Effects of Ayahuasca Use on Brain Function and Mood Correlation

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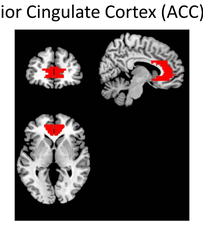
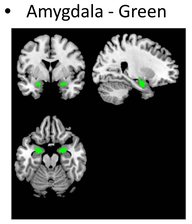
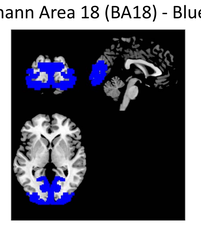
INTRODUCTION

- Ayahuasca is used through out South America and other parts of the world, including in Albuquerque, New Mexico, in religious and spiritual practices. With the growing popularity of ayahuasca, it is important to understand how it effects brain function and mood.
- It is a $5HT_{2A}$ agonist that induces hallucinations when ingested. It is made by combining two plants, *Banisteriopsis caapi* and *Psychotria viridis*, into a tea. These ingredients contain *N,N*-dimethyltriptamine (DMT) and monoamine oxidase inhibitors (MAOIs). The MAOIs allow the DMT to become psychoactive (Tupper 2008).
- This study attempts to determine the changes in functional connectivity and how those changes correlate with mood in the brains of long-term Ayahuasca users, specifically those who use ayahuasca in a religious setting, by comparing the fMRI scans between two groups. The two groups consisted of Ayahuasca users and controls.
- Our hypotheses were:
  - Ayahuasca users will have increased resting blood oxygen level dependent (BOLD) signal in frontal cortical regions in comparison to controls.
  - Ayahuasca users will have altered connectivity between the amygdala and the inferior frontal regions.

METHODS

- All of the data was collected with informed consent in Albuquerque, New Mexico at the Mind Research Network (MRN).
- The fMRI scans were collected at MRN using Siemens 3T scanners. During the scanning session, each participant was scanned with their eyes opened . Over the 30 minute scanning session a T1-weighted scan, a T2-weighted scan, and two echo-planar BOLD-weighted resting state scans were collected.
- Those participants who are part of the religious group and took part in the Ayahuasca religious ceremony were scanned the day after ingesting the ayahuasca tea.
- The experiment began with 37 subjects, but was trimmed to 33 due to 4 not meeting exclusion criteria. We ended up with:
  - Groups:
    - Control: 16
    - Ayahuasca: 17
  - Gender:
    - Male: 20
    - Female: 13
  - Age:
    - Range: 20-60
    - Mean: 39.45
  - Handedness:
    - Right: 29
    - Left: 4
- Using the CONN toolbox (Whitfield-Gabrieli and Nieto-Castanon 2012), three regions of interest (ROI) were explored using both ROI-ROI connectivity and ROI-voxel connectivity. The ROI's were:
  - Anterior Cingulate Cortex (ACC) – Red
  - Amygdala - Green
  - Brodmann Area 18 (BA18) - Blue

- The CONN toolbox (Whitfield-Gabrieli and Nieto-Castanon 2012) looks at functional connectivity by exploring the time course from a specific seed (ROI) and comparing it to the time course of voxels across the brain. Connectivity is found when time course correlations are found between the seed and other voxels.
- SPSS was then used to correlate reported general negative mood and functional connectivity found in CONN.
- All statistical tests used a p< 0.05 FDR-corrected threshold. The voxel-wise analyses used p<0.001 uncorrected at the voxel level and a cluster-wise p<0.05 FDR corrected threshold.

RESULTS

Seed-Voxel

Figure 1 shows between-group connectivity when the seed is the ACC. Ayahuasca users show greater connectivity based from the ACC. The connectivity is shown to the entorhinal and the perirhinal areas.

Voxel P<0.001 uncorrected
Cluster P<0.05 FDR corrected

T(1,31) min = 3.37
K min = 422 (min. number of voxels in a significant cluster)

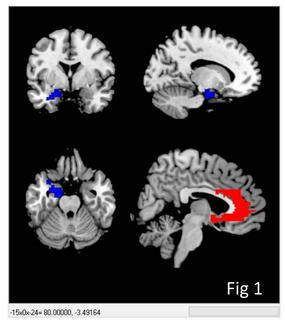


Fig 1

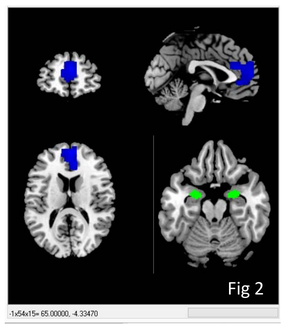


Fig 2

Figure 2 shows between-group connectivity when the seed is the amygdala. Ayahuasca users show greater connectivity based from the amygdala. The connectivity is shown to the dorsal lateral prefrontal cortex and the dorsal anterior cingulate cortex.

Voxel P<0.001 uncorrected
Cluster P<0.05 FDR corrected

T(1,31) min = 3.37
K min = 1942 (min. number of voxels in a significant cluster)

Figure 3 shows between-group connectivity when the seed is BA18. Controls show greater connectivity based from BA18. The connectivity is shown to the dorsal frontal cortex, the premotor cortex, and the dorsolateral prefrontal cortex.

Voxel P<0.001 uncorrected
Cluster P<0.05 FDR corrected

T(1,31) min = 3.37
K min = 391 (min. number of voxels in a significant cluster)

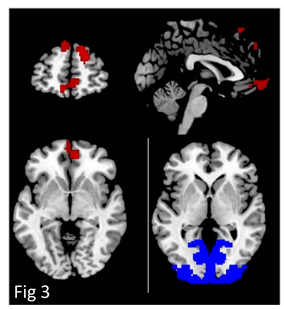


Fig 3

Mood Correlation

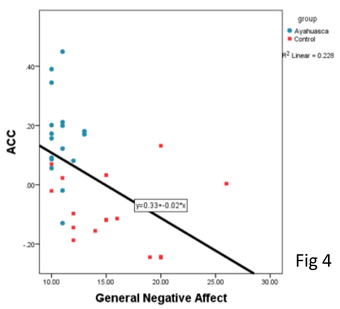


Fig 4

Figure 4 shows the correlation between the ACC functional connectivity and the self reported general negative affect scores. The Ayahuasca group's lower general negative affect scores correlated with their higher between-group connectivity when the seed was the ACC.

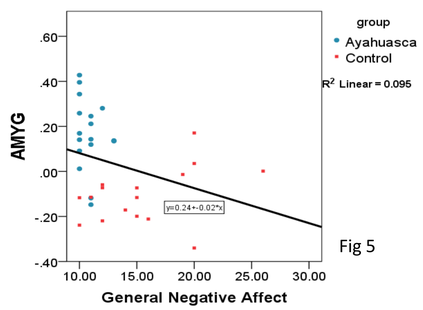


Fig 5

Figure 5 shows shows the correlation between the amygdala functional connectivity and the self reported general negative affect scores. The amygdala showed similar, but not identical, results to the ACC. The amygdala results were close to significance, but ended up not passing the significance threshold.

Figure 6 shows the correlation between BA18 functional connectivity and the self reported general negative affect scores.

The Control group's higher general negative affect scores correlated with their higher between-group connectivity when the seed was BA18.

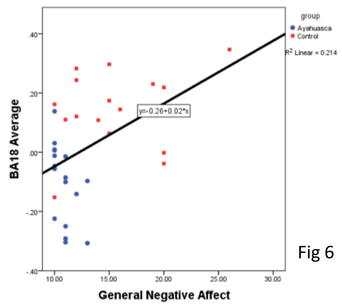


Fig 6

CONCLUSIONS

- Out of our 3 ROI's, all of them showed between group connectivity results.
  - One of the 3 ROI's showed that the control group had more significant connectivity than Ayahuasca users when based in that ROI. The ROI was BA18, with greater connectivity to frontal regions.
  - Two of the 3 ROI's showed that Ayahuasca users had more significant connectivity than controls when based in that ROI. These 2 include that ACC and the amygdala, both showing increased connectivity to areas near each other.
- Our original hypothesis that Ayahuasca users will have altered connectivity between the amygdala and the inferior frontal regions was supported by our findings (Fig. 5). This may suggest that Ayahuasca users can process emotional stimuli in a better way than controls.
- Our second original hypothesis was not supported by the results provided by the CONN toolbox.
- The mood correlations showed that lower general negative affect is correlated with higher functional connectivity in the ACC and that higher general negative affect is correlated with higher functional connectivity in BA18.
- The mood correlation findings, like the amygdala findings, may suggest that Ayahuasca users have increased ability to process emotional stimuli. This raises questions about the way hallucinogens affect emotional processing.

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