Magnetic resonance imaging textural changes are more sensitive than volumetric changes in the amygdala of cocaine use disorder patients

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Introduction

- Neuroimaging can improve the treatment response classification accuracy compared to using clinical measures alone in psychiatric diseases like PTSD, MDD, and substance use disorders[1,2].
- Yip and Konova[3] have shown that dense temporal sampling can maximize clinical insights by capturing the clinically meaningful transition phase during ongoing therapy of addiction patients.
- Several substance use studies[4,5] have shown the volumetric changes in the amygdala and hippocampus regions.
- We have investigated and compared the sensitivity of the volumetric and textural changes over time in the amygdala of cocaine use disorder patients subjected to repetitive transcranial magnetic stimulation.
- We are motivated by the recent studies[6-7] on the early detection of Alzheimer's using textural analysis.
- We have validated that textural changes are seen earlier than volumetric changes in the amygdala.

Methods

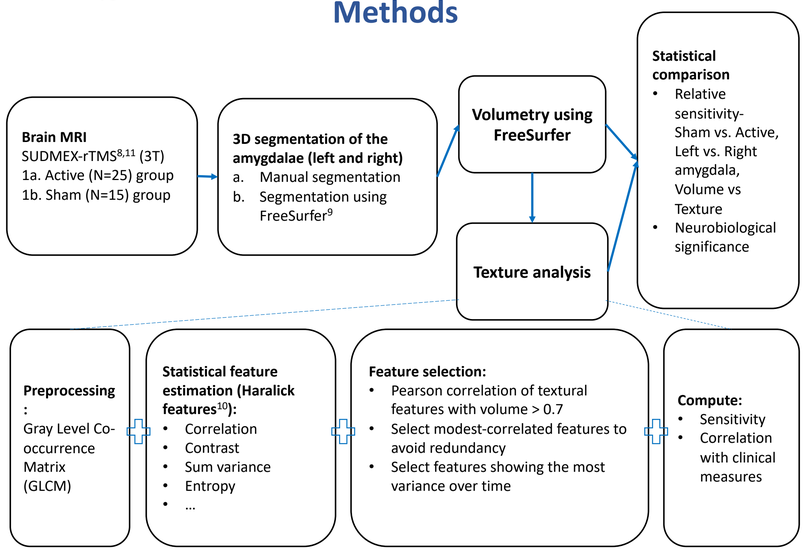

***Figure 1**: Pipeline for volumetric and textural analysis*

- SUDMEX database: 54 participants who underwent the repetitive Transcranial Magnetic Stimulation (rTMS) treatment
- Treatment location:
  - Sham group- left temporalis muscle
  - Active group- left dorsal-prefrontal cortex
- Treatment duration: One year, imaged at five-time points, baseline(t_0), two weeks (t_1), one month ($t_{1\text{-}4}$, only for Sham), three months(t_2), six months (t_3), one year (t_4)
- 40 subjects- 15 Sham, 25 Active treatment
- Acute phase (0-2 weeks): 5000 pulses/day for ten days, Maintenance phase (only active) (2 weeks – 1 year): 10000 pulses/week
- Other 14 participants' - inconsistency in timepoint data or reported to have received both active and sham treatment (avoid confounds)
- Amygdala segmentation using FreeSurfer's *recon-all* command on the 3T T1-MPRAGE
- We computed the Haralick features for textural analysis.
- Our reference manual amygdala segmentation ensured less than 5% coefficient of variation.
- A five-subject pilot study (2 Active, 1 Sham, 2 Active + Sham) was performed to understand the volumetric changes compared to textural changes.
- Feature selection approach:
  (i) Select features with a correlation>0.7 with the left and right amygdala volumetry
  (ii) Select modestly correlated features (correlation < 0.5) to avoid redundancy
  (iii) Select the features with higher sensitivity and temporal variance to volume
- Comparison: Volume vs Texture, Left vs Right amygdala, Sham vs Active groups
- Correlate results with clinical and cognitive measures to interpret additional clinical information.

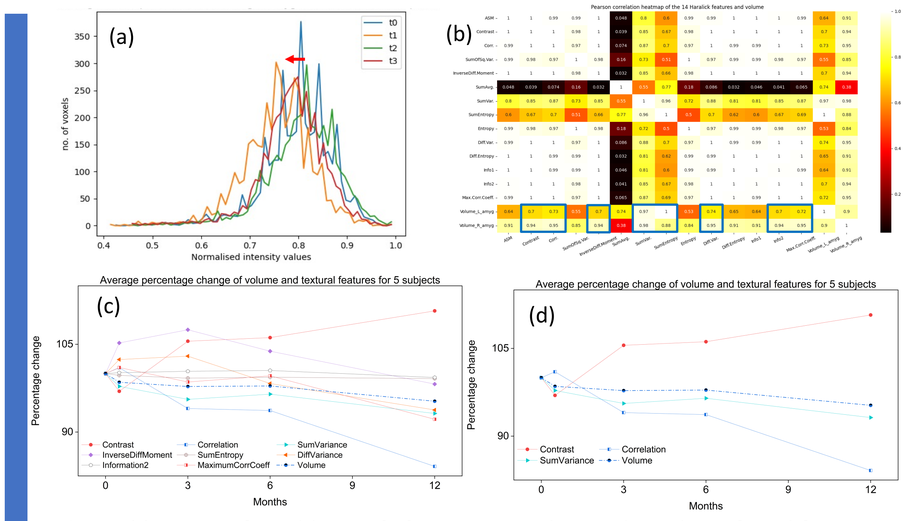

***Figure 2**: (a) Histogram of amygdala region for four time points, red arrow indicates the significant shift in intensity (b) Pearson correlation of Haralick features with left and right amygdalae, blue boxes indicate shortlisted features that pass the 0.7 threshold, (c) average percentage change (5 subject pilot study) of volume and 14 Haralick features, and (d) best-performing features*

Results

- Histogram analysis of ROI shows variation in intensity across time points.
- Figure 2b shows the Pearson correlation coefficient of the 14 Haralick features and the left and right amygdala. The features which didn't cross the threshold were excluded. This pipeline (Figure 1) was performed for all five subjects within the pilot study, and we have visually inspected the features that have shown higher percentage changes than volume.

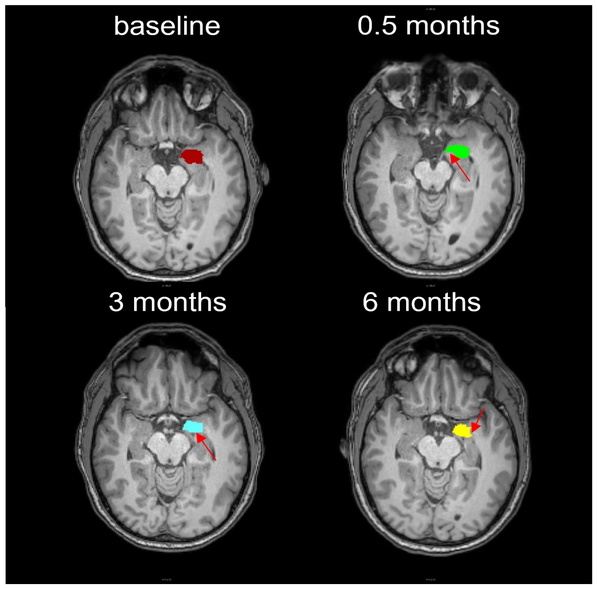

***Figure 3:** Left amygdala volume changes (arrows) over time in a cocaine use disorder patient*

- The average left amygdala volume over all the 25 patients in Active group was lower than the right.
- The left amygdala showed a higher percentage change than the right, probably because the treatment was close to the left amygdala.
- The average standard deviation (SD) of volumetric changes of the Sham group (~8.3%) was lesser than that of the Active group (~11%), indicating the effectiveness of the active therapy.

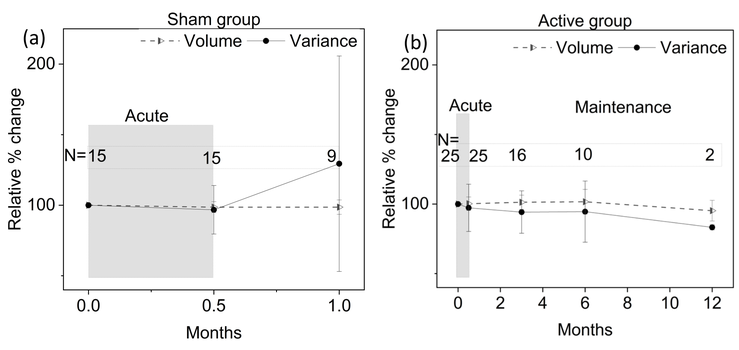

***Figure 4:** Comparison of volumetric and textural changes in the (a) Sham and (b) Active patient populations*

- The Active group witnessed increased modulation of the amygdalae volume (red arrows, Figure 3) than that of the Sham group.
- Figure 5 shows that the sensitivity of the selected textures is higher than the volume in both groups.
- It is observed that the slope decreased with an increase in months during the unblinded or open-label maintenance phase (Figure 4).

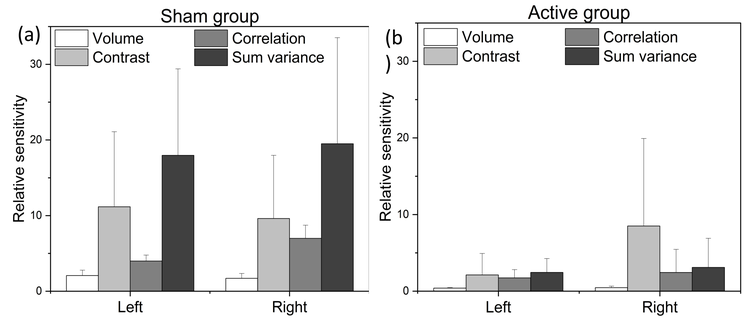

***Figure 5**: Comparison of the relative sensitivity (change over time) for volumetric and textural changes in the (a) Sham and (b) Active groups.*

Discussion and conclusion

- Volume vs Texture: The sensitivity of the textural features is higher than that of the volume across the whole dataset. During atrophy or any neuronal death, the ROI has a statistical variance that impacts the GLCM and in turn, affects the textural features and shows up earlier than actual volumetric changes.
- Left vs Right amygdala: The left has changed more than the right, correlating with the location of the therapy. The increased slope of changes in volumes has been noted during the double-blinded randomized clinical trial acute phase, which qualifies them for treatment responders.
- The Sham group has data until one month and cannot be compared with Active group responders.
- The variance of the GLCM of the amygdalae shows increased sensitivity than volume during both phases (acute and maintenance) of the rTMS therapy.
- In conclusion, the sensitivity of amygdalae texture changes in cocaine use disorder patients subject to rTMS is more than volumetric changes in 40 patients imaged over time.

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