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## INTRODUCTION

Patients who undergo anterior temporal lobectomy (ATL) to treat temporal lobe epilepsy (TLE) often experience worsened or de novo psychiatric symptoms. There is evidence to suggest that the pathophysiology of epilepsy and mood disorders are linked both functionally or structurally in the brain.[1,2] While several studies have examined the role that changes in hippocampal volume may play in predicting post-surgical depression, the role of the amygdala in such prediction has been overlooked, despite extensive literature demonstrating its contribution to emotion processing and expression.[3,4] The goal of this project was to determine if change in amygdala volume is a predictor of depression and/or anxiety in TLE patients who undergo ATL, with specific attention given to side of surgery.

## METHODS

Data was collected from 32 patients who underwent ATLs (19 right, 13 left, matched samples). Pre- and post-surgery Personality Assessment Inventory (PAI) data were collected on 14 ATL patients. The following PAI subscales were utilized in this analysis: Anxiety: PAIANX; Anxiety Related Disorder: PAIARD; Depression: PAIDEP). Volumetric analysis was performed on pre- and post-surgical T1 MRIs using Freesurfer's longitudinal processing function. Left and right amygdala volumes, change scores, and amygdala asymmetry ratios were calculated taking into account whole brain volume. 55% of the patients were seizure-free after 1 year (RTLE= 8, LTLE= 9); 29% received an Engel Class score of 2 or 3 (RTLE= 7, LTLE= 2)

## RESULTS

The two experimental groups, right TLE and left TLE, showed no significant differences either pre- or post-ATL: age, age of seizure onset, full-scale IQ or amygdala volume or asymmetry (Table 1).

**Table 1: . Clinical and Demographics Characteristics of each TLE group**

| | RTLE | LTLE | Significant (?) |
|---|---|---|---|
| N (female) | 18 (12) | 13 (10) | NS |
| Age (years) | 45 ± 12 | 48 ± 12 | NS |
| Years of Education | 15 ± 2 | 15 ± 3 | NS |
| Time between surgery and Second Test (months) | 15.4 ± 24.7 | 14.7 ± 16.2 | NS |
| Age of seizure onset (years) | 21 ± 11 | 25 ± 14 | NS |
| L amygdala volume, pre-/post- surgery | 0.18 ± 0.04/0.17 ± 0.04 | 0.17 ± 0.07/0.03 ± 0.03 | NS/0.0 |
| R amygdala volume, pre-/post- surgery | 0.19 ± 0.06/0.03 ± 0.05 | 0.21 ± 0.08/0.17 ± 0.06 | NS/0.0 |
| Amygdala Asymmetry | 0.03 ± 0.08/-0.73 ± 0.42 | 0.11 ± 0.06/0.62 ± 0.48 | 0.005/0.0 |
| **Psychiatric Scores, pre-/post- surgery** | | | |
| PAIANX | 57 ± 12/48 ± 6 | 53 ± 9/59 ± 13 | NS/NS |
| PAIARD | 53 ± 12/49 ± 12 | 51 ± 9/60 ± 16 | NS/NS |
| PAIDEP | 59 ± 11/54 ± 9 | 51 ± 7/64 ± 18 | 0.042/NS |

All measures are shown as means ± standard deviation. Amygdala volume was calculated as a ratio with total gray matter volume. Amygdala was calculated as the difference between right and left maygdala volume rations over the combined right and left amygdala volume. Group comparisions were examined throug independent sample t-test. Abbreviations: Personality Assessment Inventory measures Anixiety (PAIANX), Anxiety Related Disorders Depression (PAIDEP).

**Table 2: Post Surgical Psychiatric Scores. Results of regression analyses for PAIDEP, PAIANX, and PAIARD scores to amygdala volume, amygdala volume change, amygdala pre-surgery, and amygdala asymmetry change measurements. Significant results are marked with an asterisk.**

| Model | PAIDEP *Adj. $R^2$=0.64, F[7,15]=4.7, p=0.02* | PAIANX *Adj. $R^2$=0.56, F[7,15]=3.7, p=0.04* | PAIARD *Adj. $R^2$=0.6, F[7,15]=4.2, p=0.03* |
|---|---|---|---|
| | **Stand. b Coef., p-value** | **Stand. b Coef., p-value** | **Stand. b Coef., p-value** |
| ATL group | -0.24, .0.68 | 1.2, 0.08 | 0.57, 0.35 |
| Left AMYG vol, pre-surg. | 6.5, 0.008* | 4.5, 0.06 | 5.8, 0.02* |
| Right AMYG vol, pre-surg. | -5.9, 0.02* | -4.2, 0.08 | -5.2, 0.03* |
| Left AMYG vol change | -0.46, 0.72 | -0.38, 0.79 | -1.2, 0.38 |
| Right AMYG vol change | 4.4, 0.005* | 2.5, 0.08 | 4.2, 0.009* |
| AMYG asym., pre-surg. | 4.7, 0.02 | 3.2, 0.11 | 4.1, 0.04* |
| AMYG asym., change | -3.9, 0.04* | -3.5, 0.08 | -5.3, 0.01* |

Results of regression analyses for PAIDEP, PAIANX, and PAIARD scores to amygdala volume, amygdala volume change, amygdala pre-surgery, and amygdala asymmetry change measurements. Significant results are marked with an asterisk.

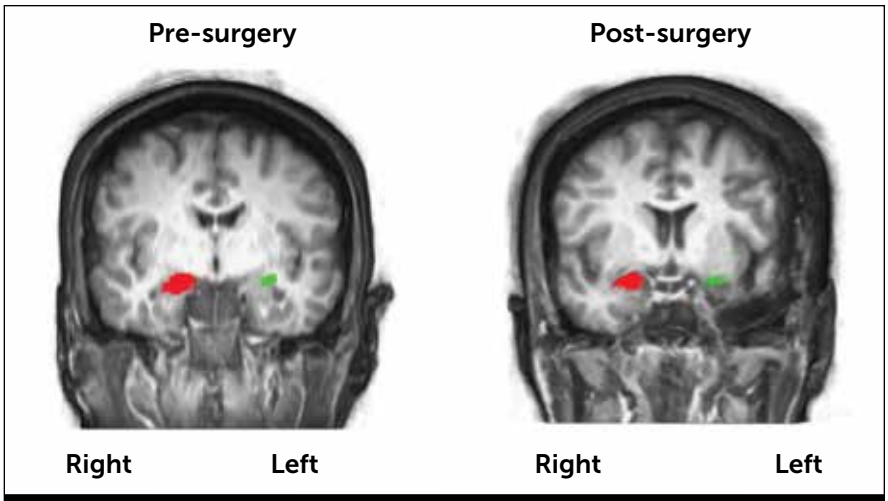



**Figure 1**

Pre- and post-surgery fMRI images from a Left TLE patient. The red and green overlays represent the right and left amygdala, respectively. The left temporal lobe resection is clearly visible in the right post-surgery image. Images shown in radiological view.

There is a change post-surgery in PAIANX (F[1,12]=6.6, p=.02), PAIDEP (F[1,12]=8.2,p=.01) and PAIARD (F[1,12]=4.5, p=.05; see Figure 2) that varies for both the left and right ATL groups, such that the RATL group symptom levels went down and LATL group levels went up.

Regression analysis showed that measures of amygdala volume, amygdala volume change, and amygdala asymmetry predict post-surgery PAIANX, PAIDEP, and PAIARD, explaining approximately 36% of the variance in each of these variables, though the individual beta coefficients were significant for only PAIARD and PAIDEP (Table 2). Examined within each ATL group, this regression model was only significant for PAIARD in the right ATL group.

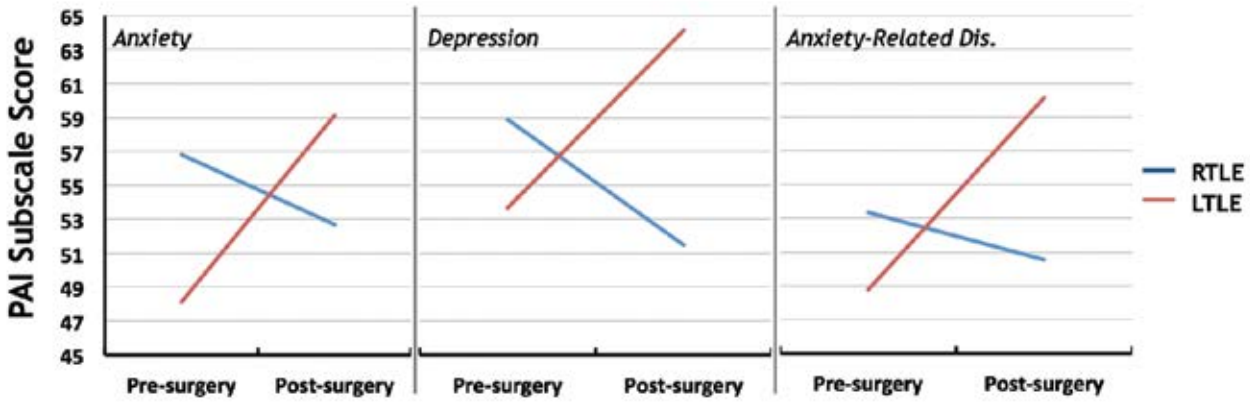
The above regression model remained significant when ATL group was included as a predictor, and also after accounting for pre-surgery PAI scores and age of seizure onset.

Correlational analyses showed that change in the ratio or asymmetry of right to left amygdala volume may result in post-surgical psychiatric symptom change in right but not left ATL patients, with loss of the right sided volume associated with decreases in PAIANX (r=-.77), PAIDEP (-.86), and PAI ARD (-.95).

## CONCLUSIONS

Psychiatric symptoms changed in both left and right TLE, however, the direction of the effects differed. The left group consistently showed a worsening of symptoms. This suggests left more than right ATL disrupts emotion regulation systems, potentially placing patients at higher risk for deleterious post-surgical emotional/psychiatric change.

A multivariate combined model of amygdala volume, volume change, and asymmetry does predict post-surgical anxiety (rumination, tension), depression, and anxiety related disorders (phobia, trauma stress response). Increases in right




**Figures 2: Comparision of Pre- and Post-Surgery PAI Subscale Scores in LTLE and RTLE Patients.** Average pre-and post-surgical PAIANX, PAIDEP, and PAIARD scores plotted pre- and post-surgery. Psychiatric scores tend to decrease in RTLE patients post-surgery, whereas scores tend to increase post-surgery in LTLE patients.

amygdala volume and decreases in left amygdala volume related to higher levels of psychiatric symptoms post-surgery, but this effect needs to be retested in larger samples as it does not distinguish the separate effects in right and left ATL. There were some indications these associations with amygdala volume may be strongest with the PAI ARD variable in the right ATL group.

When viewing psychiatric symptoms alone, preliminary results suggest left ATL patients may fare worse post-surgery in terms of psychiatric symptoms. In contrast, associations with volume reveal that right ATL patients may be more sensitive to the ipsilateral amygdala loss than left patients, with reduction in this pathologic zone reducing levels of depression, anxiety, and anxiety/stress related symptoms.

The data suggest the catalyst of symptom change differs in the two ATL groups, with the left group more susceptible to causes less related to brain structure and more related to diminished dominant hemisphere functions (e.g., language/memory), and their negative impact on communication or vocational skills. In contrast, psychiatric symptom change in right ATL appeared more closely aligned with structural change (loss) in the ipsilateral amygdala, reducing pathologic emotion processing. An effect that may be related to the tendency for the right hemisphere to be dominant for emotion processing and regulation.

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