Emotional/Psychiatric Symptom Change and Amygdala Volume After Anterior Temporal Lobectomy

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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 amygdala volume rations over the combined right and left amygdala volume. Group comparisons were examined through independent sample t-test. Abbreviations: Personality Assessment Inventory measures Anxiety (PAIANX), Anxiety Related Disorders Depression (PAIDEP).
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 PAIARD (-.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 amygdala asymmetry does predict post-surgical anxiety (rumination, tension), depression, and anxiety related disorders (phobia, trauma stress response). Increases in right
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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