Multi-modal pattern recognition: an application to schizophrenia.

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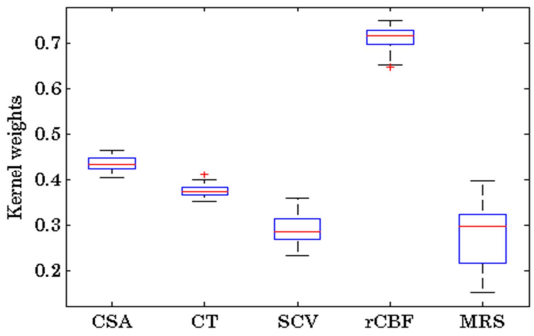
PURPOSE To establish which MRI modalities are most accurate in distinguishing patients diagnosed with schizophrenia from healthy controls and whether combining modalities offers increased performance.

METHODS Twenty-four patients diagnosed with schizophrenia and 24 age- and gender-matched controls were included. Clinical diagnoses of all participants were established using face-to-face interviews conducted by a consultant psychiatrist. Brain imaging was performed at the Clinical Research Image Centre in Edinburgh, Scotland. Imaging was performed using a Siemens Verio 3T scanner using a matrix head coil with 12 elements. A structural brain image was acquired using a T1-weighted magnetisation prepared gradient echo sequence prescribed parallel to the AC-PC line with a repetition time (TR) = 2300ms, echo time (TE) = 2.98ms, inversion time (TI) = 900ms and flip angel = 9º; yielding 160 contiguous 1mm axial slices of 256 x 256 voxels. Perfusion imaging was performed to quantify regional cerebral blood flow (rCBF) using the PICORE Q2TIPS pulsed arterial spin labelling sequence (22 slices, TR = 3000ms, TE=14m, TI1 = 700ms, T1-stop = 1400ms, TI2 = 1600ms.). The regional concentration of metabolites in the brain were imaged using proton magnetic resonance spectroscopy (1H-MRS) using the point resolved spectroscopy (PRESS) sequence with the following parameters: TR = 3000 ms, TE =80 ms, 128 averages, 2048 data points, spectral width 2000 Hz. For each metabolite spectrum, unsuppressed water reference spectra were acquired (16 averages). 1H-MRS spectra were acquired in the left and right dorsolateral prefrontal cortex and the anterior cingulate cortex. The T1-weighted images were pre-processed using Freesurfer[1] in order to compute the cortical thickness (CT), cortical surface area (CSA) and subcortical volumes (SCVs). Regional cerebral blood flow (rCBF) maps were computed using ASLtbx, a toolbox developed by Wang et al.[2] The MRS data were processed using LCModel[3] and the concentrations of GABA glutamine, glutamate, glutathione, choline, creatine and NAA were selected; 18 participants per group were available for the MRS data. To perform multi-modal pattern recognition we used the SimpleMKL framework[4]. The main premise of this method is to create a kernel that encodes the discriminatory information from all modalities. In this case, MKL is achieved by computing the weighted sum of all kernels

$$\boldsymbol{K}_{MKL} = \beta_{CSA}\boldsymbol{X}_{CSA}\boldsymbol{X}_{CSA}^T + \beta_{CT}\boldsymbol{X}_{CT}\boldsymbol{X}_{CT}^T + \beta_{SCV}\boldsymbol{X}_{SCV}\boldsymbol{X}_{SCV}^T + \beta_{rCBF}\boldsymbol{X}_{rCBF}\boldsymbol{X}_{rCBF}^T + \beta_{MRS}\boldsymbol{X}_{MRS}\boldsymbol{X}_{MRS}^T$$

where β represents the kernel weights. Performance was assessed using leave-one-out cross validation whereby all but one pair of matched subjects' data is used to train the model and the left out pair are used as a test case. Area under the receiver operator characteristic curve (AUC) was used to assess performance.

RESULTS The combined discriminative power of all five modalities was achieved an AUC of 0.77. In some cases, the individual modalities achieved higher performance: AUC for CSA – 0.71, AUC for CT – 0.70, AUC for SCV – 0.62, AUC for rCBF – 0.82 and AUC for MRS – 0.61. The weights for each modality can be seen in Figure 1. We observe that the weight for rCBF is the most highly weighted modality.



DISCUSSION This is the first time that structural brain data, rCBF and MRS data have been jointly assessed for discriminating schizophrenia from controls. An increase in discriminative power was not observed on combining modalities. rCBF was the most highly weighted modality. Predictive probabilities (the probability of belonging to the SCZ group) were not correlated with the level of antipsychotic medication. These results imply that perfusion imaging is a highly sensitive marker for schizophrenia. Future work should assess the specificity via differential diagnosis of psychiatric disorders.

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