High Resolution Spatial Temporal Analysis of Whole-Head 306-Channel Magnetoencephalography & 66-Channel Electroencephalography Brain Imaging in Humans During Sleep

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Collaborators

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- Eugene Zawadzki, PhD, Codebris, San Diego
- Arlene Schlosser, Polysomnography Sleep Expert, Dept Psychiatry, UC San Diego (ret)
Alternating Cerebral Hemispheric Activity and the Lateralization of Autonomic Nervous Function
Werntz DA, Bickford RG, Bloom FE, Shannahoff-Khalsa DS
Alternating Lateralization of Plasma Catecholamines and Nasal Patency in Humans
Kennedy B, Ziegler MG, Shannahoff-Khalsa DS
Life Sciences, (1986) 38, 1203-1214.
Ultradian sleep rhythms of lateral EEG, autonomic, and cardiovascular activity are coupled in humans
Shannahoff-Khalsa DS, and Yates FE
In 1972, Goldstein et al. [1] measured EEG with the intent to look for hemispheric asymmetries coupled to rapid eye movement (REM) and non-rapid eye movement (NREM) sleep cycles. Their results in seven humans showed that left hemisphere EEG power dominated during REM sleep and that right hemisphere EEG dominated during NREM sleep. They found the same relationship in three of four cats and three of five rabbits, with one cat and two rabbits showing opposite coupling [1]. They concluded that “the difference in hemispheric amplitude relationships during NREM and REM sleep may eventually prove to be a neurophysiological concomitant of the changes in brain function during these stages.”

Our understanding of psychophysiological states are now more broadly defined by the inclusion of the ultradian ultradian rhythms of the autonomic and central nervous systems (ANS and CNS) that play a key regulatory role in mind-body states. These neural rhythms are a unique step in the evolution of the nervous system that have mostly been ignored or missed in our understanding of physiology, mental activities, mood swings, and in the treatment of psychiatric disorders. The multilevel physiological approach reviewed in this book provides a new "big picture" for how the body's major systems (ANS, CNS, neuroendocrine, endocrine, etc.) are regulated, integrated, and coordinated by the brain's hypothalamic-pituitary-adrenal axis (HPA axis) and its hypothalamic-pituitary-adrenal (HPA) axis. This discovery has implications for psychiatry, psychology, medicine, biology, and philosophy. The book also describes the translational neuroscience of the discovery that includes methods of selective unilateral autonomic activation and their therapeutically potential.
306 Channel MEG Elekta Neuromag Triux System
(Figure from Elekta Neuromag® TRIUX™)
MEG 102 channel sites

1 magnetometer + 2 opposing gradiometers at each of the 102 sites
3 x 102 = 306 channels
102 channels - 6 midline channels = 48 possible homologous pairs

Pink = frontal region
Blue = parietal region
Green = temporal region
Yellow = occipital region
EEG Channels 1-60

Pink = frontal region 3 pairs
Blue = parietal region 3 pairs
Green = temporal region 11 pairs
Yellow = occipital region 9 pairs

26 Homologous Pairs
7 midline unpaired channels
6 Frequency Bands Analyzed

1) Low Delta (0.1 - 2 Hz)
2) Delta (2 - 4 Hz)
3) Theta (4 - 8 Hz)
4) Alpha (8 - 16 Hz)
5) Beta (16 - 30 Hz)
6) Gamma (30-50 Hz)
Subject 1 Whole-Head G2 L-R Power for all 6 Frequency Bands

Low Delta

Delta

Theta

Alpha

Beta

Gamma
Subject 1 Whole-Head G2 L-R Power for all 6 Frequency Bands (detrended)
Fast Orthogonal Search (FOS) Analysis for Detecting Ultradian Rhythm Periodicities

FOS Spectra - Subject 1 M1 Whole Head L-R Detrended

FOS Spectra - Subject 1 G2 Whole Head L-R Detrended

FOS Spectra - Subject 1 EEG Whole Head L-R Detrended

FOS Spectra - Subject 1 G3 Whole Head L-R Detrended
FOS - Whole Head vs Back Half vs Front Half

FOS Spectra - Subject 1 M1 Whole Head L-R Detrend

FOS Spectra - Subject 1 M1 Back L-R Detrend

FOS Spectra - Subject 1 M1 Front L-R Detrend
FOS - 4 Zones - Frontal vs Occipital vs Parietal vs Temporal

FOS Spectra - Subject 1 M1 Frontal L-R Detrended

FOS Spectra - Subject 1 M1 Parietal L-R Detrended

FOS Spectra - Subject 1 M1 Occipital L-R Detrended

FOS Spectra - Subject 1 M1 Temporal L-R Detrended
Selected bins for periods:

1) 20-65 min
2) 70-100 min
3) 105-150 min
4) 155-205 min
5) 210-265 min
6) 270-300 min
Data

- Elekta Neuromag proprietary file format (*.fif)
- 4 subjects
- 603.1072 Hertz recordings rate
- 389 channels
  - 74 EEG (60 EEG + EOG, EMG)
  - 2 sets of gradiometers each with 102 channels
  - 102 magnetometers
  - 9 stimulus (not used with our data sets)
Resources / Tools

- XSEDE Comet
- MATLAB
- FieldTrip Toolbox
  http://www.fieldtriptoolbox.org
- Open Science Framework
  https://osf.io
- SeedMe / SDSC HPC Share
  https://hpcshare.sdsc.edu

XSEDE
Processing Steps

1. Transform the Neuromag data files into Matlab format files
2. Combine each subject’s multiple files into a single, continuous data set

<table>
<thead>
<tr>
<th>Subject</th>
<th>Number of *.fif files</th>
<th>Total # of signal points</th>
<th>Total continuous duration (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>9,313,200</td>
<td>4.29</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>10,623,600</td>
<td>4.89</td>
</tr>
<tr>
<td>3</td>
<td>18*</td>
<td>9,578,400</td>
<td>4.41</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>11,221,200</td>
<td>5.17</td>
</tr>
</tbody>
</table>
Processing Steps (cont’d)

Subject 3 channel 20

Subject 3 RMS, M1, frontal L-R mean, beta
Above: before    Below: after fillgap
Processing Steps (cont’d)

3. Separate out 2 gradiometers (G1, G2), magnetometer (M1), and EEG data

4. Perform band-pass filtering (6 bands + unfiltered)

4 subjects x 366 channels x 4 signal types x 7 bands = 40,992

5. Run Root-Mean-Square (RMS) calculation (Matlab code from A. Bolu Ajiboye)

<table>
<thead>
<tr>
<th>Subject</th>
<th># of signal points</th>
<th># of RMS points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9,313,200</td>
<td>15,444</td>
</tr>
<tr>
<td>2</td>
<td>10,623,600</td>
<td>17,617</td>
</tr>
<tr>
<td>3</td>
<td>9,578,400</td>
<td>15,884</td>
</tr>
<tr>
<td>4</td>
<td>11,221,200</td>
<td>18,608</td>
</tr>
</tbody>
</table>
Processing Steps (cont’d)

6. Remove movement artifacts
   a. Simple clipping above certain value
   b. Cut off x% spikes
   c. Matlab functions: filter(), filtfilt(), smooth(), medfilt1()
   d. Matlab hampel()*
   e. Matlab movmean()*

* gave good results which we used
7. Determine homologous pairs
   a. 48 MEG pairs
   b. 26 EEG pairs

8. Calculate left minus right (L-R) homologous channel pairs, not including the unpaired midline channels
Processing Steps (cont’d)

9. Removed bad channel pairs

10. Calculate L-R means for whole head, front & back, 4 regions (frontal, parietal, temporal, occipital)

11. Detrend

<table>
<thead>
<tr>
<th>Subject</th>
<th>M1 (%)</th>
<th>G2 (%)</th>
<th>G3 (%)</th>
<th>EEG (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.1</td>
<td>10.4</td>
<td>6.3</td>
<td>26.7</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>6.3</td>
<td>0</td>
<td>42.3</td>
</tr>
<tr>
<td>3</td>
<td>8.3</td>
<td>20.8</td>
<td>12.5</td>
<td>42.3</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>2.1</td>
<td>19.2</td>
</tr>
</tbody>
</table>
L-R Mean and Sleep Stage Coupling

Subject 1 M1 Whole Head L-R Mean Average for All Stages

Subject 1 G2 Whole Head L-R Mean Average for All Stages

Subject 1 EEG Whole Head L-R Mean Average for All Stages

Subject 1 G3 Whole Head L-R Mean Average for All Stages
L-R Mean and Sleep Stage Coupling

Subject 1 M1 Whole Head L-R Mean Average for All Stages

Subject 1 G2 Whole Head L-R Mean Average for All Stages

Subject 1 EEG Whole Head L-R Mean Average for All Stages

Subject 1 G3 Whole Head L-R Mean Average for All Stages
Subject 1 - Summary of the bar graphs for correlations of sleep stage 4 vs REM for the L-R power values of greater negative values (more right hemisphere dominance) for stage 4 vs REM

These results are based on whether stage 4 was more or less negative compared to REM. NREM Stage 3 results are not included, but by quick glance it is clear they are similar but a bit weaker.

Below are the list of anomalies that do not support the observation of the simple hypothesis, where stage 4 NREM is more negative than REM sleep. Our primary hypothesis checks out with the best result for the whole head data.

**Whole-Head:** 1 of the 24 are opposite to the hypothesis
G3 gamma

**Front/back:** 5 of 48 are opposite to the hypothesis
EEG beta front, gamma front, theta back
G2 gamma front (but barely)
G3 gamma back

**Four regions:** 16 of 96 are opposite to the hypothesis
EEG beta frontal, beta temporal, gamma frontal, low delta temporal,
G2 low delta frontal, low delta parietal
G3 beta parietal, gamma parietal, low delta frontal, low delta parietal
M1 alpha parietal, beta parietal, delta parietal, gamma parietal, low delta parietal, theta parietal
Visualizing Spatio-Temporal Datasets

- 2D ‘Cascade’ Plots
- 2D Contour Maps
- 2D ‘Heat’ Maps
- 2D Topographic Brain Maps
- Animations
- Principle of ‘Small Multiples’
- 3D ‘Stacked’ Scatter Plots
- 3D Spatiotemporal Isosurfaces
Challenges

- Thousands of lines of custom code in Matlab and Python
- XSEDE systems unable to support OpenGL hardware acceleration in Matlab
600 Hz sampled data reduced to 1 sample per second.
Let’s Start With Just a Temporal Visualization

- Provides some useful insights
- Legend would be off the page
- Colors are duplicated
- Cannot identify bad channels
'Cascade' Plots Are Common in EEG Viz

• Scrolling cascade plots are EEGLab default
• 32-channel sample EEGLab dataset more manageable than 102 channels
• Still no idea where channels are spatially located
• Cannot include vertical axis labels for Power
Cascade Plot of G2 102 Channels

- We can now see bad channels
- Still no idea where channels are spatially located
2D Contour plot With 100 Contour Lines

Subject 1 G2 Delta Power, 102 Channels x 15444 Seconds
2D Heat Map

- Similar to 2D contour plot but filled
- Even more easy to detect bad channels
- Still no easy way to identify spatial locations of channels
2D Surface or Mesh

- Can be considered a combination of time series and heat map
- Includes the use of height or ‘elevation’ as measure of Power
- Still cannot easily identify spatial location of channels
Heat Map Aligned With Hypnogram
Heat Map Aligned With Hypnogram
Example from EEGLab of 2D Brain Topo Maps using a combination of heat map and isolines.
2D Topographic Brain Maps

Example from EEGLab of 2D Brain Topo Maps using a combination of heat map and isolines.
2D Brain Topo Map Animation
2D Brain Topo Map “Small Multiples”

Adding a temporal component using an image sequence.
At some point we run out of space or it becomes prohibitively difficult to identify trends or anomalies.
Combine Spatial With Temporal Visualization Modes

Stack temporal image sequence of 2D Brain Topo Maps like a loaf of bread.
102 MEG channel time series aligned vertically and merged with stacked 2D Brain Topo Maps.
Use scaled and colored ellipsoids to create a stacked 3D scatter plot.
For 102 MEG channels it is still difficult to explore internal ‘midline’ structures. Visualization tools do not typically include this in their repertoire of viz methods.
Useful for datasets which are spread out spatially.

Visualization of COVID-19 daily deaths for U.S. Counties, March 12 - Sept. 1, 2020
This is a Job For Spatiotemporal Isosurfaces!!

AVS

XSEDE
What Is An Isosurface?

• 3D analog of 2D isoline/contour line
• Continuous constant value in a 3D space
What Is An Isosurface?

“An isosurface is a three-dimensional analog of an isoline. It is a surface that represents points of a constant value (e.g. pressure, temperature, velocity, density) within a volume of space; in other words, it is a level set of a continuous function whose domain is 3D-space.”
2D Topographic Brain Maps

Multiple ‘Stacked’ 2D Topo Brain Maps

3D Spatiotemporal Volume Schematic

Subject 1 G2 Alpha

3D Spatiotemporal Isosurface

Step 1

3D Spatiotemporal Volume

Step 2

2D Topographic Brain Maps

Step 3

Multiple ‘Stacked’ 2D Topo Brain Maps

Step 4

3D Spatiotemporal Isosurface
Spatiotemporal Isosurfaces
“Morphological gradient” from left to right.
Low freq. Bands distinctly different from high freq. bands.
Stage 4 (and 3) activity have similar structure.
Activity in higher frequencies like Beta ‘mirror’ lower freqs., i.e. what’s red in one is blue in the other, etc.
Gamma activity varies for waking state at different times during the night.
Stage 4 activity consistent.
Beta mirrors lower frequency bands.
High Beta activity during REM as expected.
Beta mirrors Alpha during middle part of night’s sleep.
Unexpectedly high Beta activity during NREM.
Left-Right Homologous Pairs

Processing Steps (cont’d)

7. Determine homologous pairs
   a. 48 MEG pairs
   b. 26 EEG pairs

8. Calculate left minus right (L-R) homologous channel pairs, not including the unpaired midline channels

Map 48 pairs to 6 X 10 grid
Subject 2 L-R, M1, Lateral View

Low Delta

Delta

Theta

Alpha

Beta

Gamma

Time (minutes)

\( \text{Hz} \)

\( \times 10^{-15} \)

\( \times 10^{-16} \)

\( \times 10^{-17} \)

\( \times 10^{-18} \)

\( \times 10^{-19} \)

\( \times 10^{-20} \)

\( \times 10^{-21} \)

\( \times 10^{-22} \)
Thank You