Predicting symptomatic outcome in mild traumatic brain injury with support vector machines: a 1H-MRS Study

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Introduction: Up to 5 million Americans are currently living with Traumatic Brain Injury (TBI) related disabilities. It is estimated that about 12-20% of Iraq and Afghanistan veterans have suffered from TBI. More so, the overwhelming majority of viable TBI patients (75%) are deemed "mild" with most injuries occurring as non-hemorrhagic and or microscopic likely rendering them undetectable by Computed Tomography (CT) or conventional MRI (Magnetic Resonance Imaging). Besides detecting acute abnormalities with imaging or neuropsychological markers of mTBI, a current challenge of researchers and clinicians alike is being able to predict the required time for symptom resolution in patients. The awareness of the time required for symptom resolution is indeed valuable as it can allow patients and caregivers to plan towards recovery and resumption of regular activity, particularly in the case of athletes and combat personnel.

The aim of the current study is to acutely predict the symptomatic outcome of mTBI patients 6 months post injury (PI) using magnetic resonance spectroscopy (MRS). Herein, we applied acute neurometabolic information to the support vector machine (SVM) algorithm in order to differentiate between patients with and without post concussive syndrome (PCS) 6 months PI. SVM is a supervised learning algorithm that is able to predict the class of previously unseen input data, having developed a pattern recognition model by "learning" pertinent features from pre-classified data.[1]

Methods: Forty-one mTBI patients [Glasgow Coma Scale (GCS) 13-15] were examined both acutely (within 10 days of injury) and chronically (~6 months PI). Participants with a history of neurological and psychiatric illness, stroke, brain tumors or seizures were excluded from this study. Acute MR examinations were carried out on a Siemens Tim-Trio 3T MRI scanner and included a T1-weighted-MPRAGE scan for anatomical reference and a Proton Magnetic Resonance Spectroscopy Imaging (^{1}H-MRSI) scan (TE/TR = 135/1300). Metabolite quantification was performed using *LCModel*. The SVM algorithm was developed using *MATLAB R2013b*. The acute metabolic information included in the SVM model were N-acetyl aspartate-to-creatine ratio (NAA/Cre) and Choline-to-creatine ratio (Cho/Cre) values measured in the thalamus and centrum semiovale (CSV). Previous work in our research lab and from others has shown that these measurements are sensitive markers for mTBI evaluation. Patient evaluation for the persistence of PCS at the chronic stage of mTBI was carried out using the Rivermead post concussive symptoms questionnaire (RPQ). Patients were deemed PCS positive (PCS+) if they experienced any of 4 or more of the major PCS symptoms (headaches, dizziness, sleep abnormalities, trouble concentrating, fatigue, memory problems and irritability). Of the 41 patients examined, data from 28 [13 PCS+, 15 PCS negative (PCS-)] patients was used to train the SVM classifier for pattern recognition. Data from 13 (6 PCS+ and 7 PCS-) patients was used to validate the accuracy of the model. An optimized Gaussian kernel was used to obtain the feature space for maximum separation of classes. A 10-fold cross validation method was used to determine the misclassification rate (MCR) of the model. The MCR (0-1) measures classifier performance by estimating the proportion of misclassified samples. A lower MCR signifies better classifier performance.

Results: *Figure 1* shows the grouping of patients in the training data set according to symptomatic outcome using NAA/Cre and Cho/Cre measurements in (a) the thalamus and (b) the CSV. In using metabolic measurements from the thalamus alone, the cross validation analysis yielded an MCR of 0.2927 in predicting the symptomatic outcome of patients in the validation data set. An MCR of 0.4390 was realized when metabolic measurements from the CSV alone were used. When metabolic measurements from both the thalamus and CSV were jointly incorporated in the model, an MCR of 0.2195 was achieved.

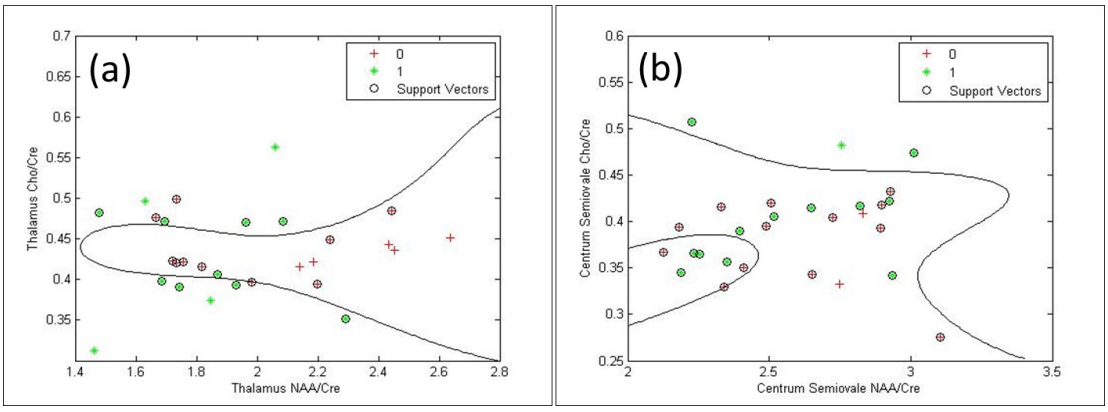

Figure 1. Plots showing the grouping of patients from the training data set according to symptomatic outcome by the SVM classification model. The model used acute metabolic measurements from (a) the thalamus and (b) the CSV in predicting whether patients would be PCS+ (green stars) or PCS- (red crosses) at 6 months post injury. The circled markers indicate patients on the support vectors demarcating each outcome class.

Conclusion: Magnetic resonance spectroscopy data applied to the support vector machine algorithm can potentially serve as a feasible approach to predicting the symptomatic outcome of mTBI patients. The inclusion of MRS measurements from multiple neuroanatomic regions can help to boost classifier performance.

References: [1] Pontil M. et al., Neural Comput. 1998 May 15;10(4):955-74.

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