Characterizing Neurochemical Signatures of Sleep Stages via Simultaneous MRS-EEG

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Background

Sleep is crucial for maintaining healthy cognitive function, yet the neurochemical mechanisms underlying its different stages in the human brain remain poorly understood. This project aims to characterize how brain metabolites fluctuate across various sleep stages using simultaneous magnetic resonance spectroscopy (MRS) and electroencephalography (EEG). Specifically, we measured thirteen metabolites including GABA, glutamate, lactate, and creatine, in anterior cingulate cortex, hypothesizing distinct neurochemical signatures may characterize different arousal states.

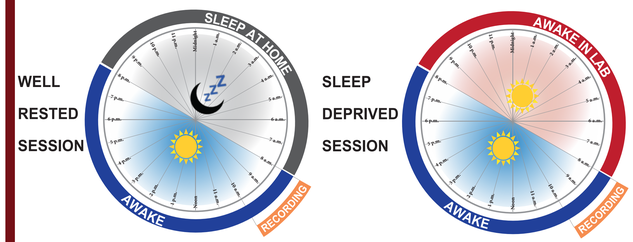
Study Design

Table1: Demographic Information of Study Participants

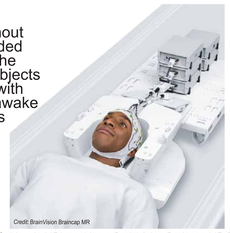
Features	MDD Group	HC Group
Number of Subjects	39	26
Sex (Female)	30	16
Mean Age (Years)	23.6 (±3.4)	23.7 (±3.1)

MDD represents individuals with Major Depression Disorder, and HC represents Healthy Control subjects

Two Imaging Visits



Subjects fasted throughout the nightand were provided with one meal before the morning MRI session. Subjects were instructed to rest with their eyes open and stay awake during the MRS scans



Scalp EEG
32-ch scalp EEG
3 EMG channels
2 EOG channels
4 carbon wire loops

MRS
HERCULES sequence
TR = 2 s
TE = 80 ms
Voxel size: 2 x 4 x 2 cm
Minimum number of transients = 320

Figure 1: Subject in MRI machine a BrainVision Braincap MR EEG cap on

Anterior Cingulate Cortex Voxel

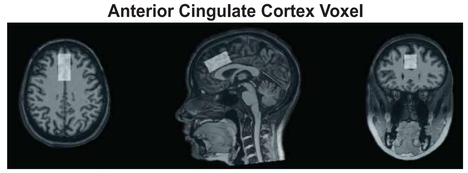


Figure 2: Anatomical MRI images showing voxelized region of interest (pathological region associated with MDD)

Table 2: Sleep States and Scoring Metrics

State 0 (Awake and Alert)		Mixed frequency Low amplitude
State 1 (Awake and Drowsy)		Presence of alpha (8-12 Hz) in >50% 8s epoch
State 2 (Transtion into Sleep)		Slow rolling eye movement and slowing EEG
State 3 (Stable Sleep)		Eyes fully closed or presesnce of K complexes and Sleep Spindles
State 4 (Arousal from Sleep)		Eyes opening after stable sleep

Framework for Evaluating the Quality of MRS Data

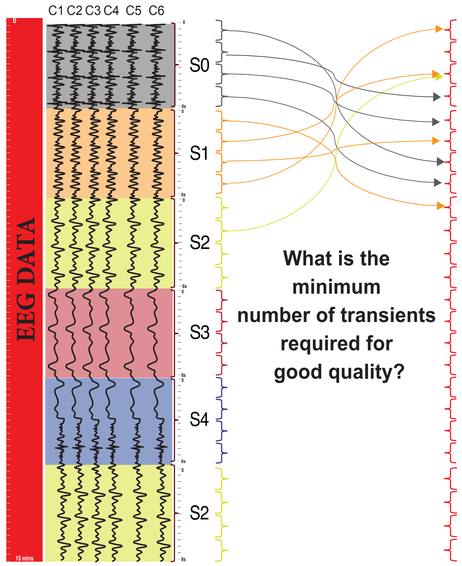


Figure 3: Simultaneous EEG data with an average length of 15 mins was segmented into 8-second windows which aligns with MRS acquisition timing. Within each 8-second classification window, we further segmented into 2-second windows which matches the length of each individual MRS spectra in Figure 4. Using multiple 2-second state-labeled EEG data, we segment MRS data for a good signal quality.

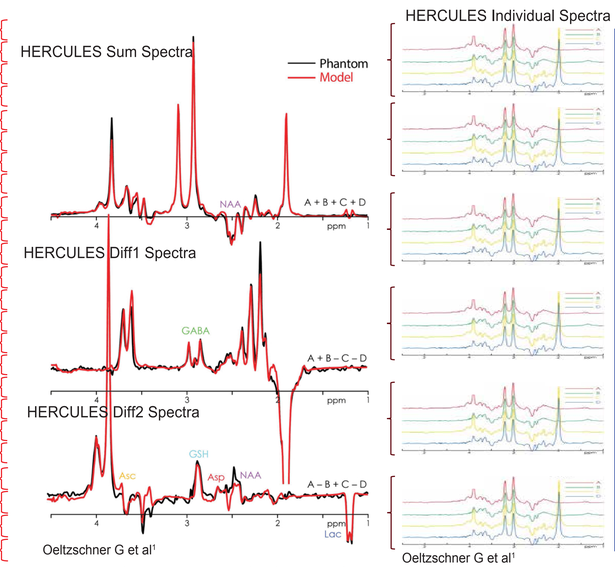


Figure 4: During MRS scan, each individual HERCULES spectra (A,B,C and D) were collected every two seconds in succession. For this reason, a full MRS spectra is optained after a linear computation on all four individual spectra collected every 8s. The output of every MRS run is the average of all 8-second spectra averages into three main spectra: Sum (which contains metabolites tCr, tCho, INs, Glx, Glu, Gln, NAA, tNAA), Diff1 (GABA and GABA+), and Diff2 (Asc, Asp, Lac, GSH, NAAG, PE).

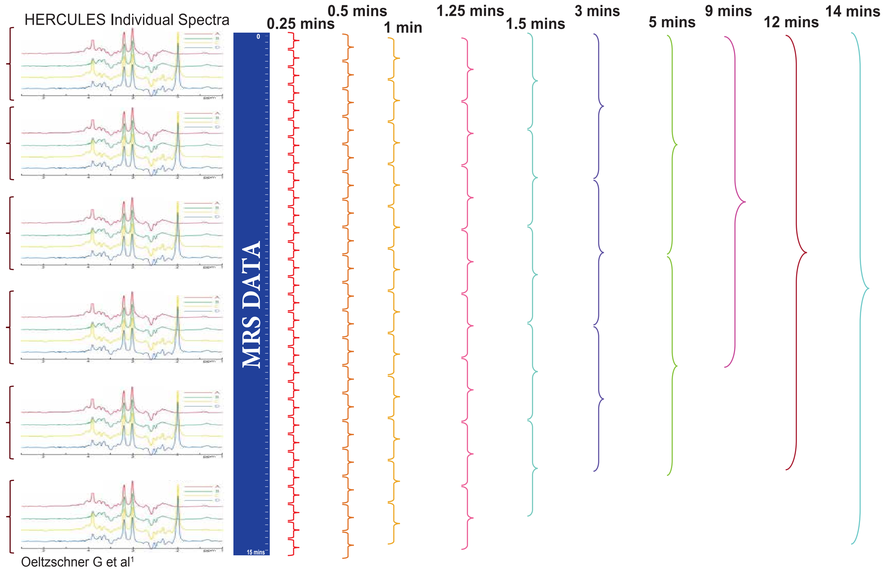


Figure 5: Prior to segmenting MRS data using EEG labeled 2-second transients, we built the framework of segmenting the data at multiple segmentation windows starting at 8 transients (four 2-second windows) all the way to 440 transients with a step size of 8 transients.

Quality Metrics for Spectroscopy Data

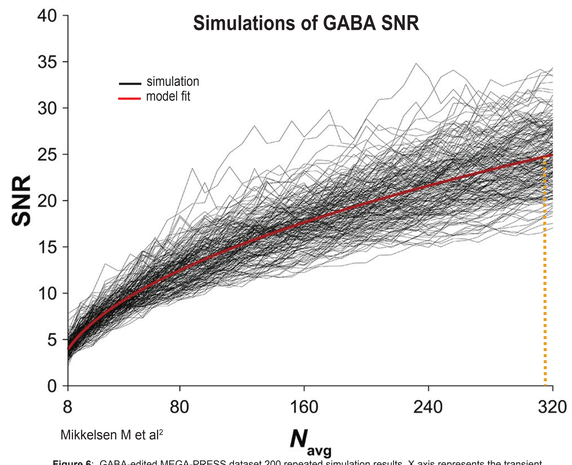


Figure 6: GABA-edited MEGA-PRESS dataset 200 repeated simulation results. X axis represents the transient numbers and y axis represent GABA SNR values. Red line is a model relationship of SNR as a function of the square root of signal averages[2]

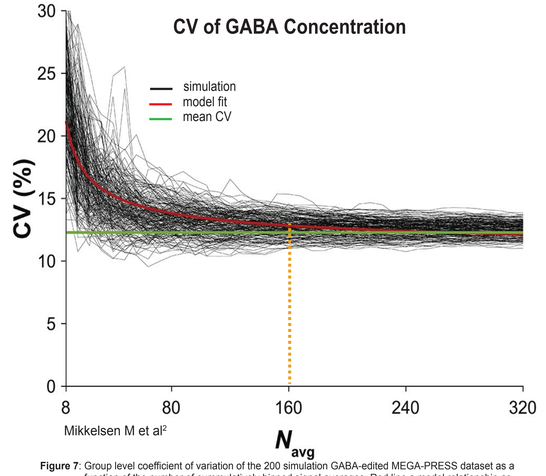


Figure 7: Group level coefficient of variation of the 200 simulation GABA-edited MEGA-PRESS dataset as a function of the number of cummulatively binned signal averages. Red line a model relationship as a function of the inverse square root of the number of signal averages. The green line indicates the coefficient of variation of the 20 datasets plotted[2]

The relationship between exact number of transients (or scan duration) needed to reliably quantify metabolites in HERCULES-edited MRS data remains elusive. Signal to noise ratio (SNR) has been used as the quality metric for segmenting MRS data. Mikkelsen et al investigated the effects of signal averaging on SNR, measurement error and group-level variance against twenty simulated datasets of GABA-edited MEGA-PRESS acquisitions with known signal integrals and fixed linewidth. They discovered that while GABA SNR increases with increasing signal averages (transients) as seen in Figure 6, the coefficient of variation (CV) in GABA concentration stabilizes and plateaus early (around 160 signal averages) as seen in Figure 7. This work informs us to account for the CV of metabolite concentration when analysing how many transients are needed to reliable quantify chemical signatures of our defined five sleep states.

Next Steps

1. Segment HERCULES-edited MRS data at different segmentation windows starting at 8 and ending at 440 with a step size of 8 transients
2. Determine the minimum number of transients needed for a state-based segmentation (signal averaging)
3. Segment MRS data by sleep and arousal states for each group of dataset (MDD and HC)
4. Find differences in chemical signatures across sleep states and among MDD and HC subjects
5. Apply analysis for aging dataset which has simultanoes EEG-MRS data of young and old subjects

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References

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