

Complexity Analysis of Resting-State and Task fMRI Using Multiscale Sample Entropy

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Abstract— Functional magnetic resonance imaging (fMRI) is a powerful tool that allows for analysis of neural activity via the measurement of blood-oxygenation-level-dependent (BOLD) signal. The BOLD fluctuations can exhibit different levels of complexity, depending upon the conditions under which they are measured. We examined the complexity of both resting-state and task-based fMRI using sample entropy (SampEn) as a surrogate for signal predictability. We found that within most tasks, regions of the brain that were deemed task-relevant displayed significantly low levels of SampEn, and there was a strong negative correlation between parcel entropy and amplitude.

I. INTRODUCTION

The blood-oxygenation-level-dependent (BOLD) signal is commonly used as a tool to measure neural activity in both resting-state and task-based functional magnetic resonance imaging (fMRI). However, typical BOLD signal analysis only provides information as to the presence and amplitude of activation at any point in time, not the complexity of the underlying signal.

In typical functional connectivity analysis, correlation is found between BOLD signal in brain regions of interest to determine connected networks. This information does not reflect some of the nuances of brain activity, including the dynamic nature of fluctuations in activation due to mental activity or changes in brain state [1], [2]. To be able to explore these nuances, we must examine signal complexity, and to examine signal complexity, new analytical techniques must be used.

Entropy is a measurement of the predictability of a signal [3], [4]. This lends itself to complexity analysis of fMRI, where entropy has been used in analysis of both resting-state and basic task-based fMRI [1], [2]. Initial studies using resting-state fMRI indicated lower levels of entropy in the neocortex of the brain and higher entropy within the rest of the brain [1]. These differences in entropy are much more pronounced in task-based fMRI than resting-state, with robust patterns across subjects noted in preliminary task-based analysis [1].

Previous work examining task-based fMRI has compared the entropy of regions of interest with regards to a particular task to the background entropy of the neocortex, subcortical regions, or whole brain at large [1]. This provides valuable

information about the relative levels of entropy in task-relevant regions overall; however, there is no specific comparison among all brain regions. This is necessary to determine whether significantly low entropy in task-relevant regions is a reflection of a commonality amongst cortical areas or a characteristic unique to salient regions. Our aim was to examine the degree of entropy across the whole brain during resting-state and task-based fMRI, to determine whether regions relevant to a particular task displayed significantly different levels of entropy as compared to other similar regions in the brain. Our analysis substantiated previous findings that cortical regions of the brain display lower entropy than subcortical, as well as more pronounced entropy profiles in task-based fMRI than resting-state. Additionally, we found that task-relevant regions did indeed display significantly lower levels of entropy as compared to other cortical regions. Finally, in all tasks, we determined that there was a strong negative correlation between the entropy of a brain region and its BOLD signal amplitude.

II. METHODS

A. Data acquisition

We examined the entropy of a resting-state and seven task scans for 412 subjects, as retrieved from the Human Connectome Project [6]. Two runs were acquired for each task within each subject, with TR = 720 ms and TE = 33.1 ms. The task topics included emotion, language, sensorimotor, gambling/risk-taking, relational processing, social processing, combination working memory/category-specific representation, and rest. Once retrieved, the scans were global-signal regressed. Within each task, fMRI volumes were divided into 246 parcels based on the Brainnetome Atlas parcellation method, allowing for parcel-wise analysis rather than voxel-wise analysis [7].

B. Parcel-wise entropy

Sample entropy (SampEn) is a particular technique for estimation of entropy that relies on fewer time points than typical entropy calculations, allowing for more accurate values for shorter time series (such as fMRI scans, which typically have no more than 1,000 time points) [5].

Within each task and resting-state scan, the SampEn of the time course from each individual parcel within each subject

*This work was supported by the NIH R01MH111416, NIH R01NS078095, NSF BCS INSPIRE 1533260, and NSF CRCNS 1822606.

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was calculated using MATLAB, with a combination of home-designed code and code from MATLAB File Exchange [8], [9]. Then, SampEn was averaged across all subjects to yield one value of entropy for each parcel within each task. The z-score of each individual parcel's SampEn was calculated relative to the mean and standard deviation of all task parcels, and parcels with a z-score magnitude higher than 1.95 ($p < 0.05$) were noted as having significantly high or low entropy.

C. Parcel power vs. entropy

Amplitude analysis of each parcel within each task was performed. The BOLD signal was averaged across subjects, resulting in an average time series of signal for each parcel within each task. From these time series, the standard deviation was calculated to determine which parcels within each task showed the greatest degree of fluctuation in BOLD signal. Then, within each task, parcel power was compared to parcel entropy, in order to ascertain the presence and strength of a correlation between BOLD signal amplitude and entropy.

Additionally, power vs. entropy was examined for a series of 500 randomly-generated datasets. Each set consisted of a series of 500 random numbers generated by MATLAB, which was then multiplied by an integer factor between one and 500. The length was chosen to be comparable to the length of a task-based fMRI scan. SampEn was calculated for each dataset, and the power of each dataset was taken to be the integer factor by which it had been scaled.

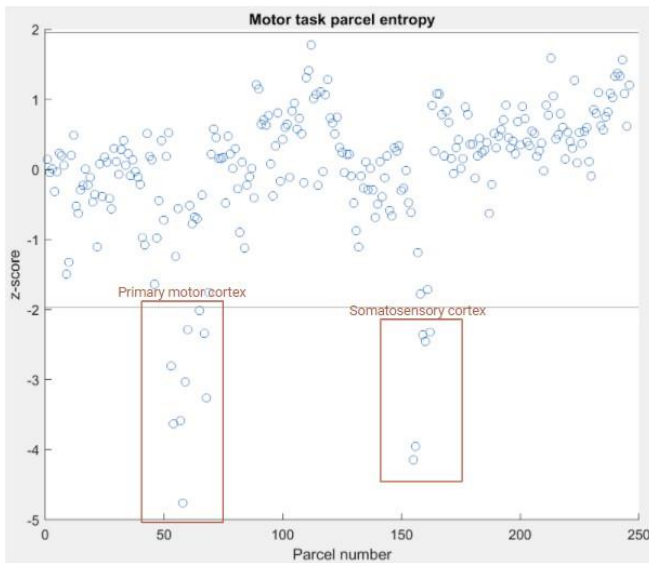


Figure 1: Parcel number vs. entropy z-score for the motor task. Task-relevant brain regions are indicated with red boxes. Note lines at $z = \pm 1.96$, indicating thresholds for parcels w/ statistical significance. See Table I in the Appendix for a list of parcel numbers and corresponding brain regions.

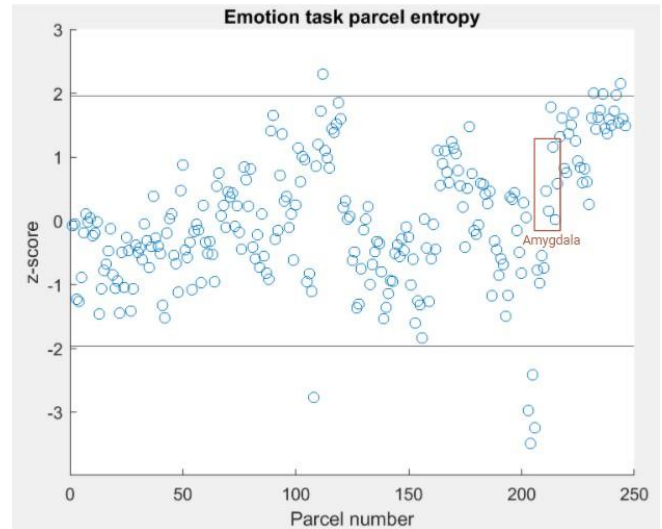


Figure 2. Parcel number vs. entropy z-score for the emotion task. Task-relevant brain regions are indicated with a red box. Low-entropy parcels 203-206 represent occipital lobe activation.

III. RESULTS AND DISCUSSION

Complexity metrics provide information about the dynamic reconfiguration of the human brain. For most tasks, parcels that corresponded to brain regions that were relevant to the task had significantly lower entropy as compared to regions that were less relevant to that task, as determined by predicted areas of activation found in the literature. This finding was stronger in tasks where areas of activation were expected to be cortical regions, such as the sensorimotor task (where primary motor and sensory cortices were expected to be salient [10]) (Fig. 1), as opposed to tasks where areas of interest were subcortical regions, such as the emotion task (where amygdala activation was expected [10]) (Fig. 2). The closest matches between expected activation and observed significant entropy were found in the sensorimotor task, the language task, and the working memory/category-specific representation task (specifically in the category-specific representation portion of this task). Additionally, the social processing task showed some match between expected activation and entropy in the basal temporal area, but the primary areas of observed low entropy were in the superior parietal lobule, which was not an area of expected activation from literature [11]. The relational processing task, emotion task, and gambling task did not display significantly high or low entropy in areas of expected activation. See Table II in the Appendix for further detail on significant entropy for each task.

Additionally, for all task scans, there was a strong negative correlation between BOLD signal amplitude and entropy for all parcels (correlation coefficients ranging from $r = -0.670$ (emotion task) to $r = -0.820$ (relational processing task)). This correlation did not appear in the resting-state scan ($r = -0.0685$) or in the randomly-generated dataset ($r = -0.001$). The indication of significantly low entropy for regions of interest across several task-based fMRI scans indicates that brain regions recruited for a task tend to have a signal that is more predictable than brain regions that are less relevant to that task. There was also a strong negative correlation between the

amplitude of BOLD signal in a brain region and the entropy of that region.

Because of the complete lack of correlation between amplitude and entropy in the resting-state scan and the set of randomly-generated time series, this suggests that the correlation between amplitude and entropy in task-based data is not a feature of SampEn; rather, it is an inherent feature of task-based fMRI. However, the causation behind this correlation within task-based fMRI is uncertain. This could truly be a feature of the fact that task-activated brain regions tend towards lower entropy; alternatively, this could be an artifact of differences in the temporal nature of the hemodynamic response displayed at differing intensities. Further exploration is necessary to discern the likely cause for this correlation.

IV. CONCLUSION

We explored sample entropy as a methodology for analyzing BOLD signal complexity in task- and resting-state fMRI. For most tasks, brain regions that were relevant to the task at hand displayed significantly low levels of entropy as compared to the baseline; this finding was more prevalent in brain regions where cortical activation was expected, as compared to subcortical nuclei activation. Additionally, for all task-based fMRI, there was a strong negative correlation between BOLD signal amplitude and entropy. This correlation was not present in the resting-state scan or a set of random data generated to mimic time series of differing amplitudes. This suggests that the correlation between amplitude and entropy is a feature inherent to task-based fMRI.

APPENDIX

TABLE I. BRAINNETOME ATLAS REGIONS AND PARCEL NUMBERS

Parcel Range	Region ^a	
	General region	Subregion
1-14	Frontal lobe	Superior frontal gyrus
15-28		Middle frontal gyrus
29-40		Inferior frontal gyrus
41-52		Orbital gyrus
53-64		Precentral gyrus
65-68		Paracentral lobule
69-80	Temporal lobe	Superior temporal gyrus
81-88		Middle temporal gyrus
89-102		Inferior temporal gyrus
103-108		Fusiform gyrus
109-121		Parahippocampal gyrus
121-124	Parietal lobe	Posterior superior temporal sulcus
125-134		Superior parietal lobule
135-146		Inferior parietal lobule
147-154		Precuneus
155-162		Postcentral gyrus
163-174		Insular lobe
175-188	Limbic lobe	Cingulate gyrus
189-198	Occipital lobe	Medioventral occipital cortex
199-210		Lateral occipital cortex
211-214	Subcortical nuclei	Amygdala
215-218		Hippocampus
219-230		Basal ganglia
231-246		Thalamus

a. See <https://atlas.brainnetome.org/bnatlas.html> for more detail on precise location

TABLE II. EXPECTED VS. NOTED TASK ACTIVATION

Task	Brain Regions	
	Areas of activation from literature	Noted areas of high/low entropy ^a
Working memory and category-specific representation	<i>WMem</i> : Dorsolateral prefrontal cortex [10]	<i>Low</i> : Fusiform gyrus (BA 37) Occipital lobe (BA 17/18/19) Precuneus
	<i>Cat-specific</i> : Fusiform face area (BA 37) Occipital face area (BA 18/19) Extrastriate body area Parahippocampal place area [12]	
Social	Medial prefrontal cortex (BA 9) Basal temporal area (BA 20/37/38) Superior temporal sulcus (BA 21/22) Extrastriate cortex (BA 18/V3) [11]	<i>Low</i> : Superior parietal lobule Middle temporal gyrus (BA 37) Occipital lobe
Relational processing	Rostrolateral prefrontal cortex (BA 10) [13] Anterior prefrontal cortex [14]	<i>Low</i> : Fusiform gyrus (BA 37) Occipital lobe (BA 17/18/19) <i>High</i> : Postcentral gyrus (BA 2)
Emotion	Amygdala Hippocampus [10]	<i>Low</i> : Occipital lobe (BA 17/18/19)
Motor	Primary motor cortex (BA 4) Supplementary motor cortex (BA 6) Visual cortex [10]	<i>Low</i> : Primary motor cortex (BA 4) Postcentral gyrus (BA 1/2/3)
Language	Temporal lobe (anterior, medial, lateral) Angular gyrus Occipital lobe Superior frontal gyrus (BA 9/46) Inferior frontal gyrus (BA 45) Ventromedial prefrontal cortex (BA 11) [15]	<i>Low</i> : Superior temporal lobe (BA 22/38) Middle/inferior temporal lobe Angular gyrus Superior frontal gyrus (BA 9/46) Medial frontal gyrus (BA 9/46) Inferior frontal gyrus (BA 45) Precentral gyrus (BA 4) Ventromedial prefrontal cortex (BA 11) Parietal lobe (BA 1/2/3) <i>High</i> : Superior temporal lobe (BA 38/41/42)
Gambling	Cingulate gyrus Striatum [16]	<i>Low</i> : Occipital lobe (BA 17/18/19)

a. Bold regions indicate those that match areas of literature activation

ACKNOWLEDGMENTS

A sincere thanks to Behnaz Yousefi, Xiaodi Zhang, Anzar Abbas, Eric Maltbie and Wenju Pan for participating in lively discussions regarding this work. This work was supported by the National Science Foundation BCS INSPIRE 1533260, National Institutes of Health R01NS078095 and

1R01MH111416-01. Data were provided by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.

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