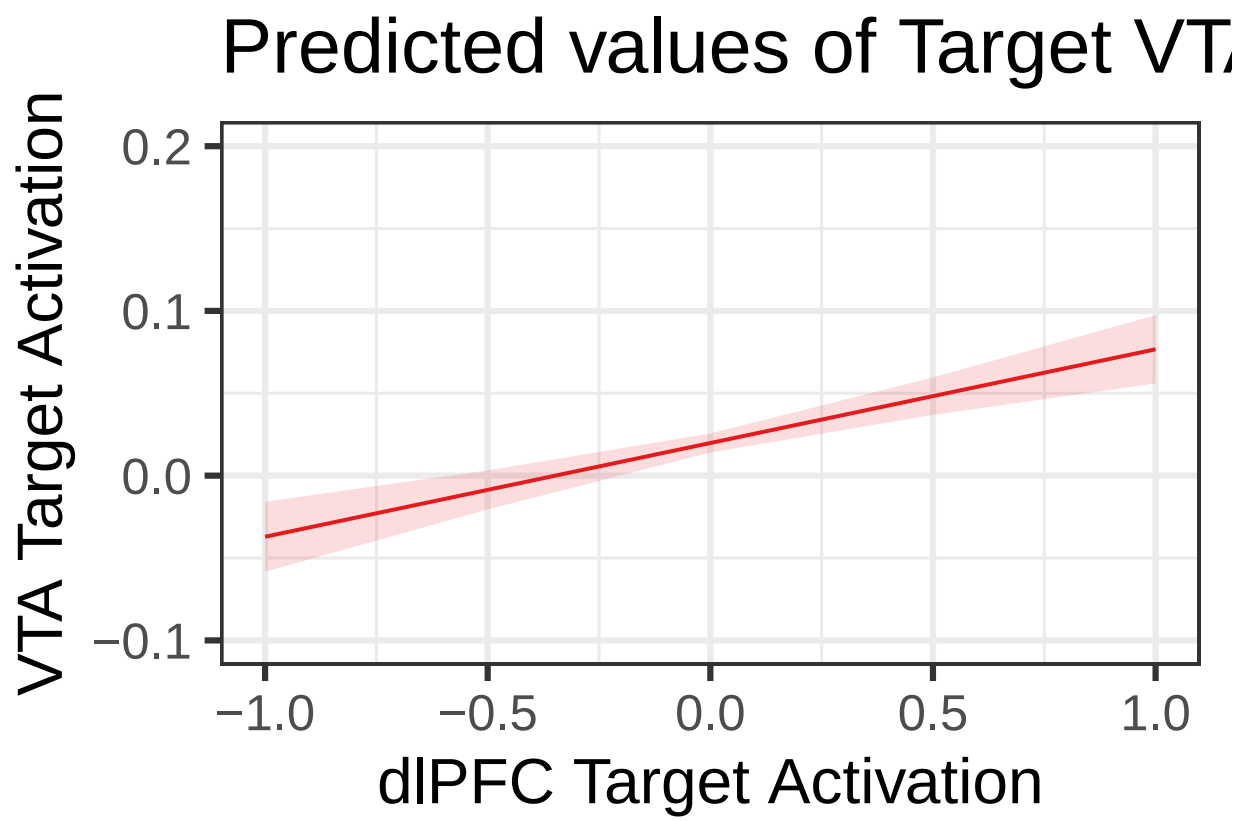
```
## refitting model(s) with ML (instead of REML)

## Data: MAP_Data_NoNA_Target
## Models:
## basemodel: Target_VTA ~ 1 + (1 | Subject)
## dlPFC_regression: Target_VTA ~ Target_dlPFC + (1 | Subject)
##                   npar     AIC     BIC logLik deviance  Chisq Df Pr(>Chisq)
## basemodel            3 -3240.4 -3222.3 1623.2  -3246.4
## dlPFC_regression     4 -3268.8 -3244.7 1638.4  -3276.8 30.436  1   3.45e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
dlPFC_plot <- lmer("Target_VTA ~ Target_dlPFC + (1 | Subject)", data = MAP_Data_NoNA_Target)
x <- sjPlot::plot_model(dlPFC_plot, type="eff", xlim =-1) + theme_bw(base_size = 24) +
  labs(x = "dlPFC Target Activation", y = "VTA Target Activation")
x = x + xlim(-1, 1) + ylim(-0.1, 0.2)
```

```
## Scale for y is already present.
## Adding another scale for y, which will replace the existing scale.
```

```
print(x)
```

```
## Warning: Removed 2 rows containing missing values or values outside the scale range
## (‘geom_line()‘).
```




```
#Analysis 4
set.seed(23)

shuffled_data <- MAP_Data_NoNA %>%
  group_by(Subject) %>%
  mutate(Novel_HPC_shuffled = sample(Novel_HPC))

HPC_regression <- lmer(Target_VTA ~  Novel_HPC_shuffled + (1 | Subject), data = shuffled_data)
summary(HPC_regression)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Novel_HPC_shuffled + (1 | Subject)
##    Data: shuffled_data
##
## REML criterion at convergence: -1971.8
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
```

```
## -3.7621 -0.6479 -0.0061  0.5976  4.2204
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0003831 0.01957
##  Residual             0.0201524 0.14196
## Number of obs: 1889, groups:  Subject, 77
##
## Fixed effects:
##                      Estimate Std. Error        df t value Pr(>|t|)
## (Intercept)         2.811e-02  3.960e-03 7.655e+01   7.097 5.58e-10 ***
## Novel_HPC_shuffled 8.858e-03  1.779e-02 1.870e+03   0.498    0.619
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr)
## Nvl_HPC_shf -0.050
```

```r
# Initialize an empty dataframe to store t-values
t_values_df <- data.frame(iteration = integer(), t_value = numeric())

# Set the number of iterations
num_iterations <- 1000

# Start the loop
for (i in 1:num_iterations) {
  # Shuffle the data
  shuffled_data <- MAP_Data_NoNA %>%
    group_by(Subject) %>%
    mutate(Novel_HPC_shuffled = sample(Novel_HPC))

  # Fit the linear mixed-effects model
  HPC_regression <- lmer(Target_VTA ~ Novel_HPC_shuffled + (1 | Subject), data = shuffled_data)

  # Extract the t-value for the coefficient of interest
  t_value <- summary(HPC_regression)$coefficients["Novel_HPC_shuffled", "t value"]

  # Store the iteration number and t-value in the dataframe
  t_values_df <- rbind(t_values_df, data.frame(iteration = i, t_value = t_value))
}

# Calculate the confidence interval for the t-values
t_value_ci <- quantile(t_values_df$t_value, c(0.025, 0.975))

# Print the confidence interval
print(t_value_ci)
```

```
##      2.5%     97.5%
## -1.606951  2.435685
```

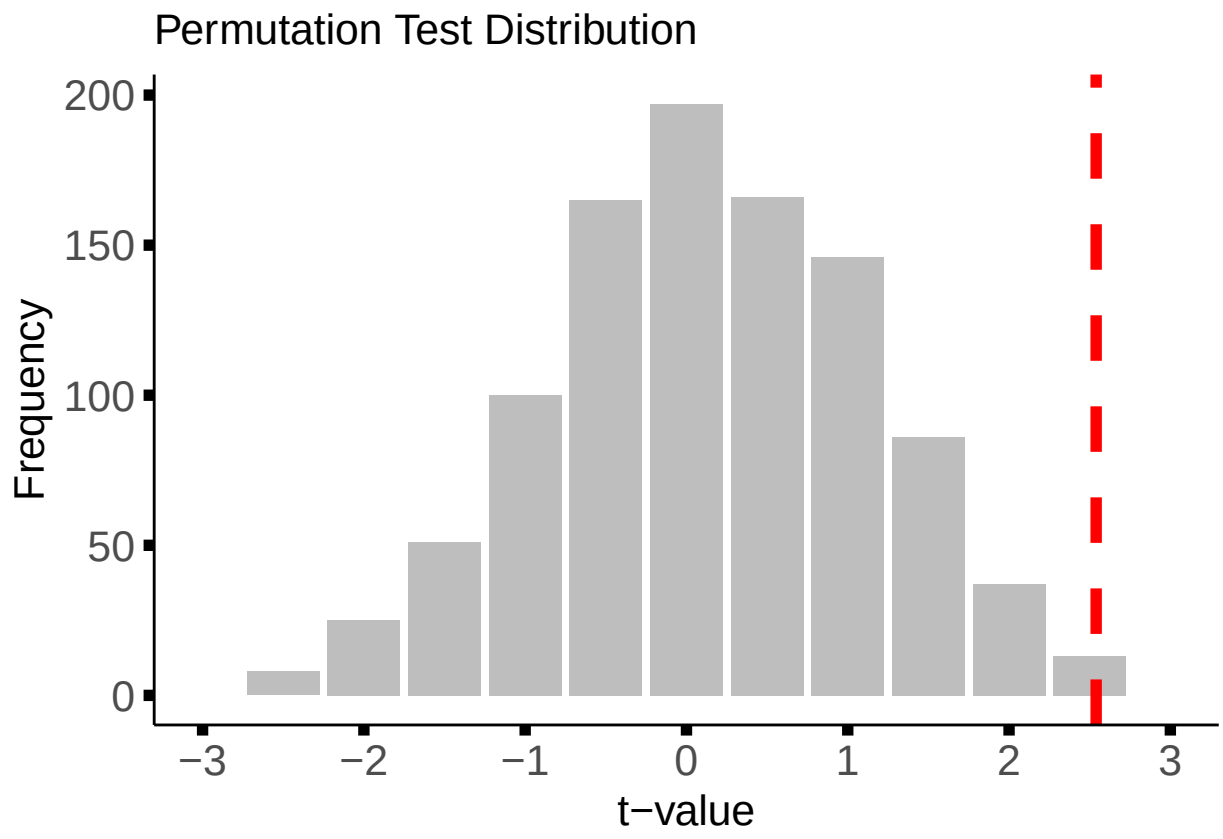
```r
# Create histogram data
h <- hist(t_values_df$t_value, breaks = 20, plot = FALSE)
```

```r
# Create ggplot object
ggplot(data.frame(x = h$breaks[-length(h$breaks)], y = h$counts), aes(x = x, y = y)) +
  geom_bar(stat = "identity", fill = "gray") +
  labs(
    title = "Permutation Test Distribution",
    x = "t-value",
    y = "Frequency"
  ) +
  geom_vline(xintercept = 2.54, linetype = "dashed", color = "red", size = 2) + # Adjusted line positio
  scale_x_continuous(limits = c(-3, 3), breaks = seq(-3, 3, by = 1)) + # Adjusted x-axis limits
  theme_minimal(base_size = 16) +
  theme(
    axis.title = element_text(size = 16),
    axis.text = element_text(size = 16),
    plot.title = element_text(size = 16),
    axis.line = element_line(color = "black", size = 0.5),
    panel.background = element_blank(),
    panel.grid.major = element_blank(),
    panel.grid.minor = element_blank(),
    axis.ticks = element_line(size = 2)  # Adjust tick size
  )
```

```
## Warning: Using ‘size‘ aesthetic for lines was deprecated in ggplot2 3.4.0.
## i Please use ‘linewidth‘ instead.
## This warning is displayed once every 8 hours.
## Call ‘lifecycle::last_lifecycle_warnings()‘ to see where this warning was
## generated.
```

```
## Warning: The ‘size‘ argument of ‘element_line()‘ is deprecated as of ggplot2 3.4.0.
## i Please use the ‘linewidth‘ argument instead.
## This warning is displayed once every 8 hours.
## Call ‘lifecycle::last_lifecycle_warnings()‘ to see where this warning was
## generated.
```

```
## Warning: Removed 3 rows containing missing values or values outside the scale range
## (‘geom_bar()‘).
```



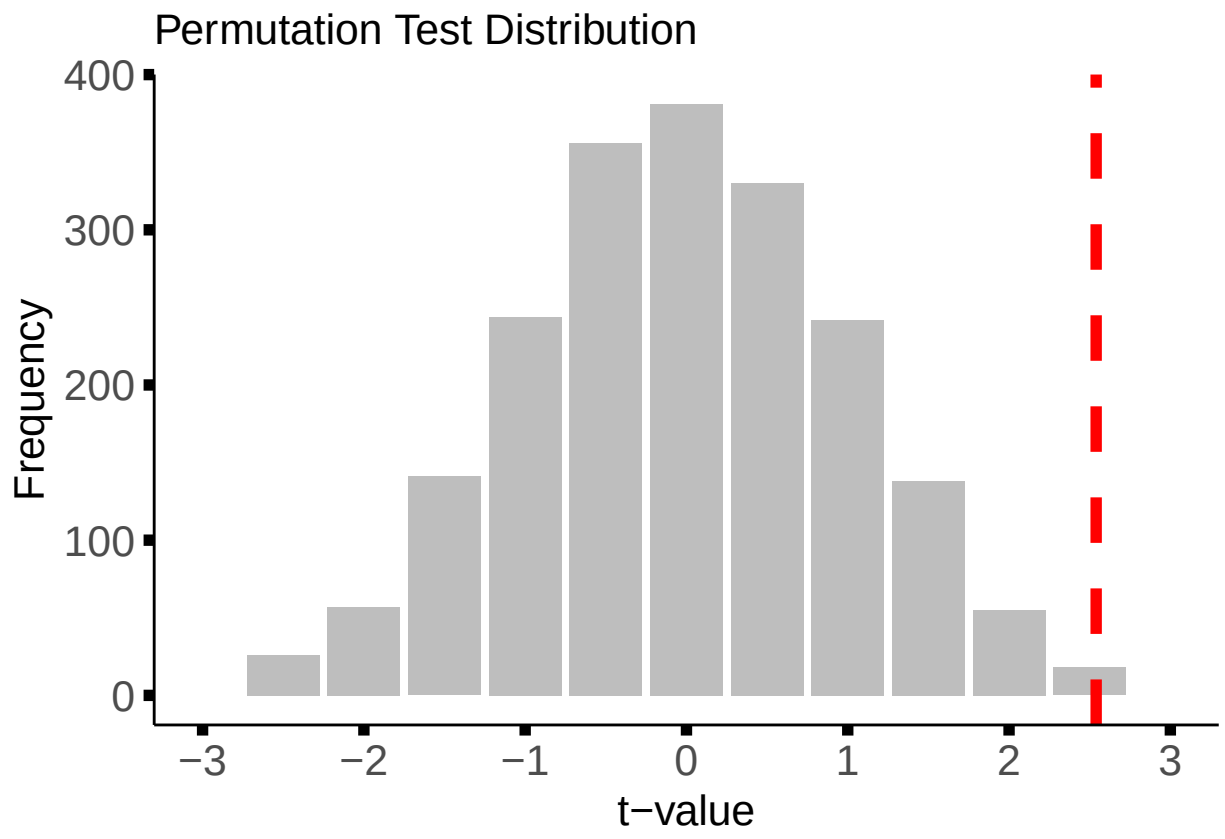

```r
#Analysis 5
#dlPFC
set.seed(23)
# Initialize an empty dataframe to store t-values
t_values_df_dlpfc <- data.frame(iteration = integer(), t_value = numeric())

# Set the number of iterations
num_iterations <- 1000

# Start the loop
for (i in 1:num_iterations) {
  # Shuffle the data
  shuffled_data_dlpfc <- MAP_Data_NoNA_Target %>%
    group_by(Subject) %>%
    mutate(Target_dlPFC_shuffled = sample(Target_dlPFC))

  # Fit the linear mixed-effects model
  dlPFC_regression_s <- lmer(Target_VTA ~ Target_dlPFC_shuffled + (1 | Subject), data = shuffled_data_dl

  # Extract the t-value for the coefficient of interest
  t_value <- summary(dlPFC_regression_s)$coefficients["Target_dlPFC_shuffled", "t value"]

  # Store the iteration number and t-value in the dataframe
  t_values_df <- rbind(t_values_df, data.frame(iteration = i, t_value = t_value))
}
```

```r
# Calculate the confidence interval for the t-values
t_value_ci <- quantile(t_values_df$t_value, c(0.025, 0.975))

# Print the confidence interval
print(t_value_ci)
```

```
##      2.5%     97.5%
## -1.789911  2.187423
```

```r
# Create histogram data
h <- hist(t_values_df$t_value, breaks = 20, plot = FALSE)

# Create ggplot object
ggplot(data.frame(x = h$breaks[-length(h$breaks)], y = h$counts), aes(x = x, y = y)) +
  geom_bar(stat = "identity", fill = "gray") +
  labs(
    title = "Permutation Test Distribution",
    x = "t-value",
    y = "Frequency"
  ) +
  geom_vline(xintercept = 2.54, linetype = "dashed", color = "red", size = 2) + # Adjusted line positio
  scale_x_continuous(limits = c(-3, 3), breaks = seq(-3, 3, by = 1)) + # Adjusted x-axis limits
  theme_minimal(base_size = 16) +
  theme(
    axis.title = element_text(size = 16),
    axis.text = element_text(size = 16),
    plot.title = element_text(size = 16),
    axis.line = element_line(color = "black", size = 0.5),
    panel.background = element_blank(),
    panel.grid.major = element_blank(),
    panel.grid.minor = element_blank(),
    axis.ticks = element_line(size = 2)  # Adjust tick size
  )
```

```
## Warning: Removed 4 rows containing missing values or values outside the scale range
## (`geom_bar()`).
```




```
#Analysis 6
# Load the car package for VIF calculation
library(car)
require(lmerTest)

dl_HPC_regression <- lmer(Target_VTA ~  Novel_HPC + Target_dlPFC + (1 | Subject), data = MAP_Data_NoNA)
# Calculate VIF for the multiple regression model
vif_values <- vif(dl_HPC_regression)
print(vif_values)
```

```
##    Novel_HPC Target_dlPFC
##     1.001979     1.001979
```

```
# Fit the mixed-effects model
full_model <- lmer(Target_VTA ~ Novel_HPC + Target_dlPFC + (1 | Subject), data = MAP_Data_NoNA)

# View model summary
summary(full_model)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Novel_HPC + Target_dlPFC + (1 | Subject)
##    Data: MAP_Data_NoNA
##
## REML criterion at convergence: -2002.9
```

```
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.7476 -0.6400 -0.0098  0.6157  4.1273
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0003796 0.01948
##  Residual             0.0197595 0.14057
## Number of obs: 1889, groups:  Subject, 77
##
## Fixed effects:
##               Estimate Std. Error        df t value Pr(>|t|)
## (Intercept)  2.623e-02  3.937e-03 7.723e+01   6.664 3.53e-09 ***
## Novel_HPC    4.635e-02  1.776e-02 1.864e+03   2.611  0.00911 **
## Target_dlPFC 7.262e-02  1.319e-02 1.865e+03   5.508 4.14e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Nv_HPC
## Novel_HPC   -0.047
## Targt_dlPFC -0.065 -0.044
```

```
# Fit reduced models
model_without_Novel_HPC <- lmer(Target_VTA ~ Target_dlPFC + (1 | Subject), data = MAP_Data_NoNA)
model_without_Target_dlPFC <- lmer(Target_VTA ~ Novel_HPC + (1 | Subject), data = MAP_Data_NoNA)

# Likelihood ratio test: Full model vs. model without Novel_HPC
anova(model_without_Novel_HPC, full_model)
```

```
## refitting model(s) with ML (instead of REML)

## Data: MAP_Data_NoNA
## Models:
## model_without_Novel_HPC: Target_VTA ~ Target_dlPFC + (1 | Subject)
## full_model: Target_VTA ~ Novel_HPC + Target_dlPFC + (1 | Subject)
##                         npar     AIC     BIC logLik deviance  Chisq Df
## model_without_Novel_HPC    4 -2010.4 -1988.2 1009.2  -2018.4
## full_model                 5 -2015.2 -1987.5 1012.6  -2025.2 6.8203  1
##                         Pr(>Chisq)
## model_without_Novel_HPC
## full_model                0.009013 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# Likelihood ratio test: Full model vs. model without Target_dlPFC
anova(model_without_Target_dlPFC, full_model)
```

```
## refitting model(s) with ML (instead of REML)

## Data: MAP_Data_NoNA
```

```
## Models:
## model_without_Target_dlPFC: Target_VTA ~ Novel_HPC + (1 | Subject)
## full_model: Target_VTA ~ Novel_HPC + Target_dlPFC + (1 | Subject)
##                            npar     AIC     BIC  logLik deviance  Chisq Df
## model_without_Target_dlPFC    4 -1987.1 -1964.9  997.54  -1995.1
## full_model                    5 -2015.2 -1987.5 1012.59  -2025.2 30.115  1
##                            Pr(>Chisq)
## model_without_Target_dlPFC
## full_model                  4.071e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
#Analysis 7: Effect of Adding Posterior HPC
base <- lmer(Target_VTA ~  1 + (1 | Subject), data = MAP_Data_NoNA)
post <- lmer(Target_VTA ~  Novel_HPC_Post + (1 | Subject), data = MAP_Data_NoNA)
HPC_regression <- lmer(Target_VTA ~  Novel_HPC + (1 | Subject), data = MAP_Data_NoNA)
HPC_PostRegression <- lmer(Target_VTA ~ Novel_HPC + Novel_HPC_Post + (1 | Subject), data = MAP_Data_NoN
summary(HPC_PostRegression)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Novel_HPC + Novel_HPC_Post + (1 | Subject)
##    Data: MAP_Data_NoNA
##
## REML criterion at convergence: -1975.6
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.7558 -0.6560 -0.0177  0.6194  4.1571
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0003592 0.01895
##  Residual             0.0200836 0.14172
## Number of obs: 1889, groups:  Subject, 77
##
## Fixed effects:
##                 Estimate Std. Error        df t value Pr(>|t|)
## (Intercept)    2.737e-02  3.925e-03 7.726e+01   6.973 9.22e-10 ***
## Novel_HPC      3.787e-02  2.170e-02 1.869e+03   1.745   0.0811 .
## Novel_HPC_Post 3.276e-02  3.122e-02 1.850e+03   1.049   0.2942
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Nv_HPC
## Novel_HPC   -0.003
## Nvl_HPC_Pst -0.067 -0.567
```

```
summary(post)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
```

```
## Formula: Target_VTA ~ Novel_HPC_Post + (1 | Subject)
##    Data: MAP_Data_NoNA
##
## REML criterion at convergence: -1978.4
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.7990 -0.6548 -0.0153  0.6169  4.1822
##
## Random effects:
##  Groups   Name        Variance Std.Dev.
##  Subject  (Intercept) 0.000362 0.01903
##  Residual             0.020104 0.14179
## Number of obs: 1889, groups:  Subject, 77
##
## Fixed effects:
##                  Estimate Std. Error        df t value Pr(>|t|)
## (Intercept)    2.739e-02  3.931e-03 7.725e+01   6.968 9.42e-10 ***
## Novel_HPC_Post 6.365e-02  2.573e-02 1.838e+03   2.473   0.0135 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr)
## Nvl_HPC_Pst -0.084
```

```
anova(base, post)
```

```
## refitting model(s) with ML (instead of REML)

## Data: MAP_Data_NoNA
## Models:
## base: Target_VTA ~ 1 + (1 | Subject)
## post: Target_VTA ~ Novel_HPC_Post + (1 | Subject)
##      npar     AIC     BIC logLik deviance  Chisq Df Pr(>Chisq)
## base    3 -1981.0 -1964.4 993.50  -1987.0
## post    4 -1985.1 -1963.0 996.56  -1993.1 6.1186  1    0.01338 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
anova(HPC_PostRegression, HPC_regression)
```

```
## refitting model(s) with ML (instead of REML)

## Data: MAP_Data_NoNA
## Models:
## HPC_regression: Target_VTA ~ Novel_HPC + (1 | Subject)
## HPC_PostRegression: Target_VTA ~ Novel_HPC + Novel_HPC_Post + (1 | Subject)
##                     npar     AIC     BIC logLik deviance  Chisq Df Pr(>Chisq)
## HPC_regression         4 -1987.1 -1964.9 997.54  -1995.1
## HPC_PostRegression     5 -1986.2 -1958.5 998.09  -1996.2 1.1074  1     0.2926
```

```r
#Analysis 8: Fam_Ant_HPC predict Target VTA
MAP_Data_NoNA <- na.omit(MAP_Data_NoNA)
basemodel <- lmer(Target_VTA ~ 1 + (1 | Subject), data = MAP_Data_NoNA)
HPC_regression <- lmer(Target_VTA ~  Novel_HPC + (1 | Subject), data = MAP_Data_NoNA)
Fam_HPC_regression <- lmer(Target_VTA ~  Fam_HPC + (1 | Subject), data = MAP_Data_NoNA)
NovFam_HPC_Reg <- lmer(Target_VTA ~  Fam_HPC + Novel_HPC + (1 | Subject), data = MAP_Data_NoNA)
summary(Fam_HPC_regression)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: Target_VTA ~ Fam_HPC + (1 | Subject)
##    Data: MAP_Data_NoNA
##
## REML criterion at convergence: -1608.2
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.6743 -0.6430 -0.0207  0.6143  4.2512
##
## Random effects:
##  Groups   Name        Variance  Std.Dev.
##  Subject  (Intercept) 0.0004927 0.0222
##  Residual             0.0200282 0.1415
## Number of obs: 1540, groups:  Subject, 77
##
## Fixed effects:
##              Estimate Std. Error        df t value Pr(>|t|)
## (Intercept) 2.926e-02  4.425e-03 7.727e+01   6.613  4.4e-09 ***
## Fam_HPC     7.604e-02  2.002e-02 1.524e+03   3.798 0.000152 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##         (Intr)
## Fam_HPC -0.095
```

```r
anova(NovFam_HPC_Reg, HPC_regression)
```

```
## refitting model(s) with ML (instead of REML)
```

```
## Data: MAP_Data_NoNA
## Models:
## HPC_regression: Target_VTA ~ Novel_HPC + (1 | Subject)
## NovFam_HPC_Reg: Target_VTA ~ Fam_HPC + Novel_HPC + (1 | Subject)
##                npar     AIC     BIC logLik deviance  Chisq Df Pr(>Chisq)
## HPC_regression    4 -1609.1 -1587.8 808.57  -1617.1
## NovFam_HPC_Reg    5 -1616.4 -1589.7 813.20  -1626.4 9.2541  1    0.00235 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```