Maximized Mutual Information: A Novel Approach for Brain Activation Detection in fMRI

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Introduction

Mutual Information (MI) has been widely used in medical informatics, especially in image realignment including fMRI image registration and realignment [1-4]. A preliminary study also attempted its application in activation detection in fMRI [5]. MI measures how much information one random variable tells about another one. In another word, as its name indicates, MI is a measure of the common information contained in two signals. One characteristic strength of MI, as suggested in its application in image realignment, is its sensitivity to the degree of similarity between two signals in comparison. As such, in this work we proposed to explore its application in fMRI activation detection, since as in the majority of fMRI statistical methods [7, 8], activation signal can be detected by examining the signal similarity between pixel time course and a template signal.

Materials and Methods

Mathematically, MI is defined as [6]: $MI(X,Y) = \Sigma P(x, y)\log P(x, y)/(P(x)P(y))$, where X and Y are two random variables, while x and y are the possible values of X and Y respectively; P(x, y) is a joint probability density function when X=x, and Y=y; P(x) and P(y) are marginal probability density function of X and Y, respectively. Usually it is hard to calculate P(x) and P(y) and P(x, y) directly. As an alternative, a histogram can be used to calculate the probability density function [6]. When applying MI on time course signals in fMRI, X and Y are pixel time course and reference time course, respectively. P(x) can be calculated using histogram H(x) which is the number of time points in X that have value x, and P(y) can be calculated similarly. P(x, y) can be calculated as joint histogram H(x, y), which is defined as the number of time points when X=x and Y=y.

Both computer simulations and finger tapping activation studies were carried out to assess the characteristics of MI. All MRI experiment data were acquired on a clinical whole body 1.5-T system (Magnetom Vision; Siemens Medical Systems, Erlangen, Germany). Functional scans were acquired with a single-shot gradient echo EPI sequence (matrix size 64*64, voxel size 4*4*4 mm^3, TR/TE/FA = 0.88s/40ms/90^o), with an activation paradigm consisting of 3 cycles of "30s OFF/30s ON" bilateral finger tapping followed by 30s resting state. Figure 1 is a simulation to illustrate the sensitivity of MI to the degree of similarity in timing between two signals, where signal 1 is timing is a periodic boxcar function of amplitude 1, and signal 2 is a time-shift boxcar function of amplitude 10 and the same period. The plot showed the MI at different time shift between the two signals. As a comparison, corresponding cross correlation (CC) coefficient (in absolute value) was also shown. These simulation results assert that MI is highly sensitive to the degree of similarity in timing between signals in comparison (i.e., pixel time course versus reference signal). Further simulation was done to investigate the sensitivity of MI to the temporal pattern/shape of signal. For this purpose, MI of two time course signals with matching timing was calculated. As an example, when one signal was a periodic boxcar function while the other was timing-matching signal with periodic triangles replacing boxcars, MI was found to be 0.77 while CC = 0.75. This indicates that the sensitivity of MI to temporal pattern/shape is not as strong as that to timing. This is a favorable feature for MI because when matching timing was found, activation would be reliably detected. Based on these simulation results, we proposed the use of maximization of MI (MMI) by temporal shifting to improve fMRI activation detection. Specifically, each pixel time course was shifted in timing until the maximal MI between reference signal and the time-shifted pixel time course was obtained.

Results

Brain activation was reliably detected using MMI in each of the subjects. Figure 2 was a representative activation map obtained in one subject where threshold of the MMI coefficient was 0.65 and the size of cluster was 3. A boxcar reference function was used. Fig. 3 shows the temporal phase histogram of the activated pixels. As can be seen, there is a characteristic hemodynamic delay of approximately 8s for the activated pixels, consisting with literature [9].

Conclusions and Discussion

By exploiting the sensitivity of MI to similarity in timing between signals in timing (i.e., pixel time course versus reference signal), MMI could reliably detect fMRI activation signal by seeking to maximize mutual information existing between each pixel time course and a reference waveform. By doing so, MMI is less affected by the variation of hemodynamic delay in brain response and able to detect more activation voxels than MI alone [5]. There are two major differences between our work and Tsai's work [5]. First, MMI was used instead of MI. Second, to simplify calculation without losing accuracy, histogram was used instead of a Parzen window density function to calculate the MI coefficient. Importantly, hemodynamic delay of the activated pixels could be intrinsically derived in the process of seeking MMI for each pixel.

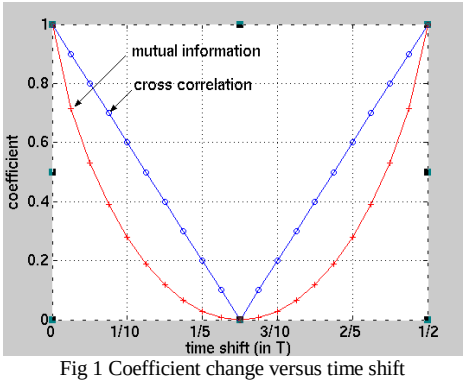

Fig 1 Coefficient change versus time shift

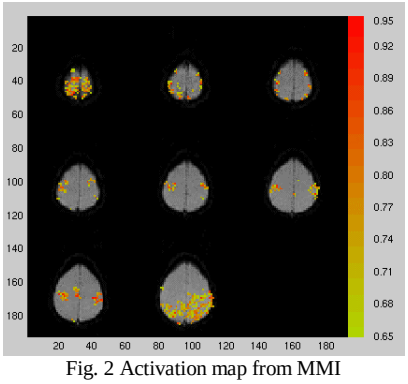

Fig. 2 Activation map from MMI

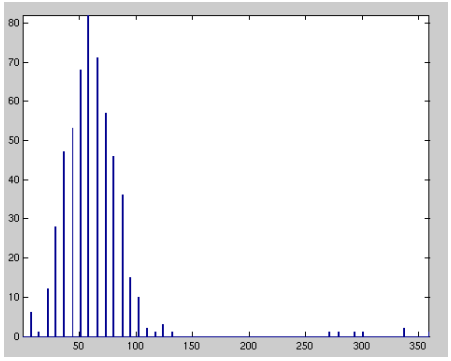

Fig.3 Phase histogram of activated pixels of Fig.2

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