***Manuscript Title: Regular Recreational Cannabis Users Exhibit Altered Neural Oscillatory Dynamics during Attention Reorientation***

**Authors:** Springer SD, Spooner RK, Schantell M, Arif Y, Frenzel MR, Eastman JA, Wilson TW.

# Supplementary Material

**Table 1. Cannabis Use Metrics**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cannabis Use Characteristics** | **Average** | **Standard Deviation** | **Range** |
| Age of First Use | 14.93 | 2.88 | 9-21 |
| Age of First Regular Use | 18.81 | 5.46 | 12-38 |
| Years of Regular Use | 9.45 | 9.45 | 1-25 |
| Years of Using Twice Weekly | 8.11 | 7.41 | 1-25 |

*n* = 21

# Supplementary Methods

### **MEG data acquisition, preprocessing, and imaging**

Neuromagnetic responses were sampled at 1kHz using an Elekta/MEGIN MEG system (Helsinki, Finland) with 306 sensors. MEG data from each participant was individually corrected for head motion and subjected to noise reduction using the signal space separation method with temporal extension (Taulu et al., 2004; Taulu & Simola, 2006). The continuous magnetic time series was divided into epochs of 4000 ms duration, with the onset of the cue defined as 0 ms and the baseline defined as the 600 ms preceding the cue onset (-600 to 0 ms). Epochs containing artifacts were rejected based on a fixed threshold method, supplemented with visual inspection. Specifically, for each participant, the distribution of amplitude and gradient values across all trials were computed, and those trials containing the highest amplitude and/or gradient values relative to the distribution were rejected by selecting a threshold that excluded extreme values. Importantly, these thresholds were set individually for each participant, as interindividual differences in variables such as head size and proximity to the sensor array strongly affects the amplitude of MEG signals (average threshold across sample = 1277.40 femtoTelsa, SD = 372.40). Of note, these thresholds did not differ by group (*p* = .89). On average, 89.81 valid and 90.51 invalid trials remained after artifact rejection and were used in the subsequent analyses. To ensure a balanced number of trials between groups and conditions, a mixed-model ANOVA was performed which showed no main effects of group, condition, nor interaction.

Artifact-free epochs were transformed into the time-frequency domain using complex demodulation (Kovach & Gander, 2016), and the resulting spectral power estimations per sensor were averaged across all trials to generate time-frequency plots of mean spectral density. These sensor-level data were then normalized with respect to the mean baseline power (i.e., -600 to 0 ms). The specific time-frequency windows used for subsequent source imaging were determined using a stringent statistical analysis involving nonparametric permutation testing of the sensor-level spectrograms across the entire array of gradiometers (see (Proskovec et al., 2018; Spooner et al., 2020; Wiesman et al., 2018).

Preceding MEG measurement, four coils were attached to the participant’s head and localized, together with the three fiducial points and scalp surface, using a 3-D digitizer (Fastrak 3SF0002, Polhemus Navigator Sciences, Colchester, VT, USA). Once the participant was positioned for MEG recording, an electric current with a unique frequency label (i.e., 293, 307, 314, and 321 Hz) was fed to each of the coils. This induced a measurable magnetic field and allowed each coil to be localized in reference to the sensors throughout the recording session. Since coil locations were also known in head coordinates, all MEG measurements could be transformed into a common coordinate system. With this coordinate system, each participant’s MEG data were coregistered to their individual to their high-resolution structural MRI.

Using a spherical head model, cortical networks were imaged at 4.0 x 4.0 x 4.0 mm using the dynamic imaging of coherent sources beamformer (Gross et al., 2001). The DICS approach utilizes the cross-spectral density matrices computed from the sensor-level complex demodulation to estimate the data dependencies. These matrices are then regularized (.0001% tSVD), time-frequency averaged across the window of interest, and inverted before multiplication with the leadfield matrices. Following convention, the source power from these images were normalized per voxel using a separately averaged prestimulus noise period (i.e., baseline) of equal duration and bandwidth (Hillebrand et al., 2005). All MEG data preprocessing and imaging used the Brain Electrical Source Analysis (BESA 7.0) software. To assess the anatomical basis of the responses identified through the sensor-level analysis, the 3D maps were computed across both conditions and then averaged across all participants. To examine the effects of cannabis use, virtual sensors (i.e., voxel time series data) were extracted from each participant’s MEG data. Specifically, for each cluster of activity identified in the grand average image, we identified the voxel with the strongest response and computed virtual sensors by applying the sensor weighting matrix derived from the forward solution to the preprocessed signal vector, which yielded a time series for the specific voxel in source space. For each coordinate of interest, the envelope of spectral power was computed for the frequency range used in the beamforming analysis. From this, we computed the relative (i.e., baseline corrected) and absolute (i.e., non-baseline corrected) response time series of each participant per task condition. For each participant, the average baseline activity was derived by averaging the absolute amplitude timeseries data across the baseline period (i.e., -600 to 0ms), and estimates of the relative response amplitude were derived by averaging across the time window used for beamforming (i.e., theta: 350-700ms; alpha/beta: 300-900ms). Finally, mixed-model ANOVAs and post hoc comparisons were conducted to evaluate changes in task-related neural oscillations during target processing as a function of task validity (within-subjects, 2 levels), cannabis use (between-subjects, 2 levels), and their interaction, while independent samples comparisons (i.e., two-sample t-tests) were made to assess differences in pre-stimulus (i.e., spontaneous) activity. Though the data reported herein encompasses the entirety of the neuromagnetic signal, to ensure that the conditional differences were not influenced by evoked responses, the same virtual sensor analyses were conducted with evoked (i.e., phase-locked) activity regressed out, and all results remained the same.