Resting state fMRI of retinotopically defined sub-regions in human visual cortex

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Introduction

Resting state connectivity is now firmly established as a robust method for measuring functional connectivity between brain regions. However, it is still not known at what spatial scale the resting state time courses cease to be unique, and are no longer statistically separable from the time courses of neighbouring spatial regions. Furthermore it is not known whether the connections between such small, unique regions will reflect connectivity patterns on a finer scale, or will merely reflect the general connectivity patterns established for larger areas. In this study we attempt to provide answers to these questions by examining the fine mapping of the human visual cortex using retinotopic mapping techniques to subdivide visual areas. This allows us to formulate direct hypotheses concerning the connectivity between sub-regions.

Methods

Six female volunteers (22-26 years, mean 24 years) with normal or corrected to normal vision participated in the study. Scanning was performed at 3 Tesla (Magnetom TRIO, Siemens, Erlangen, Germany). Retinotopic mapping and resting state data were acquired with a phased array occipital coil (Stark Contrast, Erlangen Germany). Excluding anatomical scans, the protocol included: polar angle mapping; a resting state acquisition of 7 minutes (140 volumes); eccentricity and hMT+ mapping; and finally a second resting state acquisition of 7 minutes. During the resting state scans there was complete darkness and the volunteers were instructed to close their eyes and not to perform structured thought processes. The retinotopic mapping and resting state acquisitions were performed using a gradient-echo EPI scan with the following parameters: matrix= 128x128, FOV 196x196 mm^2 ,1.53x1.53x1.5 mm^3 voxels, 30 slices, interslice gap 15%, TE/TR = 33/3000ms, FA 84° , partial Fourier acquisition 6/8, bandwidth 1628 Hz/Pixel. A relatively high spatial resolution was used in order to exploit the high sensitivity of the occipital coil.

For the resting state data the standard motion correction, slice time correction and linear trend removal were applied in addition to a low pass filter using a 3 data point smoothing kernel, that corresponds to a cut-off frequency of 1/6 Hertz.

Automatic gray and white matter segmentation was performed using BrainVoyager (Brainvoyager QX, 1.4.10, Brain Innovations, Maastricht, The Netherlands). The segmentation mask was inflated and dorsal and ventral streams defined on the basis of the polar angle encoded retinotopic mapping. The borders of visual areas were manually drawn on a flat map on the basis of phase reversal at the boundary between regions in the polar angle encoding. The central region was defined as that corresponding to the central 1° of the visual field. In this way regions of interest corresponding to the central and to the peripheral areas of V1 through to V4 were identified. The regions of interest (ROI) of hMT+ were defined in Talairach space.

Partial correlation coefficients between regions were computed using the inverse covariance matrix with an in house program. Significance was obtained using a t-test on the partial correlation coefficients rejecting the null-hypothesis of zero partial correlation with a FDR-corrected threshold of $p = 0.05$. The partial correlation coefficient approach was chosen because it will identify unique connections between regions with all other contributions partialled out.

Results

The dorsal and ventral streams were treated separately. The connectivity pattern for whole regions in each stream showed unique connections to hierarchical regions in the same hemisphere and homologous regions in the opposite hemisphere (fig 1a). When central and peripheral regions were considered separately then the central to central (fig. 1b) and peripheral to peripheral (fig 1c) connectivity patterns were similar to those for the whole regions, whereas hardly any connections between central and peripheral regions were found (fig 1d).

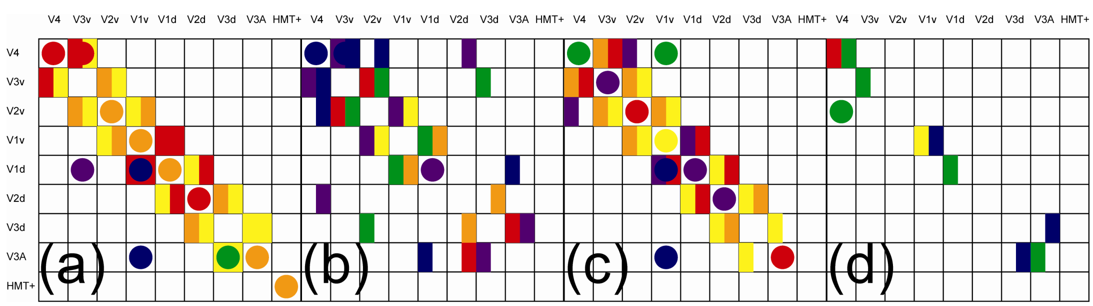

Figure 1. Significant connections between regions. Circles indicate inter-hemispheric connections with the column indicating the left region. Bars indicate intra-hemispheric connectivities, with the left bar in each box representing left hemisphere. The colour scale denotes the significance of the connection on a hot-body scale. (a) connectivity of whole areas, (b) central to central connections, (c) peripheral to peripheral and (d) central to peripheral or vice versa.

Each visual hemifield was further split into four octants using the polar mapping results and connectivity between the octants was investigated. Within hemispheres significant connections were only found between either the same octants in hierarchically ordered areas, or between different octants in the same area. Of the 13 connections between the same octants in hierarchically ordered areas, 9 pairs of regions are physically adjacent to each other, and 4 are not, implying that the connectivity does not rely on the octants being adjacent.. Furthermore the three strongest inter-hemispheric connections are all between the same octant and region, for example between the third octant of left and right V1d. The other two inter-hemispheric connections are weaker, and still between homologous visual areas, but not in the same octant.

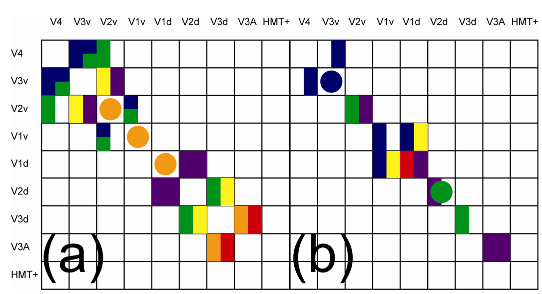

Figure 2. Connections between octants. As in figure 1 bars denote intra- and circles inter-hemispheric connections. (a) shows significant connections between the same octant, (b) shows significant connections between different octants. As each region is split in two it is possible to have more than one connection to another. In the two instances where this occurred the coloured bar is replaced by two small squares. Note that HMT+ was not included in this analysis. In (a) the expectation is that inter-hemispheric connections should lie on the diagonal, and intra-hemispheric ones on the off-diagonal lines. In (b) connections between different octants are most likely if they are in the same region, and so the expectation is that these should lie on the diagonal.

Discussion

The nature of the partial correlation coefficient approach implies that if a significant connection is found then there is a correlation that is unique to the pair of regions in question. The peripheral to peripheral and central to central connections show a strong similarity to those of the whole areas, whereas the markedly reduced pattern of central to peripheral connectivity indicates that central and peripheral regions have distinct time courses. At the scale of the octants the hierarchical connection pattern is most evident in regions higher than V1, where however a strong interhemispherical connectivity is found. In conclusion the partial correlation approach is capable of identifying meaningful unique connections in resting state connectivity even at the scale of an eighth of a retinotopic region.