Improving the detection of mTBI via Complexity Analysis by adopting an appropriate symbolization technique. A Magnetoencephalography Resting – State Study

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***Abstract*— Diagnosis of mild Traumatic Brain Injury (mTBI) was difficult due to the variability of obvious brain lesions using magnetic resonance imaging (MRI) or computed tomography (CT) scans. A promising tool for exploring potential biomarkers for mTBI is magnetoencephalography which has the advantage of high spatial and temporal resolution. By adopting proper analytic tools from the field of symbolic dynamics like Lempel-Ziv complexity (LZC), we can objectively characterize neural network alterations compared to healthy control. LZC is an estimator of the complexity of the system by enumerating the different patterns of the sequence. LZC needs first to binarize the time series using mean amplitude as the threshold. This procedure oversimplifies the rich information of brain activity captured via MEG. For that reason, we adopted neural-gas (NG) algorithm which has already been used for multichannel common symbolization. NG can transform a time series into more than two symbols by learning brain dynamics with a small error. To compare LZC with the NG symbolization approach, we adopted a proper complexity estimator called complexity index (CI).**

The whole analysis was presented to magneto-encephalographic (MEG) recordings of 30 mild Traumatic Brain Injury (mTBI) patients and 50 normal controls in δ frequency band. We compared CI and LZC via a classification procedure with k-NN and Support Vector Machines. Our results demonstrated that mTBI patients could be separated from normal controls with more than 97% classification accuracy based on CI with highest values considering to right frontal areas. In addition, a reversal relation between complexity and transition rate was demonstrated for both groups. These findings indicate that symbolization complexity could have a significant predictive value in the development of reliable biomarkers to help with the early detection of mTBI.

Keywords—component; complexity; MEG; mTBI; Symbolization; Lempel-Ziv; Symbolic Dynamics

I. INTRODUCTION

Mild traumatic brain injury (mTBI) is one of the most important cause of brain insult [1 – 3] including approximately the 90% all of brain injuries [2]. Approximately 5 to 20% of the irremediable patients [4] still suffer from post-concussion symptoms several months after the initial injury [3]. Management of mTBI is crucial due to its deleterious effects on certain brain functions [5 – 7]. One of the most successful techniques to investigate the brain abnormalities caused by mTBIs is magnetoencephalography (MEG). Using advance signal processing and statistical methods, it is possible to specify the mTBIs.

Through MEG, it is possible to analyze the recorded time series into functional connectivity networks in order to map the mTBIs. Four studies [8-11] are already published using the current dataset investigating the functional connectivity nature of these injuries. Both intra [8, 9] and inter-frequency functional brain networks [10, 11] have been investigated for potential biomarkers for the diagnosis of mTBIs. A complementary approach to brain networks is to explore the complexity of brain activity on a single sensor level.

To our knowledge, this is the first study of exploring LZC of MEG resting state in mTBIs . A previous study found lower LZC for TBIs compared to control using MEG resting-state demonstrating also correlations of LZC with several neuropsyhological measures [12]. Theoretically, a loss of neurons and synapses can cause a reduction of complexity in Alzheimer's patients and the healthy elderly populations [13,14]. Moreover, it was found that less matured brains and neural circuits show lower LZC [15]. We therefore hypothesized that symbolic dynamics and namely metrics related with symbolic time series like complexity indexes can be valuable biomarkers for mTBIs.

In summary, we compared two alternative ways of symbolizing single-sensor MEG activity: the binarization using the mean amplitude as a threshold and the NG algorithm [16]. Complexity was estimated with two different algorithms, the LZ for the binarized time series [17] and the CI based on symbolic time series without any restrictions of the number of codebooks/symbols [18]. Our aim is to quantify the classification accuracy of the two groups with both methods and to underline the importance of appropriate methodology for revealing the (ab)normal complexity of brain activity.

II. METHODS

A. Participants

Current study analyzed thirty right-handed individuals with mTBI (29.33 ± 9.2 years of age) [11] and 50 age- and gender-matched neurologically intact controls (29.25 ± 9.1 years of age). All subjects provided informed consent and all procedures were approved by the appropriate review boards at participating institutions. Resting state MEG activity was recorded from each subject, using a 248-channel Magnes WH3600 system (4D Neuroimaging Inc., San Diego, CA) with a sampling rate of 1017.25 Hz and for approximately 3-5 minutes of eyes closed. Axial gradiometer recordings were transformed to planar gradiometer field approximations using the *sincos* method of Fieldtrip [19].

B. Elimination of Non-cerebral activity

A fourth order two-pass Butterworth filter between 0.5–80 Hz and a notch filter at 60 Hz were used for filtering of recordings and to remove line noise, respectively. The extended Infomax algorithm [20] was used to estimate independent components (ICs) on individual channel recordings. The data were then whitened and reduced in dimensionality using Principal Component Analysis with threshold set at 95% of the total variance [10, 11]. The statistical values of kurtosis and skewness of each IC were used to eliminate ocular and cardiac artifacts, respectively. An IC was considered as artifact if more than 30% of its z-score values were outside ±2 [4, 9, 10]. Finally, the data were back-projected to the original 248-channel MEG space using the artifact-free ICs.

C. Complexity Estimation

Complexity analysis was performed after first filtering each MEG time series on the δ frequency band [0.5 4 Hz] using a zero-phase filter of 3rd order in both directions using *filtfilt* function in matlab. We then transformed MEG signals into a finite number of symbols. In the case of LZC, the symbols were two [0,1] while in the case of NG, the symbols were optimized based on the reconstructed error [19-21].

1) Lempel-Ziv Complexity: LZC is an algorithm that enumerate different substrings in the binarized symbolic time series STS^{LZ}=[01110…]. Here, we transformed δ oscillations into a binary time series using the mean amplitude as a threshold.
For more details see the LZC algorithm [17].

2) Neural Gas (NG) Algorithm and Complexity Index (CI):

As an alternative way to transform a MEG signal into symbols is to adopt a proper algorithm that can learn the manifold of a reconstructed phase space and finding a mapping between trajectories and symbols (alphabet). Here, we reconstructed each MEG sensor activity across each group in a common reconstructed space and then we applied NG algorithm in order to get the number of symbols that can describe the original signal with less error . For details on the procedure see [21-23].

Each concatenated MEG sensor time series across each group was first embedded in a multidimensional space as described in equation (1)

$$x(n) = [y(n);\ y(n+T);\ .....;\ y(n+(d_E - 1)T)] \quad (1)$$

where the time lag T is determined using mutual information and one of the ways to determine embedding dimension dE is the false nearest neighbors test [24].
Afterward, using NG and the reconstructed error between original MEG time series and the one described by the codebook derived from the application of NG, we fixed the number of symbols for each time series. Here, using as a threshold the reconstructed error < 8% , we found that k=6 symbols can describe the brain activity of each MEG sensor. Finally,each MEG sensor was transformed to a symbolic time series STS^{NG}=[1 2 3 4 5 6 2 1 …] with k=6.

3) Transition Rate:

We estimated an index of how fast the activity within each MEG sensor changes from one state to another [25]. The function that describes the transition rate is given below :

$$TR = \frac{no\ of\ transitions}{length(STS) - 1} \quad (2)$$

A value of 0 means no transition while a value of 1 can be interpreted as an unstable system where always ‘jumb’ from one state to the other.

D. Classification Scheme

We accessed the predictability of both complexity estimators (LZC and CI) via machine learning techniques. We first detected the most informative MEG sensors using laplacian score [26] after applying a threshold extracted by a bootstrapping technique. We shuffled the labels of the two groups and we reestimated laplacian score for each feature. Then, we applied a threshold to the original laplacian scores derived by the mean + 2 st.ds of 1.000 laplacian scores estimated via the randomization procedure. The aforementioned procedure was repeated separately for each of the complexity indexes.

We estimated the classification performance of each complexity index to discriminate healthy controls from mTBIs via k – nearest neighbor (k-NN) algorithm and Support Vector Machines (SVMs)

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E. Expore Differences on Complexity over Brain

To explore topological differences on complexity value , we applied Wilcoxon rank-sum test per sensor ($p < 0.05$) between the two groups in both LZC and CI via NG algorithm.

III. Results

A. Classification Performance on Complexity

TABLE I. CLASSIFICATION PERFORMANCE FOR SYMBOLIZATION

Complexity Classification Performance				
	Accuracy (%)	Sensitivity (%)	Specificity (%)	# of Selected features
kNN	97.49±1.574	97.02±1.764	98.27±2.977	51/248
SVM	96.99±1.57	96.28±1.73	98.17±2.737	
Transition Rate Classification Performance				
	Accuracy (%)	Sensitivity (%)	Specificity (%)	# of Selected features
kNN	98.75±0	100±0	96.67±1.27e-13	15/248
SVM	98.7±0.2462	99.98±0.2	96.57±0.5715	
Feature Combination				
	Accuracy (%)	Sensitivity (%)	Specificity (%)	# of Selected features
kNN	98.19±1.072	97.3±1.541	99.67±1.005	243/496
SVM	97.69±0.9124	100±0	93.83±2.433	

TABLE II. CLASSIFICATION PERFORMANCE FOR LEMPEL-ZIV

Complexity Classification Performance				
	Accuracy (%)	Sensitivity (%)	Specificity (%)	# of Selected features
kNN	52.33±3.441	73.9±4.258	16.37±5.127	167/248
SVM	50.43±2.71	63.2±3.122	15.237±3.628	
Transition Rate Classification Performance				
	Accuracy (%)	Sensitivity (%)	Specificity (%)	# of Selected features
kNN	80.19±2.938	79.58±4.152	81.2±3.655	181/248
SVM	75.28±2.59	65.9±3.86	90.9±3.572	
Feature Combination				
	Accuracy (%)	Sensitivity (%)	Specificity (%)	# of Selected features
kNN	76.5±3.193	65.88±3.737	94.2±4.174	385/496
SVM	74.25±2.718	63.26±4.027	92.57±4.016	

B. Statistical Differences on complexity

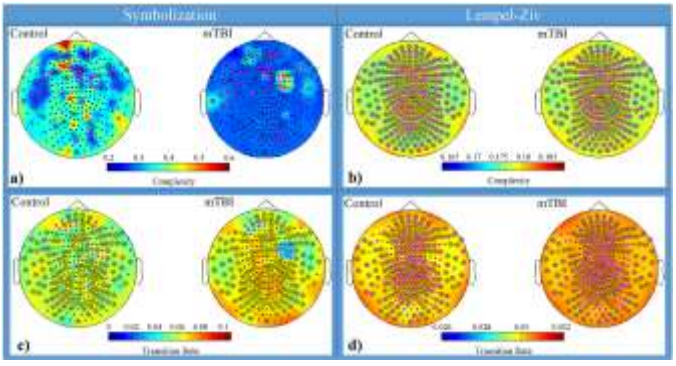

Fig. 1. Representation of averaged complexity across the subjects of each group (a and b) and its correnspoding transition rate (c and d). The black cyrcles represent the statistical significant values (p-value < 0.05) and the magenta points represented the selected (for each case) features for the described classification scheme and resutls of table I and II.

IV. Discussion and Conclusion

After

a) .

Acknowledgment

The preferred spelling of the word “acknowledgment” in America is without an “e” after the “g”. Avoid the stilted expression “one of us (R. B. G.) thanks ...”. Instead, try “R. B. G. thanks...”. Put sponsor acknowledgments in the unnumbered footnote on the first page.

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