Connectivity in controls and epilepsy: demonstration of a metabolic network by MRSI

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Introduction   While resting fMRI connectivity studies have linked the thalamus and hippocampus in humans (1), whether such connectivity maps are manifest metabolically is unknown. Our goal is to establish whether such a network can be detected through 1H spectroscopic imaging data. For disease states such as epilepsy, understanding the network is potentially important, especially given the availability of neurostimulator devices that may modulate function by propagating through network loci. We use 1H MRSI data from a subcortical set of loci with a common factor analysis to assess for metabolic connectivity in control volunteers and patients with epilepsy (medial temporal lobe and neocortical epilepsy). Not only is the subcortical network readily detected in resting connectivity studies, we believe that it is important to evaluate this system in epilepsy as it may be thought to participate in nearly all seizures and epilepsy types. The subcortical loci evaluated in this study include the bilateral anterior and posterior hippocampus, thalamus, and bilateral basal ganglia and insula, 12loci in total.

Methods   All MRSI data were acquired using a Varian Inova whole body MR system with TEM head coil. Two slices were studied in each subject, first angled through the medial temporal lobes and second through the mid-thalamus. Shimming was performed using a high resolution field map through user defined regions of interest to provide typical whole slice shim homogeneity of 11Hz through the medial temporal lobes. A modified LASER sequence (TE/TR 72/2000) was used with 24x24 phase encoding, 10mm slice with nominal voxel size of 0.64cc. A semi-automated single voxel reconstruction was used to optimize consistency of voxel selection.

A total of 56 subjects were studied (19 controls, 23 MTLE, 13 neocortical patients). All patient volunteers had partial onset epilepsy, were recruited during the process of their surgical evaluation and studied pre-operatively. 12 loci were obtained per subject (6 each hemisphere): striatum, anterior and posterior thalamus, anterior and posterior hippocampus and insula. For patient volunteers the two hemispheres were separated by "ipsi" on the same side as seizure onset ("contra" is the opposite side to seizure onset). For control volunteers, "ipsi" was defined as Left. A common factor analysis with varimax rotation, which is commonly used to detect the structure within a dataset in terms of its linked variables, was used in each group. Two factors were evaluated in each group, since in each group, $p<0.005$ for a single factor model, thereby rejecting the null hypothesis (i.e., for each volunteer group, more than 1 factor was needed to explain the variance in the data).

Results Figures 1A and B show the 12 loci coefficients for the two factors. In the first factor, controls demonstrate extensive correlation between the thalamic loci and the R posterior hippocampus. The MTLE group demonstrates large correlations throughout the thalamus but also include moderate involvement of the hippocampi and striate. The NEO group appeared substantively different with the greatest correlation in the bilateral hippocampi and lesser involvement of the thalamic loci.

Fig. 1A: Factor 1
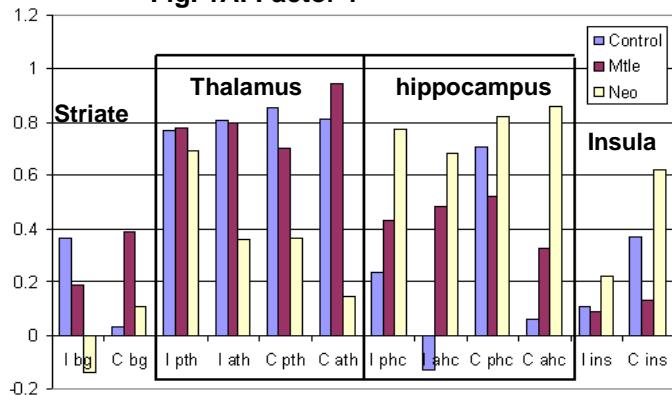
Fig. 1B: Factor 2
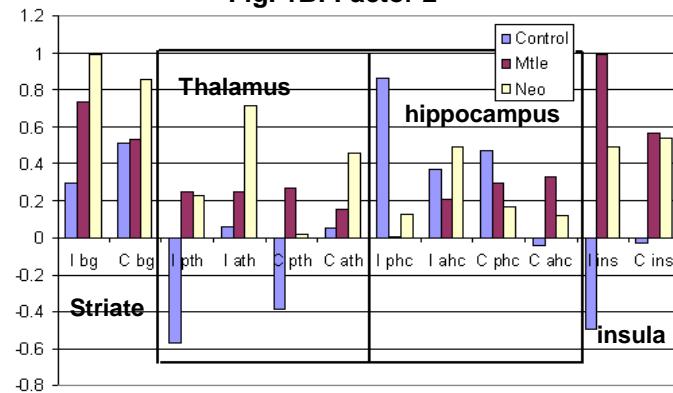
Conclusions   These data show that in healthy brain, common factor analysis demonstrates at least two significant factors linking the subcortical network. The first factor, "thalamic", shows considerable metabolic connectivity between the thalami and the right posterior hippocampus consistent with fMRI connectivity studies. The second factor, "memory (verbal)", shows connectivity between several left subcortical regions (left hippocampus, left insula, left thalamus) and also the striate, a region important for memory consolidation (2). In comparison to the controls, the MTLE group also shows limbic connectivity between the thalami but with greater involvement of the hippocampi. The NEO group is different, with less involvement of the thalami, and greater connectivity within the hippocampi. This suggests that the limbic network is a strong common factor for both control and MTLE subjects, and suggests that the network in MTLE is a distortion of existing networks. In comparison, the NEO group demonstrates strong connectivity within the hippocampi. These data show that MRSI data can be used to ascertain regional metabolic connectivity.
References: (1) Stein 2000; (2) Albouy 2008