Multivariate Pattern Analysis of Entropy estimates in Fast- and Slow-Wave Functional Near Infrared Spectroscopy: A Preliminary Cognitive Stress study

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***Abstract*— Functional near infrared spectroscopy (fNIRS) is a modality that can measure shallow cortical brain signals and also contains pulsatile oscillations that originate from heartbeat dynamics. In particular, while fNIRS slow waves (0 Hz to 0.6 Hz) refer to the standard hemodynamic signal, fast-wave (0.8 Hz to 3 Hz) fNIRS signals refer to cardiac oscillations. Using a cognitive stress experiment paradigm with mental arithmetic, the aim of this study was to assess differences in cortical activity when using slow-wave or fast-wave fNIRS signals. Furthermore, we aimed to see whether fNIRS fast and slow waves provide different information to discriminate mental arithmetic tasks from baseline. We used data from 10 healthy subjects from an open dataset performing mental arithmetic tasks and assessed fNIRS signals using mean values in the time domain, as well as complexity estimates including sample, fuzzy, and distribution entropy. A searchlight representational similarity analysis with pairwise t-test group analysis was performed to compare the representational dissimilarity matrices of each searchlight center. We found significant representational differences between fNIRS fast and slow waves for all complexity estimates, at different brain regions. On the other hand, no statistical differences were observed for mean values. We conclude that entropy analysis of fNIRS data may be more sensitive than traditional methods like mean analysis at detecting the additional information provided by fast-wave signals for discriminating mental arithmetic tasks and warrants further research.**

I. Introduction

It has been long understood that heartbeat dynamics come from a highly nonlinear system with complexity originating from feedback loops between baroreflex sensors and sympathovagal interactions [1]. In fact, many cardiac-related systems exhibit such nonlinearity and complexity [2]–[4].

With functional near infrared spectroscopy (fNIRS), brain tissue hemoglobin concentration is measured as a proxy for neural activity [5]. To this extent, a comparative analysis between fNIRS slow waves (0 Hz to 0.6 Hz) and fast waves (0.8Hz to 3Hz) still has much room for study.

Analysis of fNIRS signals commonly focus on the hemodynamic low-frequency band ($<$ 0.6 Hz) as the high-frequency band ($>$ 0.8 Hz) is thought to be sensitive to systemic physiological or instrumentation noise [6]. However, a recent study investigated the heart rate component (1 Hz to 1.9 Hz) fNIRS, for example, finding it a useful metric for cognitive stress [7]. Moreover, past research in Ghouse et al. [8] assessed complexity estimates in fNIRS signals that had both hemodynamic and heart rate frequencies, and demonstrated complementary areas of neural activity. Hence, a proper assessment of the information carried out by the pulsatile activity in fNIRS should be performed.

Accordingly, the aim of this preliminary study was to assess similarity between neural representations of fNIRS in slow- and fast-wave frequencies. To this end, complexity estimates and mean estimates in the time domain were extracted on fNIRS-derived series, independently for series including slow and fast waves. For the complexity quantification, we used entropy analysis based on reconstructed phase space, which is derived by applying a delay-coordinate map as specified in Takens' theorem [9]. Sample entropy (SampEn) [10] and fuzzy entropy (fuzzyEn) [11] are two entropy measures in the phase space that assess irregularity based on approximations of the correlation integral. Particularly, SampEn compares states using a Chebyshev distance with a heaviside binary membership function to determine class membership. Instead of using a binary membership function, fuzzyEn uses a continuous "fuzzy" membership function. Furthermore, Distribution entropy (distEn) analyzes the spatial complexity of the attractor and reduces the use of fixed parameters in its evaluation [12].

To assess differences and similarities in the spatial neural representations between slow-wave and fast-wave signals, we performed a searchlight representational similarity analysis [13], [14], i.e. a multivariate pattern analysis (MVPA) that has shown power in assessing whether modes (such as a theoretical model, behavioral data, empirical data, etc) contain similar neural representations for cognitive states. Particularly, we performed a representational similarity analysis on mental arithmetic and baseline activity using publicly available data provided by Shin et al. [15]. Furthermore, on both fast-wave and slow-wave fNIRS data, a searchlight decoding analysis [16] was used to determine which frequency band contains neural representations that can decode (i.e., classify) whether a mental arithmetic activity is being performed with above-chance accuracy, for a given searchlight center.

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II. Materials and Methods

A. Experiment Design

A publicly available dataset was used to obtain fNIRS signals, as reported in [15]. Briefly, twenty-nine healthy subjects (aged 28.5 $\pm$ 3.7) were recruited for the study, fifteen of which were females and fourteen males. Three trials were performed with ten repetitions of mental arithmetic and baseline experimental conditions for each subject. Thirty-six fNIRS series were acquired for each subject with a 10 Hz sampling rate.

The experiment design had 60 seconds of resting state to start data acquisition from a subject, after which an instruction on the screen telling them which task was to be performed–either an arithmetic problem or a ”-” for a baseline. The subject performed the task indicated for 10 seconds, with a subsequent 15 seconds of resting state before the next instruction. After 20 repetitions of these instructions and tasks (10 second repetition per task), a 60 second rest was performed. A total of three trials were performed, for a total of 30 repetitions per task.

Data randomly chosen from ten subjects (five female and five male) were retained for further analyses in this preliminary study.

B. fNIRS signals

Thirty six channels of optical densities were resolved from source detector pairs comprising 760nm and 850nm wavelengths covering the frontal, lateral parietal and posterior cortical regions. The modified Beer Lambert law was used to convert the optical densities to deoxyhemoglobin (Hb) and oxyhemoglobin (HbO). Total hemoglobin was derived from adding the two hemoglobin signals after the preprocessing described in the next section.

C. Preprocessing

Figure 1 illustrates the preprocessing pipeline. After applying the modified Beer-Lambert law, band-pass frequency filters were applied to extract hemodynamic (0Hz to 0.6 Hz) or cardiac pulsatile signal (0.8 Hz to 3 Hz) from fNIRS [17]. A wavelet filtering approach using a Daubechies 5 wavelet, nine level decomposition was used to further reduce instrumentation noise such as movement in the oxy- and deoxyhemoglobin signals [18]. The signals were separated into epochs, with each channel at each activity block being referenced to the mean of the previous 5s. Total hemoglobin (THb) was computed as the addition of both Hb and HbO.

D. Entropy Analysis

For the three fNIRS-derived signals, i.e., time series for HbO, Hb, and THb, entropy measures including SampEn, fuzzyEn, and DistEn were calculated. To this extent, a delay-time τ and embedding dimension m are needed to reconstruct attractors using delay-coordinates [9]. τ was selected as the first zero of the autocorrelation, and an m was found using the false nearest neighbors approach [19].

For SampEn and fuzzyEn, a radius $R = 0.2\sigma_x$ was used as the threshold to determine whether states were neighbors,

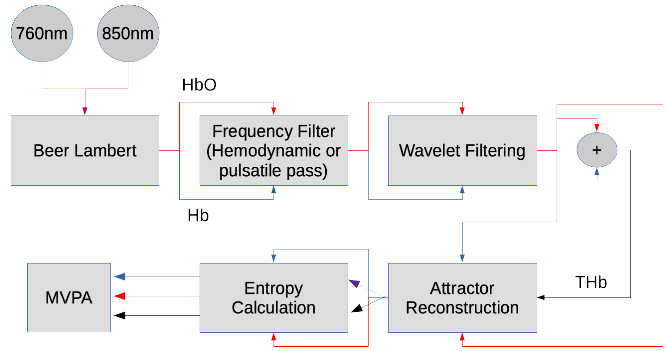

Fig. 1. Analysis pipeline used for each fNIRS signal in the dataset

where σ_x is the standard deviation of each fNIRS-derived time series [20]. While fuzzyEn used an exponential decay function to weigh the distances between the states with a fuzzy power $n = 2$ [11], DistEn utilized Scott's method to determine the bin size for the empirical probability density function represented by a histogram [21]. Shannon entropy was calculated from the histogram to obtain the reported DistEn value.

E. Searchlight Representational Similarity Analysis

A searchlight is a region of interest comprising fNIRS detectors within a radius. The center of the searchlight sphere (or circle for 2D maps) is swept through all detector positions for further analyses. Due to the montage file from the open dataset being in normalized spatial units on a unit box, searchlights radius were derived as to have each searchlight comprise at least three channels rather than being defined by a physically meaningful distance. Each searchlight had a shape of $Nrepetitions \times Nchannels \cdot Nseries$, where series correspond to hemoglobin concentrations. To derive dissimilarity between mental arithmetic and baseline representations (which are random vectors), the distance correlation is used [22], [23]. Other correlation measures such as Pearson or Spearman are based on random variables rather than random vectors, thus are not applicable.

Due to there being only two experimental conditions (baseline or mental arithmetic), the representational dissimilarity matrix is a 2×2 matrix, thus and because comparing representational dissimilarity between modalities requires only the upper triangle [13], the output for each searchlight becomes a single value. Representational dissimilarity outputs were obtained for each searchlight center corresponding to each detector location for each measure (entropies or mean value in the time domain).

F. Searchlight Decoding Analysis

A pipeline of a standard transformation (to make the features zero mean with unit variance) and a linear support vector machine classifier were used to decode (classify) whether a searchlight could discriminate between mental arithmetic or a baseline condition. For each measurement (entropies or mean value), each decoding takes a number

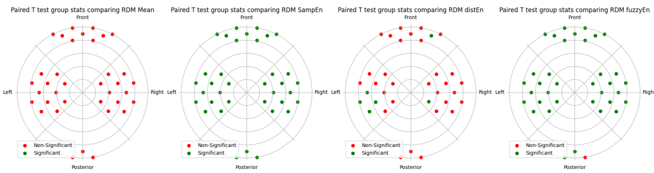

Fig. 2. Results of a paired t test across subjects to assess whether fast and slow wave fNIRS for a searchlight center had a significantly different representational dissimilarity between mental arithmetic and baseline.

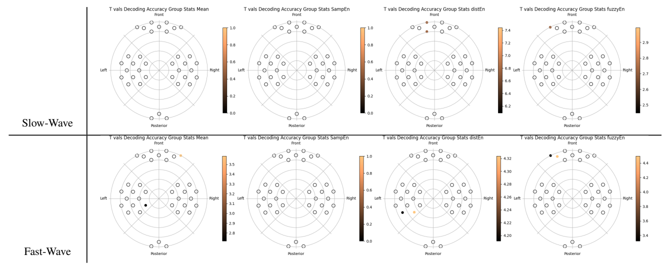

Fig. 3. Results of a the group analysis using a t-test across subjects to assess whether a searchlight center is significantly better than chance at decoding either a mental arithmetic or baseline activity. The top row is the slow wave results, the bottom row is the fast wave results. Non-colored spots indicate non-significant results.

of $3 \cdot Nchannels$ features an inputs considering the three fNIRS-derived signals, i.e.,HbO, Hb, and THb series. A 10 fold cross-validation was used to obtain a mean accuracy map for each searchlight center.

G. Statistical Analysis

Group analysis was performed using paired t-tests to see whether representational dissimilarity between mental arithmetic and baseline for fast-wave fNIRS and slow-wave fNIRS were significantly different at a searchlight center. Uncorrected statistical significance α was set to 0.05 and a $p < 0.00139$ was considered significant according to a Bonferroni correction for multiple comparison for 36 channels.

For each searchlight center, a one-sample, one-sided t-test was performed on the 10 decoding accuracy results over the subjects to test whether they are samples of a random variable with mean 50%; in other words, we performed a statistical test indicating whether the cross-validation accuracy values are significantly different from chance. A $p < 0.01$ was used without corrections to assess whether the decoding searchlight accuracy was significant.

III. Results

A. Group Statistics of Representational Similarity Analysis

Results from the representational similarity analysis can be seen in fig. 2. For the mean value, no searchlight has significantly different representations between slow and fast wave fNIRS, whereas the entire cortical surface is significantly different for fuzzyEn and SampEn. As for distEn, the posterior parietal cortex, the right frontal cortex and the medial right parietal cortex reveal representation differences.

B. Group Statistics of Decoding Analysis

Searchlight decoding results for fast and slow wave fNIRS can be seen in fig. 3. Mean estimates show significant searchlights only in fast wave fNIRS, in the the medial left parietal cortex and right frontal cortex. However, there are no clusters of more than one searchlight. SampEn shows no significant searchlight in either fast or slow wave fNIRS analysis. DistEn, on the other hand shows a significant cluster in the frontal left medial cortex in slow wave while in fast wave there is a significant cluster in the posterior parietal cortex. FuzzyEn shows significant activity in the left lateral frontal cortex, with a cluster of at least two searchlights in the fast wave fNIRS analysis.

IV. Discussion

In this study, representations of neural activity were compared between fNIRS slow waves (0 Hz to 0.6 Hz) and fNIRS fast waves (0.8 Hz to 3 Hz) for both linear measures of mean value and complexity measures derived from entropies (SampEn, fuzzyEn, distEn) in the phase space. The fNIRS signals were taken from a publicly available dataset, described in [15]. Ten subjects were analyzed during during mental arithmetic and a baseline experimental conditions. Representational similarity analysis was performed, showing that representational dissimilarities were not significantly different between fast and slow wave fNIRS in the mean measurements, while fuzzyEn and SampEn measures had significant differences across the entire cortex. DistEn had representation dissimilarities that were significantly different between slow and fast fNIRS in the posterior parietal cortex. As for decoding, only fuzzyEn and distEn were able to reveal clusters of significant searchlights. DistEn revealed the frontal left cortex in the slow-wave fNIRS while in fast wave the posterior parietal cortex provided information to discriminate the experimental conditions. FuzzyEn only provided clusters of significance in the fast-wave fNIRS, in the frontal left lateral cortex.

Considering the mean estimate is a linear estimate corresponding to the direct current value of the signal, it is not surprising that representational similarity analysis found no significant differences between fast or slow waves, as the band pass highly attenuates the direct current component, thus, the mean value is merely scaled by the filter. Regarding SampEn and fuzzyEn, how the filters affect the regularity of state space is not as easily understood, however Borges et al. show that high pass filtering results in lower mean entropy but higher variance than low-pass filtering [24]. This effect may correspond to the significantly different mean representational similarity across subjects seen. However, distEn appeared more selective than fuzzyEn or SampEn in detecting representations dissimilarities that are different, particularly with a cluster of significance in the lower left parietal cortex. Note that this area corresponds to where literature expects the neural correlate of mental arithmetic activity to be [25], [26].

When applying the decoding analysis to finely parse through which regions on the cortical surface contain information to discriminate mental arithmetic from baseline in either slow or fast wave fNIRS, only fuzzyEn and distEn provided clusters of significant activity of at least two searchlight centers. Particularly, distEn revealed a cluster in the fast wave signal in the posterior parietal cortex that corresponds to the region that representational similarity analysis showed was significantly different between fast and slow wave fNIRS data. Furthermore, clusters in the frontal left cortex were found in slow-wave distEn and fast-wave fuzzyEn, which are also in agreement with previous findings [25], [26].

Of interest is also the switching of cortical regions with fast and slow wave fNIRS in distEn between parietal cortex and frontal cortex in the decoding analysis. Further research is still needed to understand the physiology that elicits these nonlinear and complex effects seen in these results. At a speculative level, it is understood that the particular parietal location involved in mental arithmetic can be the angular gyrus, as seen in brain injury studies [27]. It is also involved in the default mode network [28], a network active during multi-modal activity, and which may contain more transient high frequency activity than regions outside of the default mode network. On the note of autonomic regulation control that are reflected in cardiac signals, the vagus nerve seems to play a role in modulating the default mode network [29]. An interesting follow-up study could be performed with a vagal nerve stimulation to see if it effects the representations seen in this study.

V. Conclusion

We conclude from this preliminary study that entropy estimates can detect different representations when using either fast- or slow-wave fNIRS data, which traditional methods like mean estimates can not.

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