Two fMRI indices as markers for Alzheimer's disease

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Introduction

In neuroscience, it is well known that regions of the brain exhibit functional synchrony [1]. Functional synchrony is characterized by regions of the brain having correlated neural activity. A well-established method to describe this synchrony in fMRI is the average cross correlation, termed the coefficients of spontaneous low frequency fluctuations (COSLOF) index. The COSLOF index has proved useful as a noninvasive quantitative marker of hippocampal synchrony for the preclinical stage of Alzheimer's disease [2]. Here, the correlation matrix determinant (COMDET) index, an alternative and complimentary index of functional synchrony, is applied. The COSLOF and COMDET indices were shown to result from generalized likelihood ratio tests of independence versus intraclass or general correlation structure [3].

Model

The standard multivariate linear regression model [4] is used to describe the voxel time courses. The model, for a set of p voxels measured at n time points, is written as $Y = XB + E$, where Y is the matrix of observed time courses, X is the design matrix, B is the matrix of regression coefficients, and E is the matrix of errors. The errors of observation, ε_i, which are rows of E, are assumed to be independent and normally distributed with p dimensional zero mean vector, and $p \times p$ positive definite covariance matrix Σ. The maximum likelihood estimator (MLE) of the matrix of coefficients is $\hat{B} = (X'X)^{-1}X'Y$ and the MLE of the covariance matrix is $\hat{\Sigma} = (Y-XB)'(Y-XB)/n$. The sample correlation matrix R is computed from $\hat{\Sigma}$. .The COSLOF index is defined to be $\hat{\rho} = (e_p'Re_p-p)/[p(p-1)]$ and the COMDET index as $\hat{\rho} = |R|$ where e_p is a p-dimensional column vector of ones. A generalized likelihood ratio test yields logarithmic functions of these two statistics, $u = -n\log\{[1-\hat{\rho}]/[1+(p-1)\hat{\rho}]\}$ and $v = -[v-(2p+5)/6]\log\hat{\rho}$ which are asymptotically χ^2 distributed with 1 and $p(p-1)/2$ degrees of freedom respectively, where $v = n-q-1$.

Results

Resting state imaging of 9 healthy aged (HA), 5 mildly cognitively impaired (MCI), and 10 Alzheimer's disease (AD) patients was performed on a 1.5T GE Signa with TR=2000 ms and TE=40 ms. Fifteen GRE sagittal slices of 64×64 were obtained. The FOV=24 cm and voxels were 3.75×3.75×7 mm with n=180 time points taken. The best slice through each hippocampus was selected and voxels extracted. The time series were low-pass filtered [2] and fit to a multivariate regression model. The correlation matrix was computed from the residuals and the asymptotic statistics were computed from sample correlation matrices. The figures below show results in which the statistics are plotted against the patients' mini mental state exam (MMSE) and each other. The plotted observations include patient number and are colored by clinical diagnosis: red for AD, yellow for MCI, and green for HA.

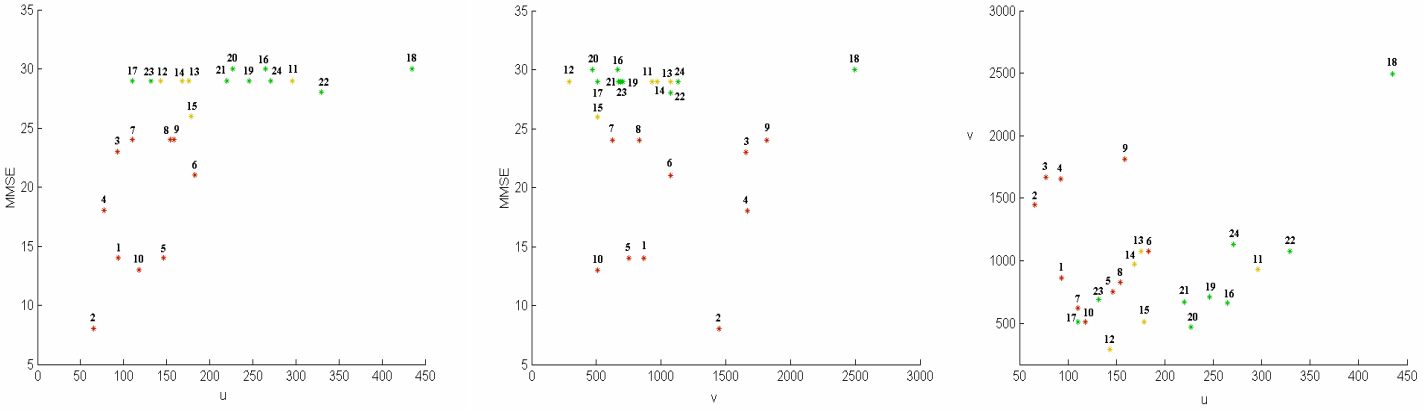

Figure 1. MMSE *vs* u (left), MMSE *vs* v (center), u *vs* v (right).

Conclusion

Two fMRI indices of hippocampal synchrony, the COSLOF and COMDET, were applied to AD, MCI, and HA patients. It was shown that each of the indices with the MMSE or both indices without the MMSE can characterize the three populations, thus eliminating the need for the MMSE.

References

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