Combining tractography and coherence measures to identify connectivity within a neural network for reading

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Introduction

The question of how a particular behaviour is supported by neural architecture is clearly of the utmost interest. The standard method of addressing this has been to use fMRI coupled with a subtractive methodology to identify those areas of neural tissue which uniquely contribute to the relevant behaviour. However, this approach has a number of potentially major drawbacks: 1) It can only reveal information about the contrast with the baseline task, so key parts of the network involved in both tasks are overlooked and the areas identified depend critically on the nature of the baseline task; 2) Measures based on the BOLD signal may not be a true representation of the underlying neuronal activity[1] 3) Allowing that fMRI can reveal relevant areas it struggles to indicate the pattern of connectivity between the areas identified. The use of temporal correlations between activations produces measures of functional/effective connectivity, but these measures are handicapped by the poor temporal resolution of fMRI. Tractography provides a potentially useful correlative methodology to identify the anatomical substrate of connections and may therefore be helpful in understanding the accuracy or otherwise of fMRI-derived networks.

Here we consider two recent studies, which used different functional methods to generate two proposed networks thought to subserve reading[2,3] Kujala et al[2] used coherence analysis in MEG with the subjects reading continuous text, while Mechelli et al[3] used DCM on fMRI data acquired from subjects reading single words. The networks identified were quite different (possibly reflecting differences in the exact task). Of particular interest is the fact that the MEG study suggested connectivity extending to the anterior temporal lobe (a region that is implicated in reading from data on semantic dementia).The focus of the current work is an exploration of evidence from probabilistic tractography for a structural substrate to support these two networks.

Method

High angular resolution diffusion weighted imaging data was collected from 11 right handed subjects using a previously described reversed, k-space distortion corrected protocol[4]. Acquisition: 3 T Philips Achieva scanner; 8 element SENSE head coil; SENSE factor 2.5; phase-encoding in L-R orientation; SE-EPI with TE = 54 ms, TR = 11884 ms, G = 62 mTm^{-1}, 112 × 112 matrix, reconstructed resolution 1.875 mm, slice thickness 2.1 mm, 60 slices, 61 diffusion sensitisation directions at b = 1200 smm^{-2} (Δ, δ = 28.5, 13.5 ms), and 1 b = 0 image. These images were then used as the source for a series of PICo probabilistic tractography[5,6] experiments incorporating q-ball[7] analysis to discern multiple fibre orientations per voxel and bootstrapping to generate the probability density functions[8]: MNI co-ordinates for each of set of ROI's identified in the two studies were converted into subject space and ROI's of radius 8mm were created around them. These ROI's were then used to seed the tractography (20,000 streamlines per voxel with the output recorded in intervals of 200). To determine whether there was evidence for an anatomical connection between each pair of ROI's the number of streamlines per voxel from the seed ROI to the test ROI was compared with the number of streamlines per voxel in the rest of left hemisphere (Mann Whitney U test). If voxels in the test ROI had significantly higher PICo frequency of connection ($p<0.001$) than voxels in the remainder of the left hemisphere it was considered to be evidence for an anatomical connection between the two areas.

Results

Figure 1 shows the relationship between the predictions from the two studies and the tractography. Where the MEG study predicts a connection tractography finds supporting evidence in 52.5% of cases (forward and backward connections are treated separately). Where there is no MEG prediction, tractography finds a connection in only 24.6% of cases. This is highly significant (Chi Squared=49.8,p=1.7x10^{-12}). By contrast for DCM the tractography finds connections in only 22% of cases irrespective of the predictions. Figure 2 shows more detailed picture of the MEG study with each possible connection represented by a circular target. Bands within the targets represent individual subjects For the predicted connections AT-OT, AT-MT, INS-ST, OT-ST and MT-OT there is very strong supporting evidence from the tractography with more than half of the subjects finding positive connections in both directions. For connections OT-PF, FM-OT, FM-PF and INS-OT there is more limited evidence with fewer of the subjects finding a positive connection and often only in one direction. For the connections FM-ORB and ORB-ST there is no supporting evidence with none of the subjects recording a significant connection.

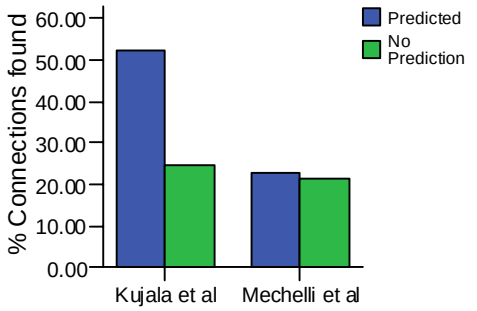

Figure 1. Accuracy of connectivity predictions

Discussion

The combination of data from coherence based measures and DWI based tractography has considerable potential to advance knowledge of brain structure/function relationships. Models derived from coherence data represent the best fit from a number of candidates. Using tractography in combination with these methods could provide a useful additional constraint -allowing improved model selection. The fit between the MEG data and the tractography results is more remarkable when we consider that different subjects were used in each case. This required the use of relatively large ROIs to ensure that the tractography seed points included the correct areas. An obvious next step would be to use the same technique with simultaneous EEG, MEG, and/or fMRI on the same subjects. The difference in data fit between the DCM and MEG studies may relate to the superior temporal resolution of MEG data, or it may indicate that the subtractive methodology, used in the DCM study, has excluded one or more key network areas through which the functional connectivity is mediated.

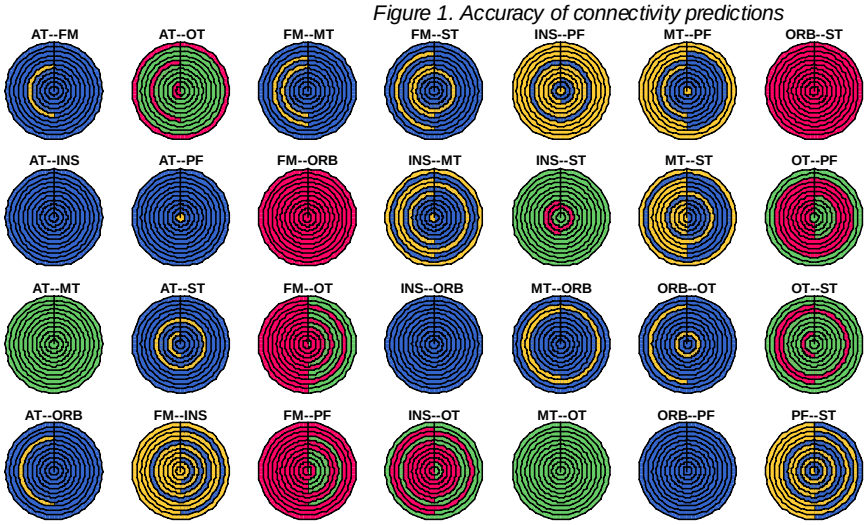

Figure 2. Prediction outcome by connection. OT = inferior occipitotemporal cortex, MT = medial temporal cortex, ST = superior temporal cortex, AT = anterior part of the inferior temporal cortex, FM = face motor cortex, INS = insula, PF = prefrontal cortex, ORB = orbital cortex.

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