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Kayla Hutton April 10, 2024

The Influence of the Left Amygdala and Left Hippocampus on Positive Valence-Dependent Emotion Recognition Processes in Temporal Lobe Epilepsy Patients

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An abstract of

a thesis submitted to the Faculty of Emory College of Arts and Sciences

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Abstract

Importance: Deficits in emotion recognition have a negative impact on quality of life. Negative valence deficits in emotion recognition can result in the misinterpretation of dangerous or sensitive situations, thereby posing a notable risk to health and safety. Pre- and post-surgical temporal lobe epilepsy patients are known to have these deficits, so discovering the brain regions associated with them and specificities regarding valence can better inform patients, surgeons, and caretakers of risks associated with different treatment options.

Objective: Investigate the relationship between 18 regions of the temporal lobe (9 bilateral regions) and valence-dependent emotional recognition processes.

Design: Observational pilot study

Participants: 88 participants; 40 healthy controls, 23 right-sided temporal lobe epilepsy patients, 25 left-sided temporal lobe epilepsy patients.

Main Outcome and Measure: Baron Cohen's "Reading the Mind in the Eyes" Test, volumetric MRI data

Results: Patients with smaller left amygdala and hippocampus had notable positive emotion recognition deficits as compared to controls; patients with smaller right amygdala and hippocampus had generalized deficits in emotion recognition, with no effect due to valence when accounting for trends in control responses.

Conclusion and Relevance: The left amygdala and hippocampus are correlated with functions relevant to positive emotion recognition processes.

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Abstract

In this study, we aimed to investigate the lateral differentiation of valence-dependent emotion recognition processes within the temporal lobe and associated subcortical structures. This information is important for informing surgical techniques and epilepsy patients of risks associated with both their disorder and the treatment options available to them. Data was collected using Baron-Cohen's "Reading the Mind in the Eyes" Test (RMET) to evaluate the emotion recognition capacities of 88 individuals - 23 of whom had right-sided temporal lobe epilepsy and 25 who had left-sided temporal lobe epilepsy. Using results from "Valence in the Reading the Mind in the Eyes task" (Hudson 2020), an analytical framework to identify trends in correct response rates between groups was designed. Groups were defined using volumetric MRI data to determine if a person had proportionally smaller left or right sides of a given brain structure (e.g. left vs. right hippocampus) and responses were analyzed by group. Epilepsy patients with proportionally smaller left amygdala volume or proportionally smaller left hippocampal volume demonstrated roughly equivalent skill in identifying positive, negative, and neutral emotions, being on average 3.3 % better at identifying positive emotions than negative emotions. This is significantly different from healthy controls and epilepsy patients with smaller right-sided volumes; on average, both are predicted to be 14.5 % better at identifying positive emotions as compared to identifying negative emotions. These findings suggest that the left amygdala and the left hippocampus have some function in identifying positive emotions.

Introduction

From an evolutionary perspective, emotion recognition is a deeply important process. Anthropologists believe that, before the development of syntactic language, humanoid social groups relied on emotion recognition processes to perform alloparenting and tool-making. As language evolved, emotion recognition processes became entwined with culture through the incorporation of language (Jablonka, Ginsburg, Dor 2012). Nowadays, social convention requires the correct assessment of the emotions of others to maintain a higher quality of life (Fulford 2013). Groups who are susceptible to deficits in emotion recognition, such as autistic people (Uljarevic, Hamilton 2013) or people with epilepsy (Edwards 2017) face social consequences when those deficits are not accommodated – particularly consequences associated with failures in nonverbal communication (Niedenthal, Brauer 2012).

Epilepsy conditions affect an estimated 65 million people worldwide, of which approximately one third are considered medically refractory and require surgical intervention to be properly treated (Devinsky 2018). However, surgical interventions inherently cause severe damage to the affected regions of the brain, which in turn can cause deficits in their associated functions. Temporal lobe epilepsy (TLE) is associated with deficits in emotion recognition (Monti, Meletti 2015); it also happens to be one of the most common forms of epilepsy, though the reason for this trend is unknown (Téllez-Zenteno, Hernández-Ronquillo 2011).

In addition to being a common form of epilepsy, TLE is also the most common cause of refractory epilepsy (Frazzini, Cousyn, Navarro 2022) and therefore has a rich and complicated history in surgical intervention (Magiorkinis 2014). Up to the famous H.M. case, in which a technically successful surgery resulted in the patient experiencing permanent and severe

anterograde amnesia, neurosurgeons were confident that removing any tissue that could possibly generate a seizure was the best course of action when treating TLE (Maugière, Corkin 2015). However, H.M. proved that being seizure-free cannot be the only goal of a conscientious surgeon – quality of life is dictated by many factors which can be severely impacted by brain surgery. Surgeons have since endeavored to understand all consequences of their procedures in an effort to minimize them.

To this aim, a wide variety of surgical options to treat refractory epilepsy have been developed, ranging from lateral amygdalohippocampectomy, in which the amygdala and hippocampus from one hemisphere of the brain are partially or entirely removed with lasers, to the current standard of anterior temporal lobectomy, in which the anterior temporal lobe is cut away entirely. These options come with differing risks and success rates (Wiebe et. al, 2001), and surgeons select the appropriate treatment option based on the balance between the pervasiveness of affected tissue and relevant side effects (Bauman, Devinsky, Liu, 2019). Currently, the temporal lobe is largely associated with memory and language function (Patel, Biso, Fowler 2023); however, there is a growing body of evidence that it is also associated with social functions such as emotion recognition (Campanella 2014, Sinha 2020, Tippet 2018).

Most studies which investigate the functional location of emotional recognition in the human brain implicate regions associated with the temporal lobe – either subcortical structures or regions of white matter connectivity. Severe impairment in emotion recognition has been connected to the insula (Tippet 2018, Campanella 2014), amygdala, (Tippet 2018, Campanella 2014), and right temporal fasciculus structures (Sinha 2020, Campanella 2014,). As previously mentioned, general deficits in emotion recognition are associated with social deficits (Nigam 2021). However, there are comparatively fewer studies which investigate valence-specific

deficits. An inability to recognize that someone is fearful is predictive of poorer quality of life (Fulford 2021), which may be related to the fact that the situations in which emotion recognition is a relevant skill have fundamentally different risks associated with valence. An inability to recognize that someone is happy can put strain on interpersonal relationships, but an inability to recognize fear can result in a lack of urgency in dire situations. A deficit-affected individual who is knowledgeable of their capacity for valence-specific emotion recognition can mitigate or accommodate the effects of deficits on their life; therefore, it is highly important to identify risk factors for these types of deficits.

Emotion recognition deficits are difficult to test for, with a few previously existing tests having been adapted to do so. Baron-Cohen's "Reading the Mind in the Eyes" Test (RMET) was originally developed to test theory of mind in autistic individuals (Baron-Cohen 2001), but has since been established as a valid measure of emotion recognition capacity (Robles et. al., 2020). However, the exam as currently structured only provides a composite score which indicates the presence or lack of a general deficit. In 2020, a study published by the American Psychological Association used survey data to establish a standard measure by which valence-specific data could be interpreted from RMET results (Hudson 2020). Our study uses a cohort of TLE patients and data from their RMET results to compare trends in valence-specific emotion recognition deficits between right-hemispheric TLE patients and left-hemispheric TLE patients as compared to a group of healthy controls.

Hypothesis and Predictions

We originally hypothesized that the right temporal lobe would be correlated with negative emotion recognition processes. We predicted that right-sided temporal lobe epilepsy patients (RTLEPs) would have a significantly worse performance as compared to left-sided temporal lobe epilepsy patients (LTLEPs) and controls in the negative valence category of RMET prompts. The analysis performed under this hypothesis showed that RTLEPs performed significantly worse in all valence categories, such that the null hypothesis could not be readily rejected, even though they were significantly worse at negative emotion recognition. However, this analysis also revealed that the LTLEPs did **not** perform significantly worse in the negative valence category – only in the positive and neutral categories. Thus, the focus of the study pivoted and a redesign was implemented. The hypothesis which is tested in this paper is as follows: Left temporal lobe structures will be correlated with positive emotion recognition processes. We predicted that temporal lobe epilepsy patients with smaller structures in the left side of the temporal lobe would have significantly worse performance in the positive valence category of prompts on the Baron-Cohen "Reading the Mind in the Eyes" Test as compared to control participants or TLEPs with smaller right-sided structures of the temporal lobe. This new hypothesis incorporated quantifiable MRI data, which allowed us to analyze specific structures, but it is important to note that it was formed after a significant portion of data collection.

Methods

RMET Manipulations

Each prompt in Baron-Cohen's "Reading the Mind in the Eyes" Test (RMET) was categorized as negative, neutral, or positive in accordance with results from a study conducted by Hudson et al. (2020). The authors used a survey method to assess each RMET prompt in accordance with a degree of "intensity" of either negative or positive valence; this degree of intensity was numerically represented through an average bootstrapped t-value for each prompt (refer to **Table 1**). These values define how far the prompt was ranked from the "neutral" point of 0. A value larger in magnitude is therefore associated with a stronger intensity of emotion. All negative t-values indicate a somewhat negative valence, and vice versa for positive values. In this study, negative valence was assigned to the 11 prompts which had an average bootstrapped t-value below -2.00, while positive valence was assigned to the 14 prompts with values above 2.00; neutral valence was assigned to the 11 prompts with t-values in between -2.00 and 2.00.

Participants

88 participants underwent MRI scanning and a test battery which included the RMET. One set of RMET results and one set of MRI data was collected per participant; however, data collection occurred from 2012-2022. The participants were sorted into three groups: Healthy Controls (HCs – n = 40), Right-Sided Temporal Lobe Epilepsy Patients (RTLEPs – n = 23), and Left-Sided Temporal Lobe Epilepsy Patients (LTLEPs – n = 25). Participants were disqualified from the study who had bilateral damage to the temporal lobe or lesions to multiple parts of the brain (i.e. large lesions which spanned multiple lobes or multiple separate lesions within the

temporal lobe). Participants who did not have available MRI data were also disqualified. Six control participants who had a composite score below 23/36 were disqualified. Each correctly answered prompt provides 1 point to the composite score, and a score below 23/36 is associated with below average or disordered function across age groups (Baron-Cohen 2001, Kynast 2021); therefore, such participants could not be confirmed as "healthy" controls.

Data Collection

The RMET was administered using a PowerPoint slideshow to display the visual prompts; participants indicated their answer to each prompt by pointing or speaking and the test administrator indicated their response on the scoresheet. These responses were documented in an Excel file. A value of 1 was assigned to each correct response while a value of 0 was assigned to any incorrect response. The percentage of correct answers in each valence category (positive, neutral, negative) was calculated for each participant in addition to the total score. Additional demographic data was collected where available, including age, years of education, Beck Depression Inventory score (BDI), and Boston Naming Test Semantic score (BNT). The Beck Depression Inventory assesses clinical depression symptoms. The inventory is a 21 prompt questionnaire with a highest possible score of 61; a score above 20 indicates moderate clinical depressive symptoms (García-Batista 2018). The Boston Naming Test assesses "naming", which is the skill associated with object recognition and definition. An examinee is shown a commonly identifiable object (e.g. giraffe, tree, helicopter, etc.) and given up to twenty seconds to name the item. An inability to recognize an item or name takes points off of the score; the test has 60 prompts, with a score of 48/60 being considered the threshold of naming deficit (Nicholas 1989).

The MRI data was processed using volumetric software designed to parcellate the brain along major sulci and gyri (Tzourio-Mazoyer 2002); this software produces volume estimates for 90 structures of the brain. To reduce multiple comparisons with areas unrelated to temporal lobe epilepsy, it was decided to only focus on the 18 structures related to the temporal lobe. The left and right hemispheric values for each of the following regions were entered into analysis: Superior Temporal Gyrus, Superior Temporal Pole, Medial Temporal Gyrus, Medial Temporal Pole, Inferior Temporal Gyrus, Insula, Hippocampus, Parahippocampal Gyrus, and Amygdala.

Statistical Analysis

A linear regression model was implemented where the independent variable was representative of the valence category; a value of "1" was assigned to the rate of positive correct responses, "-1" to the rate of negative correct responses, and "0" to the rate of neutral positive responses. The dependent variable represented a prediction of the rate of correct response for each category and group. While the valence categories of responses are not themselves numerical in nature, this configuration of the data allowed for the simultaneous comparison of the means of all three categories for the three participant groups, as well as a quantitative measure of difference in performance between the three valence categories. It also allowed for the analysis of covariates with significant effects on performance. The covariates analyzed in conjunction with the categories were age, years of education, BDI, and BNT. The raw data for responses categorized by TLEP group can be found in **Table 2** and are graphed in **Figure 1**.

For the analysis, each epilepsy patient was recategorized as "Left-Side-Smaller" (LSS) or "Right-Side-Smaller" (RSS) for each brain region. For example, a patient with a smaller left hippocampus would be categorized as LSShipp, but the same patient could have a smaller right

amygdala and be categorized as RSSamy. This grouping allowed for the categorical variable to be based on quantifiable MRI data as opposed to diagnostic criteria. The linear regression predictive model was generated and used in RStudio software (RStudio Team 2020). Each category was analyzed twice: once in an unencumbered fashion without the inclusion of covariates, and once with the inclusion of the four aforementioned covariates. One participant had a left:right amygdala ratio of 1.0 and was therefore excluded from the amygdala analyses.

The linear equation for a group's unencumbered analysis model (shown here as LSSamy's) is as follows:

y = (Control Slope - LSSamy Slope Adjust) * x + (Control Intercept - LSSamy Int. Adjust)

Where y is Rate of Correct Response, x is representative of one of three valence categories, Control Slope is the slope of the HCs's trend, LSSamy Slope Adjust is the difference between the Control Slope and the predicted slope of LSSamy, Control Intercept is the prediction of the neutral score, and LSSamy Int. Adjust is the difference between the HC neutral score prediction and the LSS patients'. Values for the unencumbered analyses can be found in **Tables 3&4** and **Figures 2&3**.

The linear equation for the a group's multivariate analysis (shown here as LSSamy's) is as follows:

y = (Control Slope - LSSamy Slope Adjust) * x + (Control Intercept - LSSamy Int. Adjust + (age * avg age value) + (education + avg education value) + (BDI * avg BDI value) + (BNT * avg BNT value))

Where age, education, BDI, and BNT are all coefficients which predict the impact of each variable's value on the Rate of Correct Response and avg [variable] value is the average

value of each value amongst the LSS group. Values for the multivariate analyses can be found in **Tables 5&6** and **Figures 4&5**.

Results

The linear regression model generated values of predicted performance based on categorization and demographic data. These values translated to graphical models which compared the predicted performance in each valence category of each group. This model found that temporal lobe epilepsy patients with smaller left amygdalas (LSSamyTLEPs) had a significantly different linear trend as compared to those with smaller right amygdalas (RSSamyTLEPs) or healthy controls (HCs) in both multivariate ($p = 0.04$, **Figure 4**) and the unencumbered ($p = 0.02$, **Figure 2**) analyses. These results indicate that performance between valence categories can be linearly approximated for RSSamyTLEPs using HC predictive trends, but not for LSSamyTLEPs.

The model also found that temporal lobe epilepsy patients with smaller left hippocampuses (LSShippTLEPs) had a significantly different linear trend as compared to those with smaller right hippocampuses (RSShippTLEPs) in the multivariate analysis ($p = 0.036$, **Figure 5**). The unencumbered analysis in conjunction with the hippocampus ratios produced a trend of borderline significance ($p = 0.0505$, **Figure 3**). These results indicate that performance between valence categories can be linearly approximated for RSShippTLEPs using HC predictive trends, but not for LSShippTLEPs.

The most relevant covariate amongst all analyses was Boston Naming Test score (BNT), with education also having a large impact. **Tables 3, 4, 5, & 6** contain the results of the unencumbered and multivariate analyses in conjunction with the hippocampus and amygdala size ratios. These tables display the values generated by the model before they were interpreted graphically. Overall, older, more depressed individuals performed worse than younger, less

depressed individuals. More educated individuals with better naming abilities performed better than less educated individuals with poorer naming abilities.

The four covariates were all relevant to this analysis, but they did not attenuate the observed trends. Age and depression were negatively correlated with performance; education and naming ability (measured by BNT) were positively correlated with performance. **Tables 7, 8, & 9** display the demographic data of each group. While the epilepsy patients were, on average, older, more depressed, less educated, and worse at naming tasks than the controls, there were no notable demographic differences between any two epilepsy groups. This means that differences in performance between any two epilepsy groups could not be attributed to any demographic factor.

The linear regression model created predictions from an aggregate of values based on a given set of data and then analyzed the significance of each of those values to its predictive power. The statistical significance of the difference in slopes between the LSSamy group and the control group shows that each group has different trends in performance between valence categories on the RMET. This difference does not exist between the RSSamy group and the controls; the predictive power of the model is maintained when the same slope is used for both groups. The only significant difference between the HCs and RSSAmyTLEPs lies in their intercepts, which are influenced both by their condition (as evidenced by BNT) and demographic variables (age, years of education). The RSSamy group has a lower intercept than the control group, which indicates a general deficit in emotion recognition that is not valence specific. Controls perform better when identifying positive emotions as compared to negative emotions, and so do TLEPs with smaller right amygdalae. Despite the fact that the LSSamy group has a

consistent performance across the three valence categories, the group's positive emotion recognition performance is comparatively much lower.

A functional deficit in recognizing positively valenced prompts on the RMET is correlated with smaller size in the left amygdala and left hippocampus of temporal lobe epilepsy patients. General deficits in emotion recognition processes are correlated with smaller size in the right amygdala and right hippocampus of temporal lobe epilepsy patients.

Discussion

Temporal lobe epilepsy patients with smaller left amygdalas have unusual and notable deficits in positive emotion recognition. This information could be highly relevant to neurosurgeons and epilepsy patients when selecting treatment options; it could also inform the families of epilepsy patients of possible areas of support and accommodation post-surgery. Furthermore, generating a more comprehensive idea of how emotion recognition functions as a cognitive process allows for society to build accommodations for people who have deficits in emotion recognition.

When accounting for covariates, LSShippTLEPs have the same trend in performance as LSSamyTLEPs in that their performance across valence categories is consistent and therefore demonstrate a deficit in positive emotion recognition as compared to healthy controls. However, it is entirely possible that one structure is being associated with this trend in error. Epilepsy patients who experience damage to their hippocampuses often experience concurrent damage to their amygdalae and vice versa (Ballerini 2022). Additionally, those patients who underwent surgery would have had both structures damaged during their operation. As the amygdala and hippocampus are almost always lesioned in tandem, the linear regression model used in this analysis is not able to discern which of the two is responsible for the appearance of a functional deficit. Therefore, it is possible that only one structure is correlated with emotion recognition processes and that the other is just also often damaged in the population which displays deficits in emotion recognition.

Another possibility is that both structures are related to emotion recognition processing. This would fit with conventional wisdom given the responsibility of the hippocampus to the

memory system and recognition functions (Lisman 2017, Tzilivaki 2023, Slotnick 2022) and the amygdala's responsibility for several notable emotional processes, including the generation of fear (Šimić 2021, Ressler 2010, Frick 2021). However, this current analysis cannot separate the impacts of each structure. It is worth noting that several major functions of the amygdala and the hippocampus are directly influenced by the other, including fear conditioning, so the idea that both structures are contributing to one process is not outside of the realm of possibility (Deng 2024, Yavas 2019).

Most people are language dominant in the left hemisphere, and most of the participants in the LSSamy group were LTLEPs. It is possible that undetected lesions to language centers in these patients may have impacted the verbal component of the RMET, but the LSSamy group has comparable Boston Naming Test scores to the RSSamy group. This means that both groups have comparable naming abilities. Any structural barrier to RMET performance would have affected both groups, so the idea that the language component of the RMET could have generated these results is unlikely. BNT did have a large impact on the predictions generated by the model, but decreased naming ability is associated with TLE (Poch 2016). Therefore, BNT score was likely conflated with epilepsy status. This is something the model cannot necessarily account for, but it did not impact the conclusion of the study.

The covariate analyses demonstrate that, while there are several contributing factors to overall RMET performance, they do not explain the difference in trends between groups. The participants in both epilepsy groups are demographically and functionally too similar – the only factor in the analysis which can account for this effect is structural difference. Temporal lobe epilepsy is highly comorbid with mesial temporal sclerosis, which damages the amygdala and hippocampus (Blair 2012). This study had a strong representation of MTS patients, so most had

damaged amygdalae and hippocampuses. These results support previous research which has indicated that the amygdala is involved with emotion recognition processes.

There are a number of limitations to this study. While most patients in the study had MRI results which confirmed the presence of lesions to the amygdala and hippocampus, there was variance between patients in terms of degree of damage and specific location of damage. 12 of the 48 epilepsy patients had their data collected post-surgical intervention, which impacts the presentation of the relevant lesions (i.e. sclerosis vs. atrophy). As previously mentioned, the analysis conducted here is not equipped to separate the effects attributable to the hippocampus or the amygdala. The linear regression model, while it does provide usable data, is not comprehensive and there is a great deal of elaboration which could be achieved using additional analytical methods. The model's requirement of a categorical grouping variable is one major barrier to that elaboration – an analysis which maintains the numeric nature of the MRI data would likely provide clearer results. Finally, this study is an offshoot analysis generated from a previous research question. Initially, the region of interest was the right temporal lobe (RTL) and the valence of interest was negative. A few sources indicated that individuals with lesions the RTL demonstrated deficits in negative emotion recognition (Tippet 2018, Sinha 2020), so we hypothesized that patients with right-temporal lobe epilepsy would demonstrate a deficit in negative emotion recognition as compared to controls. While the RTLEP group did demonstrate this deficit, it also demonstrated a deficit in positive emotion recognition. This led to the conclusion that no, RTLEPs did not demonstrate a notable and particular deficit in negative emotion recognition. However, the more interesting trend that the data produced was between the left temporal lobe and positive emotion recognition. Given that the results associated with the left temporal lobe were statistically significant, surprising, and relevant, we redirected our focus.

The analysis performed here is the same as what would have been performed if the initial hypothesis had been supported, but this study does need to be independently corroborated as the data collection and the first steps of analysis were performed before the generation of the relevant research question.

With this data, we hope to expand the study cohort and analyze more specific groups, thereby answering questions about inter-structure relationships. For example, would deficits be exacerbated for LSSamyLSShipp RTLEPs? **Table 10** showcases that the current subgroups are too small to meaningfully analyze; however, with new participants would come a broader dataset, thereby allowing for more detailed analysis. As specified earlier, a future study should be conducted to corroborate these results. However, beyond simply replicating what was done here, focus should also be put into identifying the role of specific nuclei of the amygdala and subregions of the hippocampus in valence-specific emotion recognition processes. Our results implicate the hippocampus as an area of interest in future research and the left amygdala and left hippocampus as somehow involved in positive emotion recognition processes.

Tables and Figures

Item	Average Bootstrapped t-value (Hudson et al. 2020)	Valence Category
20: Friendly	14.87	Positive
30: Flirtatious	12.29	Positive
31: Confident	10.91	Positive
21: Fantasizing	12.79	Positive
3: Desire	9.29	Positive
25: Interested	8.75	Positive
16: Thoughtful	8.29	Positive
6: Fantasizing	7.25	Positive
28: Interested	5.81	Positive
18: Decisive	5.25	Positive
15: Contemplative	4.43	Positive
13: Anticipating	3.97	Positive
1: Playful	3.47	Positive
29: Reflective	3.95	Positive
19: Tentative	1.68	Neutral
27: Cautious	1.33	Neutral
9: Preoccupied	0.87	Neutral
36: Suspicious	0.34	Neutral
24: Pensive	0.23	Neutral
33: Concerned	-0.38	Neutral
22: Preoccupied	-0.74	Neutral
35: Nervous	-0.69	Neutral
12: Sceptical	-1.1	Neutral

32: Serious	-1.33	Neutral
34: Distrustful	-1.66	Neutral
10: Cautious	-2.51	Negative
4: Insisting	-2.17	Negative
14: Accusing	-2.13	Negative
23: Defiant	-3.35	Negative
7: Uneasy	-4.36	Negative
11: Regretful	-3.75	Negative
5: Worried	-3.72	Negative
17: Doubtful	-5.25	Negative
8: Despondent	-4.92	Negative
2: Upset	-5.01	Negative
26: Hostile	-5.18	Negative

Table 1 - Results from Hudson et al (2020) Study: Valence Categorization Table of RMET Prompts: *t-values referenced are from "Valence in the Reading the Mind in the Eyes" Test, Hudson et al (2020). RMET prompts rated by valence of target word and image (n = 164). For this study, 11 prompts with avg. t-values below -2.00 were categorized as negative; 14 prompts with avg. t-values above 2.00 were categorized as positive; 11 prompts with avg. t-values between -2.00 and 2.00 were categorized as neutral.*

Diagnostic Status	Avg. Rate of Correct to Response - Negative Valence	Avg. Rate of Correct Response - Neutral Valence	Avg. Rate of Correct Response - Positive Valence
Control (n = 40)	0.711	0.807	0.855
RTLEP (n = 23)	0.526	0.605	0.683
LTLEP (n = 25)	0.625	0.622	0.654

Table 2 - Average Ratios of Correct to Incorrect Responses Per Valence Category by Diagnostic Status: *Participants were initially categorized based on their hemispheric epilepsy status (TLEP: Temporal Lobe Epilepsy Patient). The negative and neutral valence categories had 11 prompts each; the positive valence category had 14. Scores were standardized to ratios for comparison.*

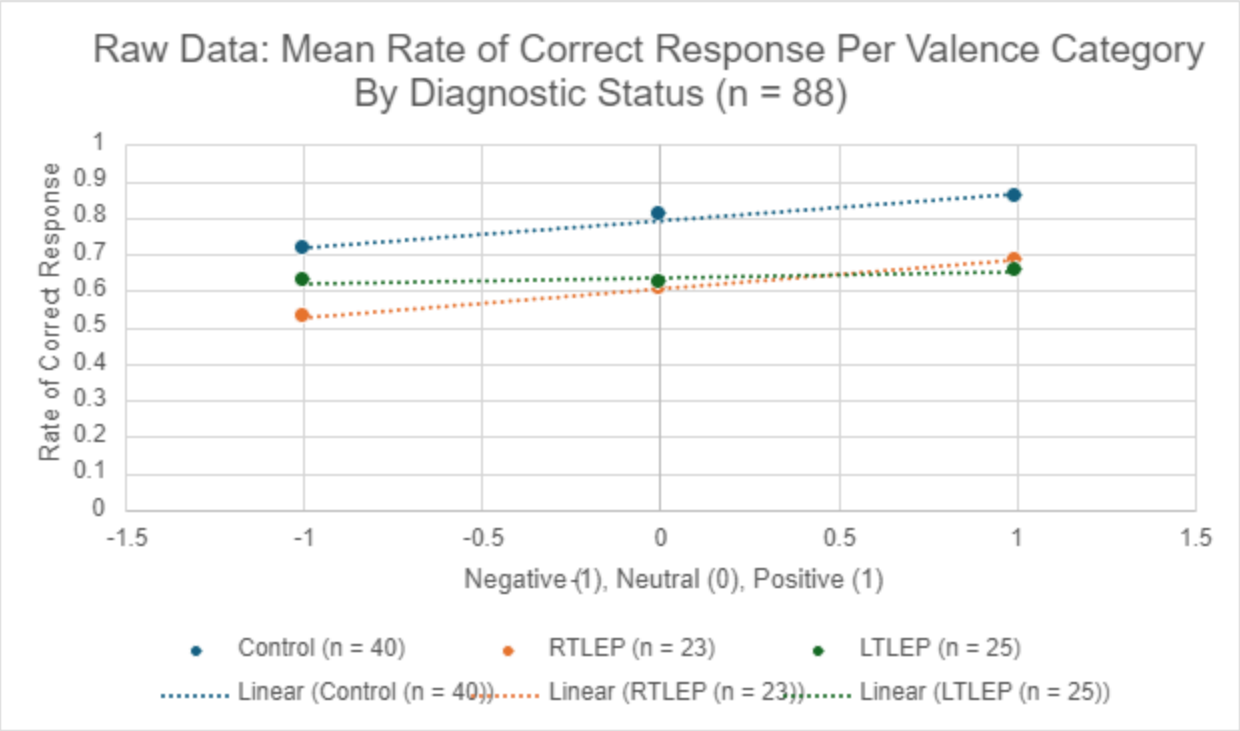

Figure 1 - Mean Value of Rate of Correct Response by Diagnostic Status: *Participants were initially categorized based on their hemispheric epilepsy status (TLEP: Temporal Lobe Epilepsy Patient). Average values for correct response rates in each valence category were calculated for each status group; the values were then fitted with trendlines:*

Controls: $y = 0.072x + 0.7912,\ R^2 = 0.9658$

RTLEPs: $y = 0.0788x + 0.6046,\ R^2 = 1.0$

LTLEPs: $y = 0.0144x + 0.6339,\ R^2 = 0.6567$

There is a stair step trend from negative to positive valence in the Control and RTLEP groups which is not present in the LTLEP group; the LTLEP group does not appear to have any specific proficiency in any valence category.

Coefficients	**Estimates**	**Standard Error**	**t-value**	**Pr (|>t|)**
Control Intercept	0.78492	0.01544	50.838	< 2e-16 ***
Control Slope	0.08070	0.01633	4.943	1.10e-05 ***
LSSamy Int. Adjust	-0.15085	0.02312	-6.525	3.56e-10 ***
RSSamy Int. Adjust	-0.19262	0.3060	-6.294	1.31e-09 ***
LSSamy Slope Adjust	-0.06210	0.02666	-2.329	0.0206 *

Table 3 – Results of Linear Regression Analysis with Lateral Amygdala Ratio Categorization: *The linear regression model generates a set of values which indicate the statistical significance of the coefficients to the prediction as well as the magnitude of their impact. A linear equation is informed by the base category values (Control), and intercept adjustments are generated for other groups (RSSamy and LSSamy) such that their addition corrects the line's trajectory. Slope adjustments are created through interactions which compare data between groups to determine differences. These values were used to generate* ***Figure 2****. The slope of LSSamy was significantly different from controls (p = 0.02) such that a prediction for an LSShippTLEP would not be accurate while using the control slope. The predicted intercepts of both LSSamy and RSSamy were significantly different from controls.*

Coefficients	**Estimates**	**Standard Error**	**t-value**	**Pr (|>t|)**
Control Intercept	0.79118	0.01555	50.887	< 2e-16 ***
Control Slope	0.07197	0.01482	4.855	2.08e-06 ***
LSSamy Int. Adjust	-0.18010	0.02610	-6.900	3.98e-11 ***
RSSamy Int. Adjust	-0.16397	0.02477	-6.619	2.06e-10 ***
LSSamy Slope Adjust	-0.05824	0.02965	-1.965	0.0505

Table 4 – Results of Linear Regression Analysis with Lateral Hippocampus Ratio Categorization: *The linear regression model generates a set of values which indicate the statistical significance of the coefficients to the prediction as well as the magnitude of their impact. A linear equation is informed by the base category values (Control), and intercept adjustments are generated for other groups (RSSamy and LSSamy) such that their addition corrects the line's trajectory. Slope adjustments are created through interactions which compare data between groups to determine differences. These values were used to generate* ***Figure 3****. The slope of LSSamy was not significantly different from controls (p = 0.0505). The predicted intercepts of both LSSamy and RSSamy were significantly different from controls.*

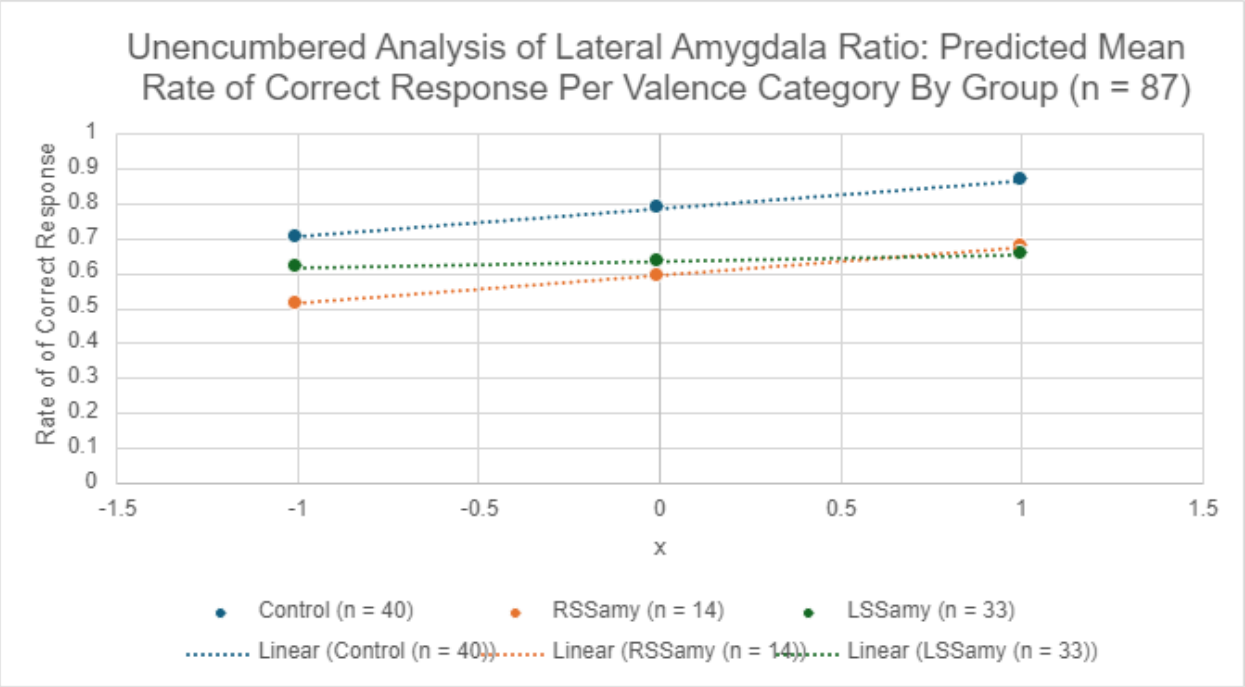

Figure 2 - Mean Value of Rate of Correct Response by Amygdala Volume: *Participants were categorized using MRI data – projected amygdala volumes for the right and left hemispheres – to determine proportion (SS: Side Smaller). A linear regression model was used to generate performance predictions based on the data set; predicted average values per valence category were calculated for each status group; the values were then fitted with trendlines:*

Controls: $y = 0.0687x + 0.749$

RTLEPs: $y = 0.0687x + 0.6113$

LTLEPs: $y = 0.0051x + 0.586$

There is a stair step trend from negative to positive valence in the Control and RTLEP groups which is not present in the LTLEP group; the LTLEP group does not appear to have any specific proficiency in any valence category.

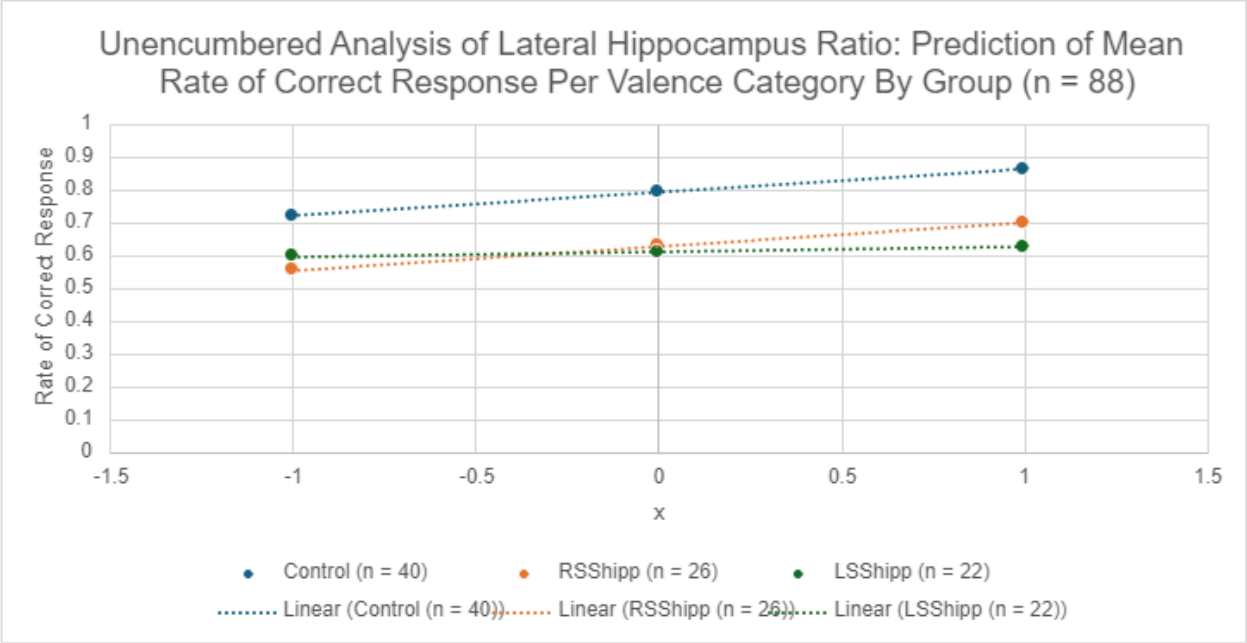

Figure 3 - Mean Value of Rate of Correct Response by Hippocampus Volume: *Participants were categorized using MRI data – projected amygdala volumes for the right and left hemispheres – to determine proportion (SS: Side Smaller). A linear regression model was used to generate performance predictions based on the data set; predicted average values per valence category were calculated for each status group; the values were then fitted with trendlines:*
Controls: $y = 0.0687x + 0.749$
RTLEPs: $y = 0.0687x + 0.6113$
LTLEPs: $y = 0.0051x + 0.586$
There is a stair step trend from negative to positive valence in the Control and RTLEP groups which is not present in the LTLEP group; the LTLEP group does not appear to have any specific proficiency in any valence category. This analysis had borderline significance (p = 0.0505)

Coefficients	**Estimates**	**Standard Error**	**t-value**	**Pr (|>t|)**
Control Intercept	0.0889728	0.1023525	0.869	0.385798
Control Slope	0.0727122	0.0160986	4.517	1.10e-05 ***
LSSamy Int. Adjust	0.0170940	0.0360631	0.474	0.636044
RSSamy Int. Adjust	0.0058781	0.0437293	0.134	0.893214
Age	-0.0029744	0.0009535	-3.119	0.002096 **
Education	0.0168585	0.0047383	3.558	0.000473 ***
BDI	-0.0034373	0.0015635	-2.198	0.029130 *
BNT	0.0093997	0.0017982	5.227	4.53e-07 ***
LSSamy Slope Adjust	-0.0557726	0.0272707	-2.045	0.042227 *

Table 5 – Results of Linear Regression Analysis with Lateral Amygdala Ratio Categorization and Covariates: *The linear regression model generates a set of values which indicate the statistical significance of the coefficients to the prediction as well as the magnitude of their correlation. A linear equation is informed by the base category values (Control), and intercept adjustments are generated for other groups (RSSamy and LSSamy) such that their addition corrects the line's trajectory. Slope adjustments are created through interactions which compare data between groups to determine differences. The coefficients of the covariates can be multiplied by an individual's value and added to the intercept (i.e. a 52 year old would have an adjustment of 52*-0.0029744 = 0.15) to create an individual prediction. These coefficients were applied to all available data; those adjustments were averaged per group to generate* ***Figure 4****. The slope of LSSamy was significantly different from controls (p = 0.04), meaning a prediction for an LSSamyTLEP would not be accurate while using the control slope. Age and BDI have a negative correlation with performance while education and BNT have a positive correlation.*

Coefficients	**Estimates**	**Standard Error**	**t-value**	**Pr (|>t|)**
Control Intercept	0.0933590	0.0977149	0.955	0.340585
Control Slope	0.0687013	0.0148697	4.620	7.08e-06 ***
LSShipp Int. Adjust	0.0320713	0.0380156	0.844	0.399939
RSShipp Int. Adjust	-0.0036224	0.0381249	-0.095	0.924405
Age	-0.0030628	0.0009353	-3.275	0.001258 **
Education	0.0164592	0.0047302	3.480	0.000623 ***
BDI	-0.0032375	0.0015002	-2.158	0.032182 *
BNT	0.0094786	0.0017354	5.462	1.47e-07 ***
LSShipp Slope Adjust	-0.0636282	0.0302006	0.0302006	0.036449 *

Table 6 – Results of Linear Regression Analysis with Lateral Hippocampus Ratio Categorization and Covariates: *The linear regression model generates a set of values which indicate the statistical significance of the coefficients to the prediction as well as the magnitude of their impact. A linear equation is informed by the base category values (Control), and intercept adjustments are generated for other groups (RSSamy and LSSamy) such that their addition corrects the line's trajectory. Slope adjustments are created through interactions which compare data between groups to determine differences. The coefficients of the covariates can be multiplied by an individual's value and added to the intercept (i.e. a 52 year old would have an adjustment of 52*-0.0029744) to create an individual prediction. These coefficients were applied to all available data; those adjustments were averaged per group to generate* ***Figure 5****. The slope of LSShipp was significantly different from controls (p = 0.036449) such that a prediction for an LSShippTLEP would not be accurate while using the control slope. Age and BDI have a negative correlation with performance while education and BNT have a positive correlation.*

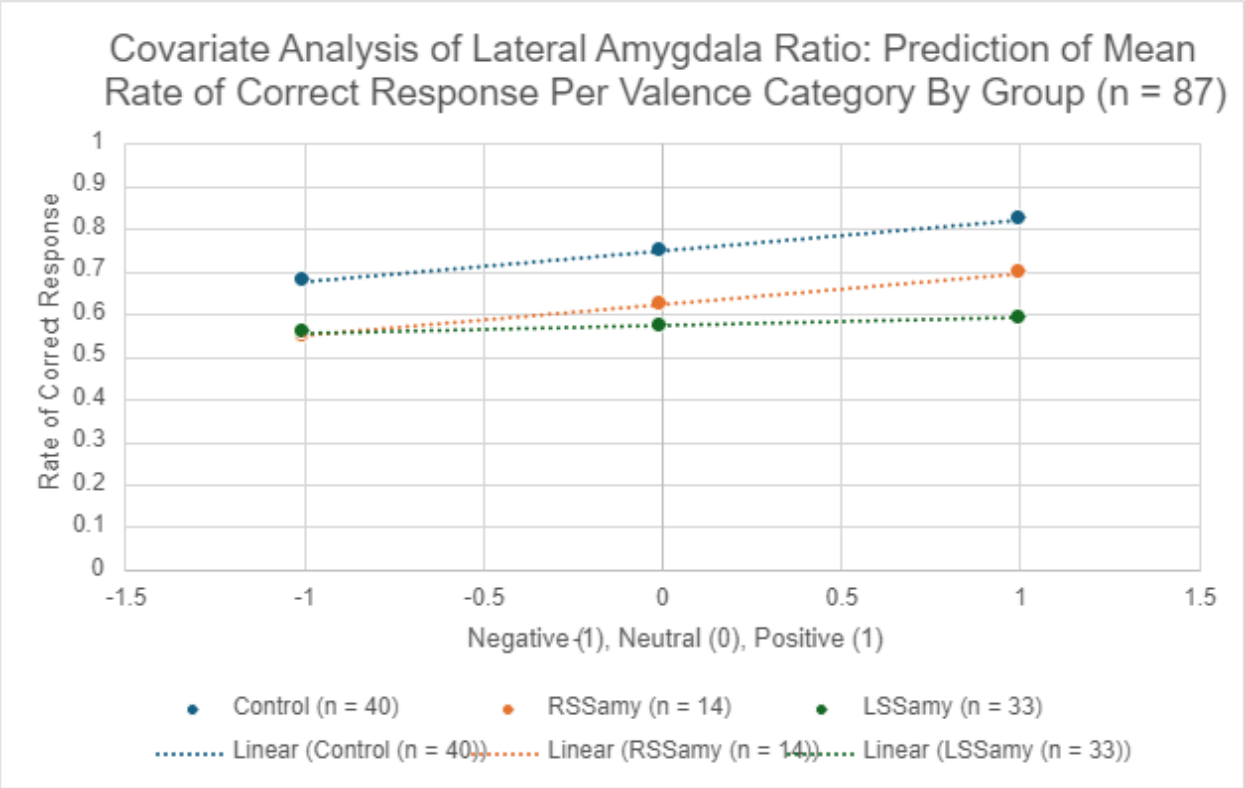

Figure 4 - Mean Value of Rate of Correct Response by Amygdala Volume Proportion Adjusted For Age, Education, BDI, and BNT: *Participants were categorized using MRI data – projected amygdala volumes for the right and left hemispheres – to determine proportion (SS: Side Smaller). A linear regression model was used to generate performance predictions based on the data set; predicted average values per valence category were calculated for each status group; the values were then fitted with trendlines:*

Controls: $y = 0.0727x + 0.7479$

RTLEPs: $y = 0.0727x + 0.6212$

LTLEPs: $y = 0.0169x + 0.5712$

There is a stair step trend from negative to positive valence in the Control and RTLEP groups which is not present in the LTLEP group; the LTLEP group does not appear to have any specific proficiency in any valence category.

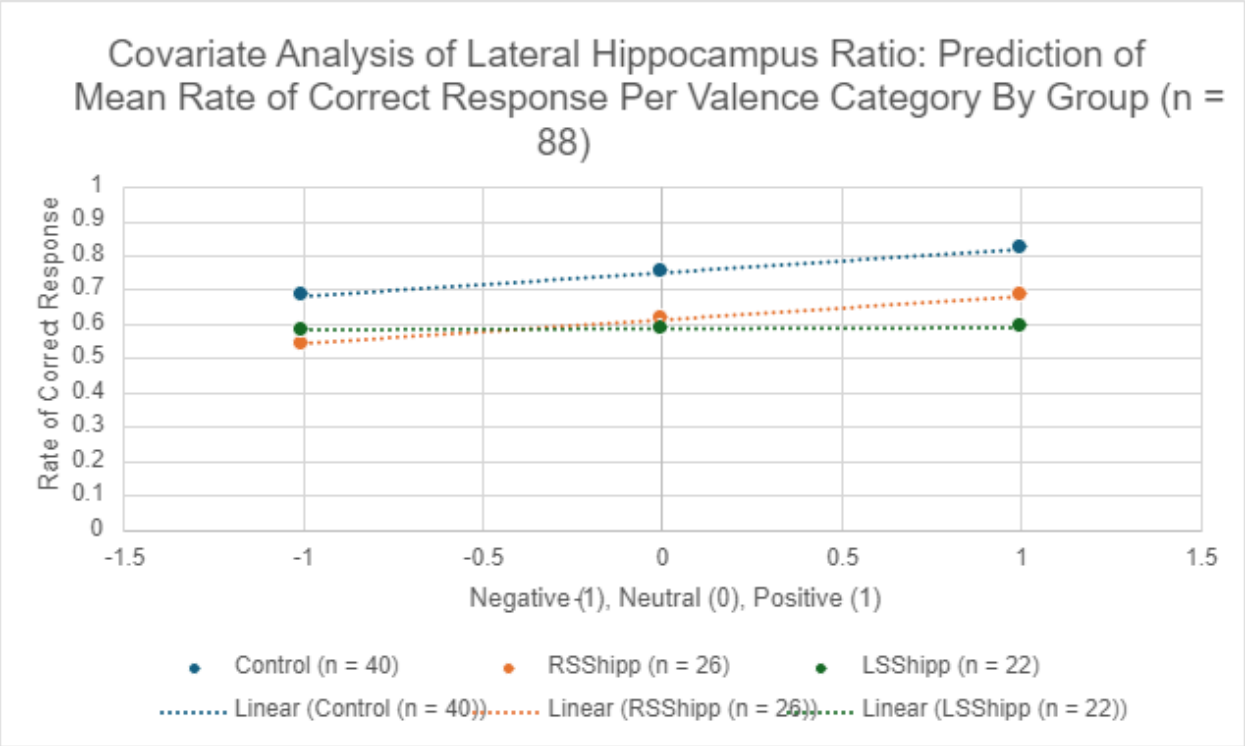

Figure 5 - Mean Value of Rate of Correct Response by Hippocampus Volume Proportion Adjusted For Age, Education, BDI, and BNT: *Participants were categorized using MRI data – projected amygdala volumes for the right and left hemispheres – to determine proportion (SS: Side Smaller). A linear regression model was used to generate performance predictions based on the data set; predicted average values per valence category were calculated for each status group; the values were then fitted with trendlines:*

Controls: $y = 0.0687x + 0.749$

RTLEPs: $y = 0.0687x + 0.6113$

LTLEPs: $y = 0.0051x + 0.586$

There is a stair step trend from negative to positive valence in the Control and RTLEP groups which is not present in the LTLEP group; the LTLEP group does not appear to have any specific proficiency in any valence category.

Demographic Data	**Controls**	**RSSamy**	**LSSamy**	**Total**
Average Age (years)	31 (n = 32)	47 (n = 14)	45 (n = 31)	39 (n = 77)
Average Education (years)	16 (n = 31)	14 (n = 14)	14 (n = 32)	15 (n = 77)
Average BDI Score	3 (n = 40)	15 (n = 12)	9 (n = 27)	7 (n = 78)
Average BNT Semantic Score	56 (n = 40)	49 (n = 14)	46 (n = 31)	55 (n = 85)
Number of Men	14	5	9	29
Number of Women	21	9	22	52
Number of Participants	40	14	33	87

Table 7 - Demographic and Covariate Data Grouped by Amygdala Volume Proportion: *Averages presented per variable by group. Groups were defined using MRI data – projected amygdala volumes for the right and left hemispheres – to determine proportion (SS: Side Smaller). One participant had a left:right amygdala ratio of 1.0 and was thus not considered in this analysis. The Beck Depression Inventory (BDI) utilizes a 62 point scale where scores above 20 indicate presence of moderate depression. The Boston Naming Test (BNT) utilizes a 60 point scale where scores below 48 indicate impaired performance on timed naming tasks. BNT is highly similar between the two epilepsy groups; this is true of all four covariates.*

Demographic Data	**Controls**	**RSSamy**	**LSSamy**	**Total**
Average Age (years)	31 (n = 32)	44 (n = 25)	46 (n = 21)	40 (n = 78)
Average Education (years)	16 (n = 31)	14 (n = 26)	14 (n = 21)	15 (n = 78)
Average BDI Score	3 (n = 40)	13 (n = 21)	8 (n = 17)	7 (n = 78)
Average BNT Semantic Score	56 (n = 40)	46 (n = 24)	46 (n = 22)	55 (n = 86)
Number of Men	14	8	7	29
Number of Women	21	18	14	53
Number of Participants	40	26	22	88

Table 8 - Demographic and Covariate Data Grouped by Hippocampus Volume Proportion: *Averages presented per variable by group. Groups were defined using MRI data; projected hippocampus volumes for the right and left hemispheres to determine proportion (SS: Side Smaller). The Beck Depression Inventory (BDI) utilizes a 62 point scale where scores above 20 indicate presence of moderate depression. The Boston Naming Test (BNT) utilizes a 60 point scale where scores below 48 indicate impaired performance on timed naming tasks.*

Demographic Data	**Controls**	**RTLEPs**	**LTLEPs**	**Total**
Average Age (years)	31 (n = 32)	45 (n = 22)	46 (n = 24)	40 (n = 78)
Average Education (years)	16 (n = 31)	14 (n = 23)	14 (n = 24)	15 (n = 78)
Average BDI Score	3 (n = 40)	11 (n = 20)	11 (n = 18)	7 (n = 78)
Average BNT Semantic Score	56 (n = 40)	48 (n = 23)	45 (n = 23)	55 (n = 86)
Number of Men	14	7	8	29
Number of Women	21	16	16	53
Number of Participants	40	23	25	88

Table 9 - Demographic and Covariate Data Grouped by Diagnosis Status: *Averages presented per variable by group. Groups were defined by clinical diagnosis (TLEP: Temporal Lobe Epilepsy Patient). The Beck Depression Inventory (BDI) utilizes a 62 point scale where scores above 20 indicate presence of moderate depression. The Boston Naming Test (BNT) utilizes a 60 point scale where scores below 48 indicate impaired performance on timed naming tasks.*

Volumetric Proportion Status	**Number of RTLEP Participants**	**Number of LTLEP Participants (n = 25)**	**Number of TLEP Participants**
RSSamy	10 (0.45; n = 22)	4 (0.16)	14 (0.30; n = 47)
LSSamy	12 (0.55; n = 22)	21 (0.84)	33 (0.70; n = 47)
RSShipp	18 (0.78; n = 23)	8 (0.32)	26 (0.54; n = 48)
LSShipp	5 (0.22; n = 23)	17 (0.68)	22 (0.46; n = 48)
LSShipp + LSSamy	4 (0.18; n = 22)	14 (0.56)	18 (0.38; n = 47)
RSShipp + RSSamy	9 (0.41; n = 22)	1 (0.04)	10 (0.21; n = 47)
LSShipp + RSSamy	2 (0.09; n = 22)	2 (0.08)	4 (0.09; n = 47)
RSShipp + LSSamy	8 (0.36; n = 22)	7 (0.28)	15 (0.32; n = 47)

Table 10 - Ratio of Patient Diagnostic Status to Hemispheric Structural Volume Proportion: *Participants were initially categorized based on their hemispheric epilepsy status (TLEP: Temporal Lobe Epilepsy Patient). They were recategorized using MRI data – projected amygdala and hippocampus volumes for the right and left hemispheres – to determine proportion (SS: Side Smaller). One participant had a left:right amygdala ratio of 1.0 and thus was only considered in the hippocampal calculations. 17% of RTLEPs and 4% of LTLEPs did not have a smaller structure in the same hemisphere as their epilepsy; 59% of participants did not have a smaller structure in their unaffected hemisphere. LTLEPs were more likely to have a smaller left amygdala; this trend does not hold true for RTLEPs.*

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