THE DEGREE OF TEMPORAL COMPLEXITY IN RESTING STATE FMRI: A POTENTIALLY NEW METRIC FOR FUNCTIONAL STUDIES IN ALZHEIMER'S DISEASE.

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INTRODUCTION: Resting state fMRI (rs-fMRI) has been an important tool to understand functional brain networks by studying correlations between fluctuations of the blood-oxygen dependent (BOLD) signal across brain regions [1]. However, the intrinsic temporal properties of the BOLD fluctuations may also contain valuable information about local brain functions. Based on the concept of information theory, transient information (TI) has been introduced as a statistical quantity to measure the degree of complexity, i.e., the difficulty involved in recognizing temporal patterns of stochastic time series [2,3]. In this preliminary study, we used TI to test whether regional BOLD fluctuations differ in the degree of complexity between Alzheimer's disease patients and normal subjects.

THEORY: The concept of TI has been introduced before [2,3], and is briefly described here. Given a sequence of bold fluctuations $\vec{S} = s_0, s_1, \ldots s_N$ the goal is to quantify the difficulty involved in recognizing temporal patterns to gain insight into the complexity of the sequence. Several information theoretic quantities were calculated. 1) Block entropy $H(L)$ is the total Shannon entropy of L consecutive observations and is defined as $H(L) \equiv -\sum_{s^L} \Pr(s^L)\log_2 \Pr(s^L)$, where s^L represents a block of L consecutive symbols in $\vec{S}$ and the sum runs over all block length L. 2) entropy rate $h_\mu$measures the irreducible randomness in $\vec{S}$, and is defined as $h_\mu \equiv \lim_{L\to\infty} H(L) - H(L-1)$. For a periodic or finite seuqnces, h_μ will become 0, as the sequences are fully predictable. Accordingly $EE + h_\mu L$ will become a horizontal line (Figure 1). 3) Excess entropy measures how block entropy $H(L)$ converges with increasing block length, and is defined as $EE \equiv \lim_{L\to\infty}\left[H(L) - h_\mu L\right]$. 4) Transient information TI is then the difference between H(L) and E taken over all L blocks and reflects the difficulty involved in recognizing the temporal patterns. $TI \equiv \sum_{L=0}^{\infty}\left[EE + h_\mu L - H(L)\right]$. Figure 1 depicts the relationships between H(L), EE and TI.

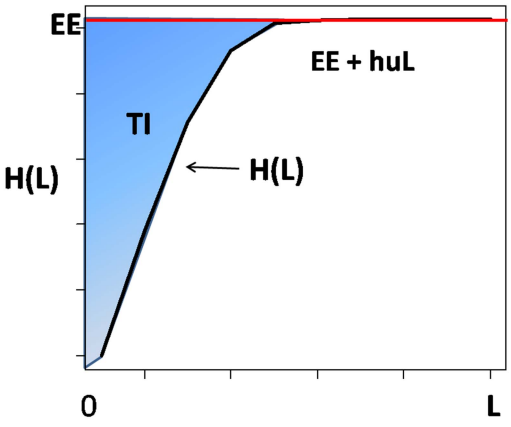

Figure 1. Sketch of block entropy growth curve H(L) as a function of block size L. The shaded area is the transient information TI.

METHODS: Rs-fMRI scans from 8 cognitive normal (CN) subjects (mean age ± std: 78 ± 7 yrs old) and 8 Alzheimer's disease (AD) subjects (mean age ± std: 80 ± 5 yrs old) were analyzed. The scans were selected from the Alzheimer's Disease Neuroimaging Initiative (ADNI). The rs-fMRI parameters were: 3 Tesla MRI, 7 minutes scan, TR/TE = 3000/30 msc, 3x3x3mm spatial resolution. In addition, we used the corresponding high resolution T1 images for anatomical registration using Freesurfer. The BOLD fluctuations were selected from two regions which are known to be affected in Alzheimer's disease [4], i.e. the posterior cingulate and precuneus. In addition, the motor cortex, which is usually spared by the disease, was selected as reference region. TI were calculated and compared between AD and CN groups using student-t test in each region.

RESULTS: Table 1 lists mean values and standard deviations of TI in each region by disease group. For BOLD fluctuations of the motor cortex, AD patients and CN subjects had similar TI values (p = 0.33). In contrast, for BOLD fluctuations of the posterior cingulate and the precuneus, AD patients had significantly smaller TI values (25%, p = 0.01 and 24%, p = 0.03, respectively) than the CNsubjects .

Conclusion: In this study, we quantified the degree of complexity in regional BOLD fluctuations using transient information, a statistical measure to characterize stochastic signals. Our preliminary results suggest that the complexity of regional BOLD fluctuations is selectively reduced in brain regions typically affected by AD. Reduced complexity implies that the brain processes in AD underlying the BOLD fluctuations are more predictable, i.e. are more periodic, than those in healthy subjects. In conclusion, transient information could provide a new metric for rs-fMRI to study brain functions in healthy conditions and disease.

	Motor Cortex	Posterior Cingulate	Precuneus
AD (mean±std)	29.1±6.8	36.7±14.1	33.2±11.4
CN (mean±std)	33.2±8.5	48.3±10.4	43.4±6.8
p-value	0.33	0.01	0.03

Table 1. Comparison of TI values in motor cortex (reference) and posterior cingulate and precuneus (affected regions) between AD and CN subjects. . Student-t test were used to test the statistic significance.

REFERENCE: [1] Raichle, et al., Proceedings of the National Academy of Sciences 98 (2): 676–82 (2001); [2] Feldman, et al., Advances in Complex Systems 7:329-355(2004);[3] Liu, et al., International Society of Magnetic Resonance in Medicine(2012); [4] Buckner, et al., the Journal of Neuroscience 25(34):7709-7717(2005);