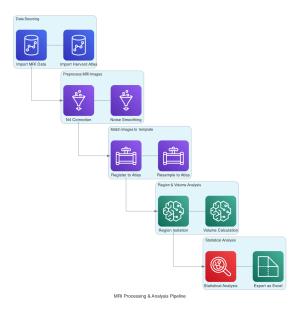
### **Abstract**

This project investigates the long-term effects of cannabis (marijuana) usage on brain structure. The dataset, obtained from OpenNeuro, comprises three main elements used for the analysis: (1) anonymized subjects with a Cannabis Use Score, (2) magnetic resonance imaging (MRI) scans taken three years apart, and (3) accompanying demographic and usage information. Working with this dataset posed several challenges. The imaging data contained noise, and the follow-up MRIs were not always acquired at the same angle or sampling resolution. Additionally, understanding how specific functional regions of the brain change through automated Python tools is a nontrivial task.

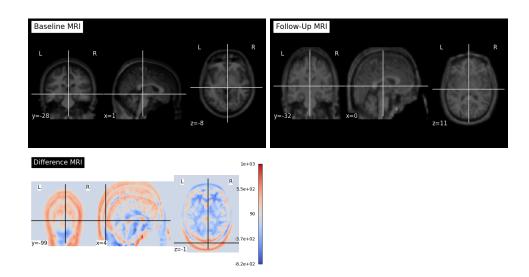
# **Design Architecture**



# **Data Analysis Tools and Methods**

The primary Python libraries employed for MRI image analysis in this project are **nilearn** and **ANTs**. *ANTs* (Advanced Normalization Tools) was used to register the MRIs by aligning them to a common orientation and shape. This step allows for valid comparisons between timepoints and against a standardized template, or "atlas." For this project, the **Harvard-Oxford Atlas** was chosen due to its widespread use in segmenting and analyzing distinct functional areas of the brain in MRI scans.

After registration, **pandas** was used to process the tabular data and combine these findings with the regional MRI difference analyses for further statistical evaluation. Specifically, linear regression models to predict CUDIT scores (cannabis use) and statistical significance testing (p-value < 0.05) were utilized to assess whether changes in certain brain regions are predictive of cannabis usage levels.



## **Hypothesis and Background**

The central hypothesis guiding this research posits that **heavy**, **long-term cannabis use is associated with structural volume changes in specific brain regions**, particularly shrinking in the temporal and frontal lobes. This assertion aligns with prior research suggesting that these regions are most susceptible to cannabinoids (Battistella et al., 2014). Despite popular belief that marijuana is less harmful than substances such as heroin, cocaine, or alcohol due to its different addiction profile, there remains a need for empirical data to determine whether prolonged cannabis use leads to functional or structural changes in the brain.

In one study on chronic cannabis users, it was noted that "...regular cannabis use is associated with gray matter volume reduction in the **medial temporal cortex**, **temporal pole**, **parahippocampal gyrus**..." (Battistella et al., 2014). Another study further corroborates potential neuroanatomical changes by stating, "In this study, we found that chronic exposure to marijuana (i) **reduces OFC gray matter volume**..." (Gilman et al., 2014). These observations highlight the importance of scrutinizing the long-term neurological implications of habitual marijuana use.

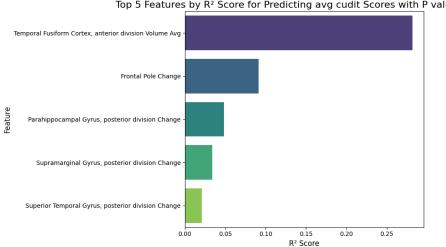
#### **Preliminary Results and Discussion**

Following the completion of registrations, difference maps were generated for each subject, highlighting volumetric changes over the three-year interval. Each difference map was then segmented by ROI (Region of Interest) to quantify these changes. The initial findings suggest that participants with higher Cannabis Use Scores exhibited more pronounced shrinkage or volume reduction in the **temporal** and **frontal** lobes. These outcomes are consistent with established research that identifies these regions as particularly vulnerable to chronic cannabinoid exposure (Battistella et al., 2014).

A subset of the ROIs demonstrated a **p-value below 0.05**, indicating statistical significance. The accompanying figure plots the correlation coefficients for the top five statistically significant regions. While these preliminary data imply a correlation between heavy marijuana use and brain structure changes, further research is needed to establish causation and to better understand potential confounding factors, such as baseline differences or concurrent substance use.

### Conclusion

This project contributes to the growing body of literature on the long-term neurological effects of cannabis. By systematically comparing baseline and follow-up MRIs, and correlating volumetric changes with Cannabis Use Scores, we provide additional evidence that heavy cannabis use may yield structural changes within the brain, particularly in areas linked to memory and cognition. Future work should incorporate larger, more diverse cohorts and examine functional outcomes to validate and extend these preliminary observations.



Top 5 Features by  $R^2$  Score for Predicting avg cudit Scores with P value < 0.05

### References

Battistella, G., Fornari, E., Annoni, J.-M., Chtioui, H., Dao, K., Fabritius, M., ... & Giroud, C. (2014). Long-Term Effects of Cannabis on Brain Structure. Neuropsychopharmacology, 39(9), 2041–2048. https://doi.org/10.1038/npp.2014.67

Gilman, J. M., Kuster, J. K., Lee, S., Lee, M. J., Makris, N., van der Kouwe, A., ... & Breiter, H. C. (2014). Cannabis use is quantitatively associated with nucleus accumbens and amygdala abnormalities in young adults. The Journal of Neuroscience, 34(16), 5529-5538. https://doi.org/10.1523/JNEUROSCI.4745-13.2014