Spectral analysis of passive listening EEG paradigms reveals consistent patterns of activation in severely brain-injured patients

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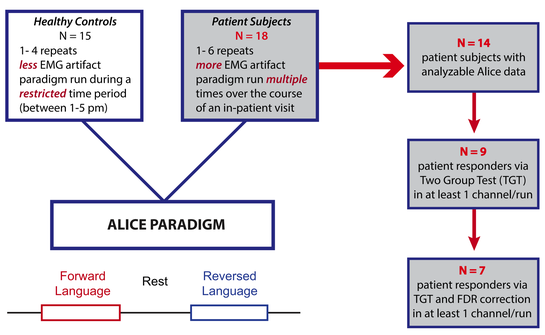
Background & Motivation

- Language-based EEG paradigms can identify covert cognitive processes in patients with disorders of consciousness (DOC) (Conte, SFN 2015; Markell, SFN 2014).
- Desynchronization in the alpha frequency band (8-12 Hz) is a marker of auditory attention (Weisz et al., 2011; Banerjee et al., 2011).
- Here we attempt to further characterize the modulation of the EEG in response to narrative language as well as the topographic distribution of responses in both healthy controls (HCs) and patient subjects (PSs).

Methods

We recorded the EEG in 15 healthy controls (7M; age range 23-55) and 18 patient subjects who sustained severe brain injuries. Participants listened to intact (FWD condition) and time-reversed narratives (BKWD condition) within each recording block. The time-reversed BKWD condition is unintelligible but preserves the overall power spectrum but not the phase information of the original speech.



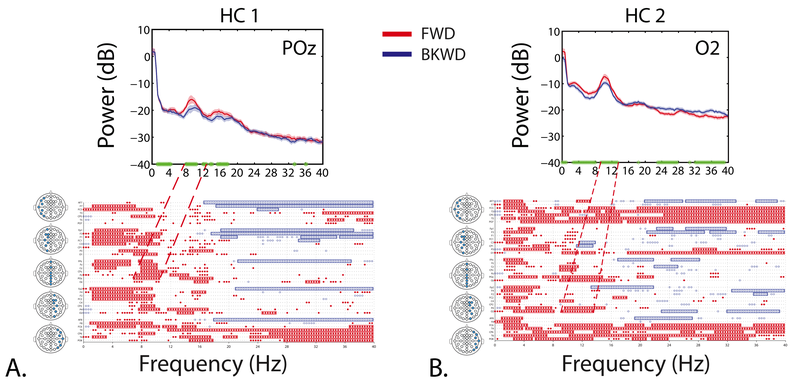
Schematic of a forward vs. time-reversed language paradigm. Forward and time-reversed English language excerpts were taken from the opening 2.5 minutes of Lewis Carroll's Alice in Wonderland with female narration. These were presented with an interleaved rest of 30 seconds. Each language block, totaling approx. 6 minutes was presented a minimum of 2x's per test session (healthy controls) and a minimum of 3-4x's for patients.

Continuous video EEG was recorded at a sampling rate of 250 Hz; bandpass-filtered (0, 40 Hz). We used the Natus XLTEK system for recordings with 37 individual collodion-pasted Ag/Cl electrodes in an augmented 10-20 montage (Impedances < 5.0 kOhm).

Multi-taper (5 tapers) power spectral estimates were calculated using a Hjorth Laplacian montage on artifact-free 3 sec EEG segments from single repeats of the Alice paradigm.

Power spectral significance differences between the conditions defined by contiguous, Two Group Test (TGT) comparisons over the entire minimum frequency resolution (2 Hz) of the multitaper estimate. All significant comparisons underwent False Discovery Rate (FDR) correction.

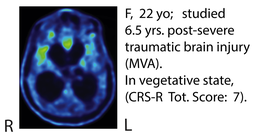
Sample Spectra - Healthy Controls



Panels A and B illustrate sample HC power spectral responses for a single repeat of the Alice paradigm in channels POz (left) and O2 (right). Both HCs show significant separations between Fwd and Bkwd speech in the alpha frequency band (8-12 Hz) (as indicated by the green stars), with a Fwd > Bkwd directionality. Additionally, HC 1 illustrates a significant difference in the low beta frequency band (14-24 Hz). Below are shown the TGT analyses for these conditions for all channels. Dashed red lines highlight channels POz and O2. Approximately half (Panel A: 49.94%; Panel B: 43.34%) of TGT identified values remain significant after FDR correction (not shown).

Sample Spectra - Patient Subjects

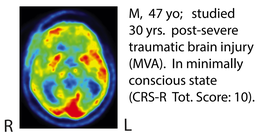
PS 1: VS



F, 22 yo; studied 6.5 yrs. post-severe traumatic brain injury (MVA). In vegetative state, (CRS-R Tot. Score: 7).

^{18}FDG-PET - global hypometabolism of the frontolateral, temporal, parietal and occipital cortices and basal ganglia with moderate preservation of the midfrontal cortices and the nucleus accumbens.

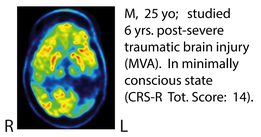
PS 2: MCS-



M, 47 yo; studied 30 yrs. post-severe traumatic brain injury (MVA). In minimally conscious state (CRS-R Tot. Score: 10).

^{18}FDG-PET – moderate hypometabolism in: sensorimotor striatum, left prefrontal, right temporal, temporal-occipital and precuneus. Almost normal metabolism: right striatum. Low metabolism: left central thalamus

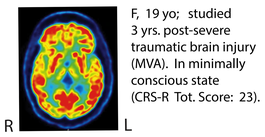
PS 3: MCS+



M, 25 yo; studied 6 yrs. post-severe traumatic brain injury (MVA). In minimally conscious state (CRS-R Tot. Score: 14).

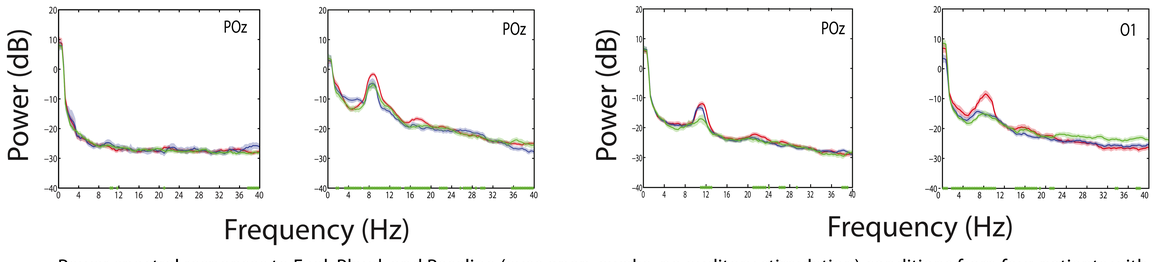
^{18}FDG-PET - shows hypometabolism in the left parieto-occipital and right lateral temporal region.

PS 4: E-MCS



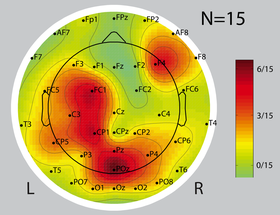
F, 19 yo; studied 3 yrs. post-severe traumatic brain injury (MVA). In minimally conscious state (CRS-R Tot. Score: 23).

^{18}FDG-PET image shown: no regions of severe hypometabolism. Not shown: hypometabolism in the left posterior occipital-temporal region.

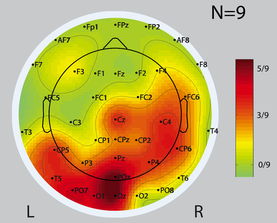


Power spectral responses to Fwd, Bkwd, and Baseline (eyes open, awake, no auditory stimulation) conditions from four patients with distinct behavioral profiles. Each panel illustrates data from a single repeat of the Alice paradigm. Baseline data in each PS was concatenated from several time periods over the course of one in-patient admission. Green stars indicate significant differences between the Fwd and Bkwd conditions. Significant separations between Fwd and Bkwd conditions in the alpha frequency range are demonstrated for MCS-, MCS+, and E-MCS patients; these differences remained significant after FDR correction. No significant differences between the Fwd and Bkwd speech condition were observed in VS.

Healthy Controls



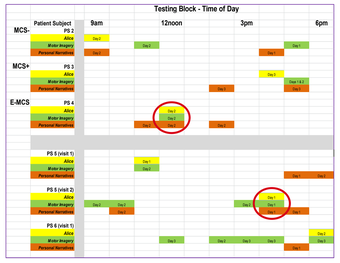
Patient Subjects



Topographic Distribution of Significant Responses

Significant separations between Fwd and Bkwd conditions in alpha frequency band (8-12 Hz) power by channel location in fifteen HCs (Two-Group Test; $\alpha < 0.05$) (top left) and nine PSs (bottom left). Cold colors represent channels where few or no HCs or PSs responded significantly, hot colors indicate channels where significant responses occurred across HCs and PSs. In the HCs, areas with the highest density of significant responses include parieto-occipital, left centro-parietal, and fronto-central regions. In the PSs, activation was most robust in parieto-occipital and right centro-parietal areas. This bias towards significant responses on the right hemisphere in nine PSs reflects a small sample statistic effect of left posterior parietal-occipital injuries.

Fluctuations in Wakefulness



This table provides evidence for diurnal state fluctuations in the assessment of patients with DOCs. Highlighted cells correspond to the occurrence of three language (2 passive, 1 active) paradigms during the testing day. For two patients, red circles indicate times during the day where we saw concordant positive responsiveness to these three paradigms.

Conclusions

- Our results demonstrate the preservation of language processing in a subset of severely brain-injured patients with limited motor output channels.
- In both patient subjects and healthy controls, the majority of significant EEG responses occurred in centro-parietal and parietal-occipital regions consistent with activation of cortical regions involved in language processing and visual imagery.
- Evidence of state fluctuations in individual patients suggests the need for repeated testing over multiple testing blocks (see Curley et al., this meeting).

References

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