Preliminary study on structural brain network topology in chronic knee OA pain

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Target audience: Clinical and preclinical Neuroscientists, Neuroradiologists

Purpose: Structural connectivity (SC) represented by the morphometric (e.g. cortical thickness) correlation among different brain regions is one of the most intriguing ways to study brain network function[1]. Graph theoretical analysis (GTA) reveals both local and global SC, which enables the understanding of the foundation for efficient information processing and complicated functional organization[2]. Recent studies using GTA have illustrated an alteration of SC related to normal aging, neuro-degenerative neuropsychiatric diseases[3] and other pain states[4]. However, we are unaware of any grey matter morphometric SC analyses in primary nociceptive disorders, including chronic pain (CP) due to osteoarthritis (OA), despite recent upsurge of interest in alterations of fibre tract[5] and functional architecture in various pain conditions[6]. The persistent and salient nature of the CP experience defined as 'pain on most days for most of the day' suggests a likely cumulative impact on the architecture of cortical networks linked to pain processing and bodily homeostasis. Therefore, we investigate whether structural network properties differ in OA-CP patients compared to healthy controls (HC).

Methods: Experiment: 31 patients (16 males; 64.2±8.3) with OA-induced CP (1-38y duration) and 21 HC (9 males; 60±7.5) with no other major medial co-morbidities were included. High-resolution 1mm-isotropic 3D T1 weighted images were performed at 3 Tesla MR scanner (GE Discovery 750) using a 32-channel head coil. 74 regions of cortical sulco-gyral structure on each hemisphere were identified according to an automatic parcellation scheme[7] and their mean cortical thicknesses (CTs) were measured using FreeSurfer software package Mac version 5.1 (www.surfer.nmr.mgh.harvard.edu) for each subject as previously presented[8]. GTA: Network analysis was performed using the GAT software package[9] (http://web.mit.edu/swg/software.htm).For each group, a 74 × 74 association matrix (AM) was generated by calculating the Pearson correlation coefficient between CTs across subjects. These data were corrected for between-group differences in age and sex. Small-world indices were obtained from the comparison of the real network with 1000 random network realizations containing the same numbers of node, edge, degree and degree-distribution. We also compared other global and local network measures, including clustering coefficient, characteristic path length, associativity, efficiency and modularity between OA and HC (two-tailed hypothesis testing, $p<0.05$). To further explore possible sex- and duration- specific reorganisations, similarity matrices based on Euclidean distance of AM were computed for male and female, short (16 subjects <8y) and long pain duration subgroups.

Results: The OA group regardless of sex and pain duration showed increased correlation strengths for many pairs of ROIs (Fig 1). Additionally, consistent with previous SC derived from CT measurements, both networks of HC and OA exhibited 'small-world' topology over a range of network densities. Although the OA group showed increased global network metrics, no significant difference was found between the two groups. However, local network measures illustrated increased connectivity in cingulate, precuneus regions and a decrease in postcentral cortex. For modularity measurement, more and different patterns of modules were identified in the OA group compared to the HC group (Fig2). Moreover, the result of the AM comparison showed large dissimilarities between subgroups for sex and PD.

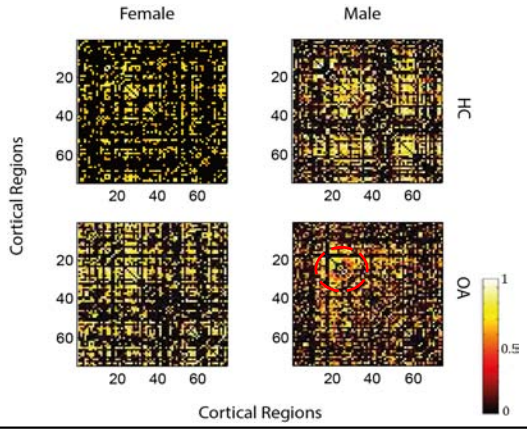
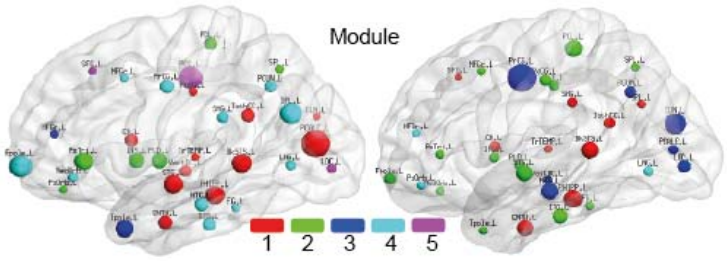


Fig 1: Thresholded CT AM of the left cortical 74-node network for female and male subjects in the HC (upper row) and OA groups (bottom row), representing the undirected weighted edges of the network. Red circle corresponds to the postcentral, precentral and precuneus cortex, which demonstrate enhanced correlations (negative and positive).

Fig 2: The modular architecture of the SC for the OA (left) group is different from modules illustrated in the HC group (right). Colours represent the number of modules. Sizes indicate the number of connections link to each node.



Discussion: To the best of our knowledge, the present study is the first investigation of large-scale SC for pain in OA using CTs. Instead of applying finer surface-based morphometry derived from region-wise CT, one previous study on OA-CP measured the gray matter density in approximated Brodmann areas. Using 'seed- based distance', they found strengthening of long distance correlations in contrast to HC[10]. However, their HC was not age- (15 years difference) and sex- matched. Importantly, the change of modularity in OA found in our study supports the hypothesis of reorganization of global SC. We found large apparent dissimilarities between different sexes and patients with short vs. long pain duration suggested possible specific reorganisations due to these factors. However, further exploration with a larger sample size is needed for a comprehensive and robust description of pain-specific characteristics of altered brain topology and their functional relevance.

Conclusion: The interregional correlation of CT and its derived network properties are a new promising approach to study cortical reorganization in CP, and we present a preliminary structural network signature of knee OA pain, a primarily nociceptive pain condition.

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