

Analysis Plan

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About

This analysis plan pertains to the fMRI-BOLD data from a movie viewing task for the HMM Video studies. At the time of writing the analysis plan, data acquisition was completed but no statistical analyses were conducted. See GitHub link for timestamps on analysis pipeline (https://github.com/jxli25/Video_HMM). Analyses will only take place once this analysis plan has been uploaded, and time stamped on the Open Science Framework. If the researchers decide to conduct additional analysis, this will be stated in any publication (“post-hoc analyses”).

Data Collection

The experiment involved showing participants a 4 minute video stimulus. Approximately 40 of these participants had a diagnosed psychotic illness, and 40 were controls. fMRI-BOLD scans were conducted on participants during movie viewing. Participants also completed the following rating scales:

- Positive and Negative Symptom Scale (PANSS)
- Hamilton Depression Rating Scale (HDRS)
- Young Mania Rating Scale (YMRS)
- Simpsons-Angus Scale (SAS) for extrapyramidal side effects
- Clinical Global Impression – Severity (CGI-S), a measure of symptom severity

- Social and Occupational Functioning Assessment Scale (SOFAS), a continuous measure of overall functioning

We from the above complete dataset, we will randomly assign 10 clinical and 10 control participants to a hold-out dataset (HOD) used for analysis.

Pre-processing

Cleaning

Scans were normalised to the the MNI152Nlin6Asym standard space. Head-motion related movement artefacts were removed. A band-pass filter was applied (high pass = 0.01Hz, low pass = 0.15Hz) to filter out large scale frequency drifts and physiological noise. Spatial smoothing was not applied.

Parcellation

fMRI-BOLD sequences were standardised and parcellated according to the Yeo-17-thick atlas.

HMM Model

Training

We will train an HMM Model on our data after subtracting a hold-out dataset of 10 control group and 10 clinical group participants. We will perform HMM analysis on the clinical and control group separately using the same settings as below. The settings as per Table 1 will be used for this model.

Table 1 HMM Model input settings for object Options on MATLAB using the HMM-MAR package

Options. _____	Setting
K	15
covtype	full
DirichletDiag	<p>Will use HOD to estimate optimal DirichetDiag out of candidate priors (0.5, 1, 2, 5, 10). For each candidate_prior, fit HMM to the training set with the specified Dirichet prior. For each trained model, compute how well it predicts the hold-out data.</p> <ul style="list-style-type: none"> - Predictive log-likelihood; use learned parameters to evaluate likelihood of the hold-out sequence - Free energy; Evaluate the variational free energy on unseen data

	Select the DirichletDiag that maximises the predictive log-likelihood on hold-out set.
cyc	300
initrep	10
initcyc	10

Outputs, Analyses and Hypotheses

Prior to statistical testing, appropriate checks will be made to check assumption are fulfilled (e.g. normalcy, variance). If unfulfilled, table will be updated with updated methods.

Decoding Brain States

To decode Brain States identified by the HMM Model, we will correlate their Fractional Occupancy with each annotated video segment.

We will further validate these associations by using 16 general terms of the Neurosynth database “anxiety, language, negative, positive, outside, task switch- ing, inhibition, conflict, feedback, pain, somatosensory, sensor- imotor, music, auditory, emotion, and face perception” (Meer et al., 2020), then correlate the spatial distribution of each brain state to the topic maps. For each BS, we will calculate the voxel-wise Pearson correlation with each of the 16 terms (Chang et al., 2013).

Research Questions

Where the same Analysis Method is used for multiple runs to answer the same Question, a correction is applied to reduce the chance of a Type I error.

Video segments refer to the 9 separate clips making up the whole video stimulus observed by all participants, first composed and used by Mavadati et al. (2013).

Table 2 Questions, relevant variables and planned Statistical Analysis

Research Question	Variable(s)			Hypothesis and Analysis Method
	Independent	Dependent	Confounding	
Are the <u>Transition Probabilities</u> between each Brain State to each other Brain State different between Clinical and Control groups? (i.e. are people with psychosis more likely to transition to different states from the same starting brain state compared to people without psychosis?)	Psychosis diagnosis	Transition Probabilities		H: There are significant differences in transition probabilities between experimental and control groups. 1. Apply a threshold of 20% to identify the most frequent transitions, and visualise this.

				2. Analyse differences between the clinical and control group for each transition probability (# BS x # BS matrix) using t-tests.
Is there a difference in the <u>Fractional Occupancy</u> of each Brain State between the Clinical and Control groups for specific video segments? For example, does the clinical group occupy Brain States similar to the Default Mode Network during emotionally salient video segments, more than the Control group?	Psychosis diagnosis	Fractional Occupancy		<p>H: There is significant difference in FO of each HN between clinical and control groups.</p> <p>Take the segmented data and calculate FO of each BS for each segment within each group. Conduct MANOVA. If a significant effect is found, interpret using post-hoc t-tests.</p>
Are the <u>Switching Rates</u> different between the Clinical and Control group for the whole video? For each video segment?	Psychosis diagnosis	Switching Rates		<p>H: There is a significant difference between switching rates between the two groups.</p> <p>Perform t-test on SRs between clinical vs control groups.</p>
Is there a difference in cardiac response in the Control group compared to the Clinical group when watching each video segment?	Psychosis diagnosis	Heart Rate PPG amplitudes	Age, Sex, Baseline (10s before movie)	<p>H: There is a significant difference in cardiac response between mean and experimental groups</p> <p>Extract HR and PPG amplitudes for each segment and analyse difference</p>

				between groups using mANCOVA and post-hoc t tests.
Is there an association between symptoms severity as measured by the scores used, and heart rate variability or switching rates?	PANSS, HDRS, YMRS, SAS, CGI-S, SOFAS	Switching Rates	Age, Sex, Ethnicity, Chlorpromazine Equivalent Psychotropic Dose	<p>H: There is a significant correlation between switching rates and clinical scores.</p> <p>For clinical group, calculate Pearson's correlation coefficient between SR and PANSS, HDRS, CGI-S AND SOFAS</p>

References

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