The Rényi entropy in data-driven analysis for pharmacological MRI

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Introduction

The analysis of pharmacological MRI (phMRI) traditionally depends upon the use of an appropriate input function, usually derived from blood plasma concentrations of the drug used in the experiment. There are a number of problems with this approach including the relationship between plasma and brain concentrations and the longer term effects of receptor activation. Because of this a number of data-driven approaches have been used where no model of the neural response is known *a priori* such as independent component analysis and wavelet cluster analysis [1]. Here we explore the use of a measure of signal complexity known as the Rényi entropy to discover voxels of interest in a data-driven manner using a dataset known to show reduced perfusion in the hippocampus.

Theory

The use of the Rényi entropy in the analysis of brain signals, including fMRI, was introduced and covered in detail in [2]. A generalisation of Shannon entropy, it allows one to discover the complexity of a signal by finding the number of components that appear in its time frequency representation (TFR). A TFR such as a spectrogram allows one to view the spectral properties of a signal as they change over time. A noisy signal would be represented by many components, that is, many concentrations of energy, while a signal of interest with what one would regard as structure or order, such as a voxel under the influence of a drug, may be made up of just a few components. That is, the signal from those voxels one is interested in may be described using less information than a signal one would regard as noise.

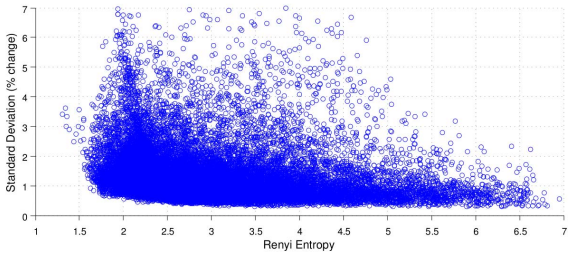


Figure 1: The standard deviation of all hippocampus voxels from all subjects on their placebo day plotted against their Rényi entropies.

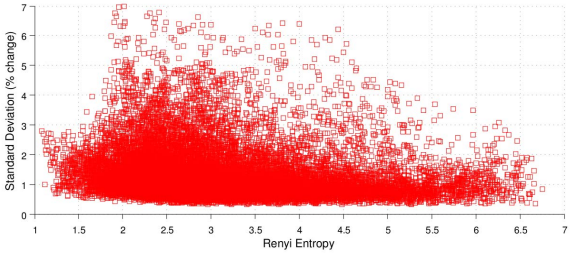


Figure 2: The standard deviation of all hippocampus voxels from all subjects on their drug day plotted against their Rényi entropies.

Methods

We have used data from a BOLD phMRI experiment where twelve healthy subjects received an infusion of either saline (placebo) or hydrocortisone (drug) after 10 minutes of baseline (out of 100 minutes in total) on alternate days [4]. Motion correction, spatial normalization and spatial smoothing were carried out using SPM5 (http://www.fil.ion.ucl.ac.uk/spm/). Segmentation was carried out according to the regions defined in [5] and only the hippocampus examined further here. Every voxel time course in the hippocampus, for each subject, on both placebo and drug days was analysed, with their values represented as percentage changes (calculated as the difference from the mean of the baseline period at every timepoint). A time frequency representation (a Morlet scalogram) was calculated for every voxel and its Rényi entropy found, as implemented in the freely available Time-Frequency Toolbox (http://tftb.nongnu.org/), a suite of MATLAB functions. The algorithm has no knowledge of spatial position and acts on each voxel independently. Standard deviations at each voxel were also recorded. Following [2] those entropies lower than 2 were noted as being of interest, the threshold used here being set at 1.75.

Results and Discussion

As can be seen in Figures 1 and 2 there is no significant difference in the standard deviations of the two groups of data, however, the drug data is shifted towards lower Rényi entropies. The most interesting voxels are those with both low standard deviation and low Rényi entropy, and we display voxels satisfying this condition in Figure 3. All those voxels with a Rényi entropy lower than 1.75 are shown in volume renderings in Figure 4 representing (a) placebo and (b) drug days. The left hippocampus is particularly interesting as several different subjects experience common low Rényi entropies in the same region.

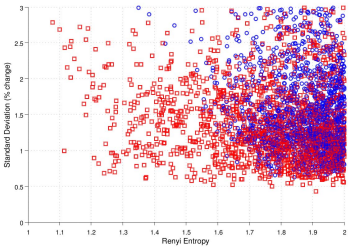
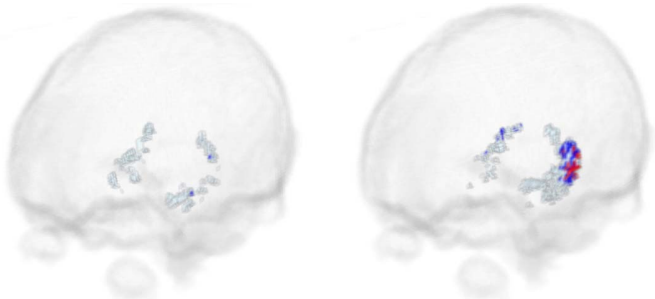


Figure 3: A zoomed portion of the previous figures combined. Placebo = blue circles. Drug = red squares.

Conclusion

These results suggest that it is possible to use Rényi entropy to discover those regions under the influence of a drug, in this case hydrocortisone, where a drop in perfusion has been caused. Further empirical and simulation testing will help discover sensible entropy thresholds for various designs of experiment. This technique is not designed to replace a conventional, hypothesis-driven analysis, but to inform of those areas with a possibly interesting signal which cannot be discovered using other approaches. It therefore merits further investigation in phMRI where one is often under informed as to an expected neural response.



(a) (b)

Figure 4: All those voxels in the hippocampus with a Rényi entropy of less than 1.75 collated over all subjects for (a) placebo and (b) drug days. Increasing colour strength signifies the number of subjects to experience a below threshold entropy in a common voxel position to others (dark blue = 2, red = 3 or more).

References

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