Replicating Impaired Resting State Functional Connectivity in Chronic Cocaine Users

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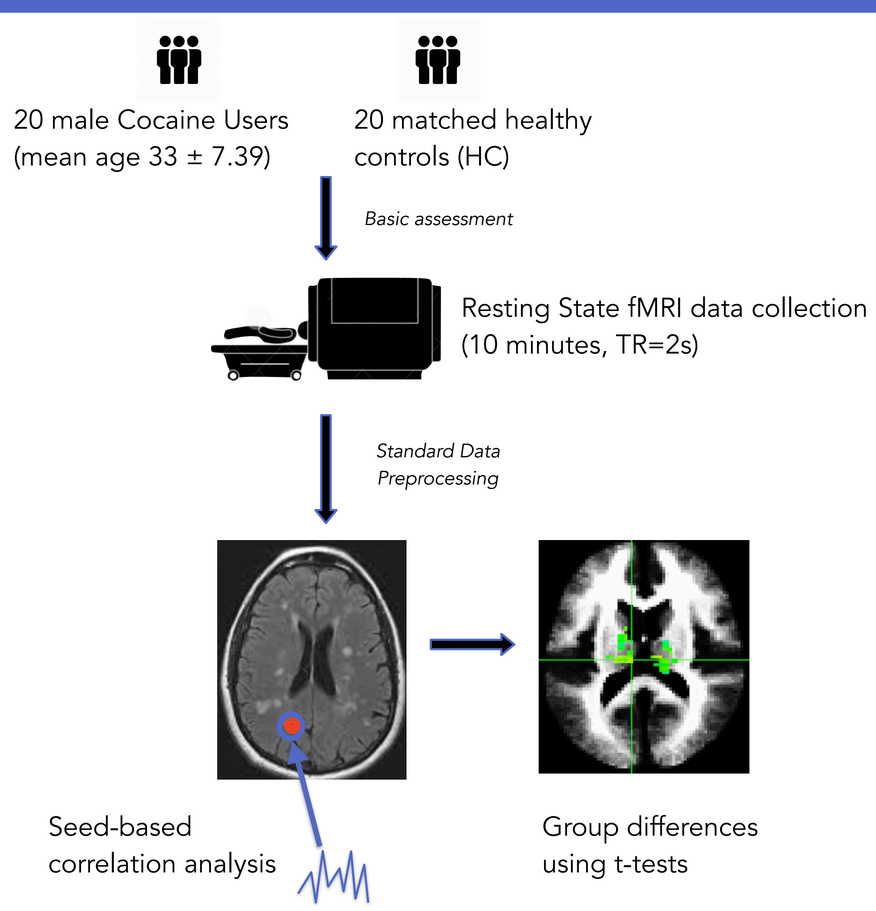
Background

The field of science, especially neuroscience is plagued by the *replication crisis*, attributed to several factors, for instance, experimental design and methods used, choice of statistical significance thresholds, and individual differences. However, reproducibility of experimental findings is key in assessing its validity. Especially in clinical settings, replicability of results across demographics is important for developing clinical treatments based on reliable biomarkers.

Studies employing resting-state functional magnetic resonance imaging (rsfMRI) to identify neurodegenerative disorders, other mental health conditions, especially addiction, have exponentially increased due to the ease of experimental design and methods employed. However, the choice of methodological approach to evaluate functional connectivity during rest may lead to differing results. Cocaine abuse has been associated with alterations in the functional connectivity of the reward-related mesocorticolimbic circuit in the brain during rest. The current work aims at assessing the validity of these findings.

Method



Seed-based correlation analysis was performed with following 7 bilateral seeds of 3mm radius:

1. **Nucleus Accumbens (NAcc)**
2. **Rostral Anterior Cingulate Cortex (rACC)**
3. **Ventral Tegmental Area (VTA)**
4. **Mediodorsal (MD) Thalamus**
5. **Insular cortex**
6. **Amygdala**
7. **Hippocampus**

Conclusion

- Cocaine users showed reduced rsFCs for a number of regions with a large part of the results in agreement with the original study.
- However, the differences highlight the need to assess the external validity of neuroscientific findings and delve into probable causes for these evidenced alterations.
- These results also question the robustness of the use of simplified seed-based rsFC approach to evaluate alterations in brain functioning.

Aim

The aim of this study is to assess the reliability of the findings of a previous resting-state functional magnetic resonance imaging (rsfMRI) study[1] that compared functional connectivity differences in United States cocaine users (CU) and matched healthy controls (HC) on a different sample (Mexican in our case) with a similar experimental setup.

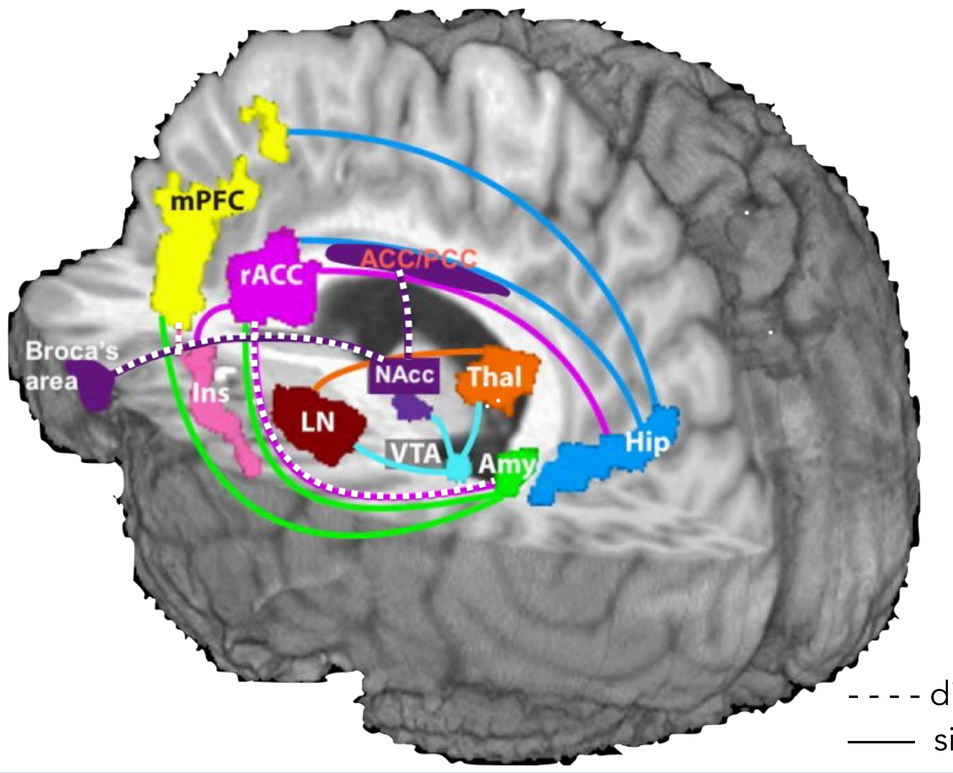
Results

Observations similar to the original study: Reduced resting-state functional connectivity strength was observed between:

- **Amygdala** and parts of prefrontal cortex, Insula, PCC,
- **Hippocampus** and prefrontal cortex, rostral and dorsal ACC, several frontal regions and left caudate nucleus,
- **Rostral ACC** and temporal gyrus and PCC,
- **Insula** and parts of prefrontal cortex and ACC,
- **Thalamus** and major parts of cingulate cortex and occipital gyrus, and
- **VTA** and the thalamus and Lentiform Nucleus.

However,

- ***rACC didn't show a direct relation with Amygdala unlike the original study but both Amygdala and rACC relate to PCC (BA 23).***
- ***Amygdala showed reduced connectivity with Substantia Nigra, a structure which is taken to play an important role in reward system.***



A distinctive finding of the study is 1) reduced resting-state FCs observed of NAcc seed with anterior and posterior Cingulate Cortex (ACC/PCC) and 2) increased connectivity with frontal regions around Broca's area.

The first observation was expected in the original study but was not found and, the second was not expected. However, increase in NAcc and Amygdala connectivity with frontal regions was observed in heroin addicts in a Chinese sample[2]

References

1. Gu H, Salmeron BJ, Ross TJ, et al. Mesocorticolimbic Circuits are Impaired in Chronic Cocaine Users as Demonstrated by Resting State Functional Connectivity. NeuroImage. 2010; 53(2): 593-601.
2. Ma N et al., Addiction related alteration in resting-state brain connectivity, NeuroImage. 2010 Jan 1; 49(1):738-44.
3. Image reference same as 1.

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