Diagnostic prediction of language impairment in Autism Spectrum Disorder using joint MEG - DTI classification

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Background and Objective: Language impairment (LI) is an important behavioral symptom associated with Autism Spectrum Disorder (ASD). While the neuronal underpinnings of LI have been investigated using DTI-based spatial WM measures [1] and temporal characteristics derived from MEG-based measures [2], neither of these individually provide a comprehensive characterization of LI. In this work, we combine information from DTI and MEG and create non-linear classifiers that can quantify LI by learning the patterns of LI in the population.

Method: The DTI images for all subjects (9 LI-ASD (LI+), 23 non-LI-ASD (LI-), 21 typically developing (TD)) were acquired on Siemens 3T Verio™ scanner using a 32 channel head coil. Diffusion tensor imaging was performed using a single shot spin-echo, echo-planar sequence with the following parameters: TR/TE=16900/70 ms, b-value of 1000 s/mm^2 and 30 gradient directions. We spatially normalized all the DTI data to a standard atlas [3] that includes labeled regions of interest (ROIs). ROIs that are hypothesized to be affected in ASD/LI were chosen as features: (right and left) superior temporal white matter (STWM), superior longitudinal fasciculi (SLF), inferior fronto-occipital fasciculi (IFOF) and inferior longitudinal fasciculi (ILF). We then skeletonized these fiber tracts using FSL-TBSS [4] and used the FA values on this skeleton as our DTI features. The MEG features included the latency of auditory evoked neuromagnetic field 100ms component (M100) and latency of magnetic mismatch field (MMF) which is a response component reflecting detection of 'change' in the auditory stream [5]. In the next step, feature selection was performed which provided us with relevant features that contributed towards the classification. We use a feature filtering method called signal-to-noise (s2n) ratio coefficients [6]. For feature vector X and class labels Y, $s2n(X,Y) = \frac{\mu(y+) - \mu(y-)}{\sigma(y+) + \sigma(y-)}$ where μ and σ are the mean and standard deviation of the classes. The optimal number of features '$\boldsymbol{n}$' is found by using a technique suggested by Guyon [7]. Finally, we implemented a 3-way non-linear support vector (SVM) classifier between, LI+, LI- and TD control population on a pair-wise basis (that is, a collection of two-class classifiers taking the three classes in pairs and averaging the output score). A leave-one-out cross validation was performed where one subject was removed and other subjects were used in feature ranking and classification. The left out subject was tested over the constructed classifier and was assigned a probabilistic score. By repeatedly leaving each subject out as a test subject, we obtained an average classification rate and a language impairment score for each subject.

Fig.1 Displaying the LOO classification performance. PDF of LOO scores is plotted for 3 classes.

Results: Fig. 1 shows the classification results. The probabilistic scores from the LOO are plotted against the normal probability density (PDF) which represents the likelihood of each score. The abnormality score ranges between +1 and -1 where a subject with low score (~< -0.9) was classified as LI+, a subject with score approximately in between -0.9 to 0.05 was classified as LI- while other subjects were classified as TD [8]. The average LOO accuracy was 71.69% (34/53) correctly classified. The top 8 features were used in each LOO. The features that were selected included MMF latency as the top ranked feature and FA regions shown in Fig. 2 with the red dots. M100 latency was selected in the top 8 features, but with low average rank (5th) compared to MMF and some of the FA features.

Discussion: In this work, we designed multivariate LI classifiers that combine information from MEG and DTI. These classifiers are based on FA of regions involved in language processing and MEG measures obtained from an auditory task. Our method shows that when information is combined from two modalities superior performance is achieved (71.69%) rather than using only MEG (64%) or only DTI (57%). The classifiers have the power to assign an abnormality score which can be potentially used as a diagnostic biomarker. Moreover, the feature ranking provides an insight into the relative importance of complementary MEG measures and DTI measures in characterizing LI. In addition, the top discriminatory features in FA values are regions that contribute most to the LI providing a physiological insight into the symptom of LI.
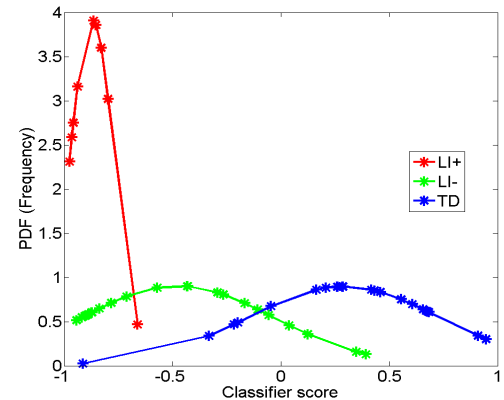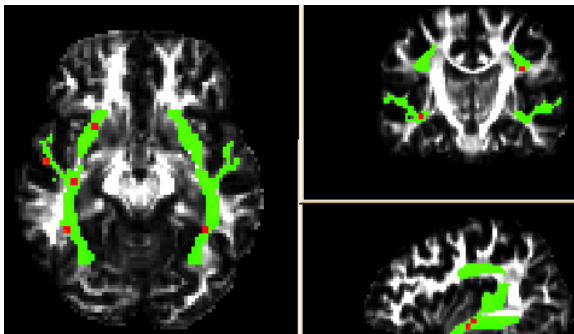

Fig. 2 Regions of interest: Green areas are the areas chosen for classification. Red dots indicate the top ranked regions.

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