MICROSTRUCTURAL ABNORMALITIES RELATED TO THE CHRONIFICATION OF OSTEOARTHRITIC PAIN: A DTI STUDY
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Target Audience: Clinicians and scientists interested in translational neuroimaging or chronic pain.

Purpose: Diffusion tensor imaging (DTI) is an MR-based technique that has been extensively used in the study of white matter architecture of the healthy brain and applied to several neurobiological disorders such as stroke, multiple sclerosis and schizophrenia. Its application to chronic pain conditions, however, has only recently started. Emerging evidence in different chronic pain conditions suggests changes in both grey and white matter integrity within brain regions, mainly the ones involved in perception and behavioural response to pain such as the thalamus, insula and anterior cingulate cortex (ACC).

Based on these observations, we aim at identifying potential key microstructural white matter and thalamic disruptions, underlyng any adaptive or predisposing changes to the networks in the brain in response to chronic knee pain due to osteoarthritis (OA). We hypothesise that pain chronification induces microstructural abnormalities, and that these changes are related to pain duration and to development of neuropathic-like symptoms.

Methods: 23 patients with chronic knee pain due to OA (mean age±SD, 66.6±8.5 years) and 23 healthy volunteers (61.1±7.6 years) were included in the study. Diffusion-weighted images were acquired using spin-echo echo-planar imaging (EPI) along 30 evenly spaced and non-collinear directions, with b=1000 s/mm², one b=0, TR=5.6 s and TE=89.0 ms.

All image processing was completed using the diffusion tools within the FSL package. Tract-based spatial statistics (TBSS) and ROI-based analyses were used to test for both group differences and correlations of DTI measures with pain duration and painDETECT scores, the latter being a widely used questionnaire for determining the prevalence of neuropathic pain components. The significances of voxel-based correlation and differences were tested using a permutation-based inference tool for non-parametric statistical thresholding (randomise tool within FSL) and expressed at corrected p<0.05 being considered significant.

Results: TBSS Analysis of the whole brain white-matter tracts did not detect any significant abnormalities when contrasting patients to healthy volunteers. ROI analysis of the thalamus however detected significant positive correlation between MD values and pain duration on the OA group (p<0.05, TFCE, corrected for multiple comparisons), considering age and gender as covariates of no-interest. Segmenting the thalamus according to the divisions proposed in Behrens et al, this finding indicates an increase in MD with longer pain duration in thalamic regions associated with sensory, prefrontal, premotor and posterior parietal regions. TBSS analysis testing for correlations between painDETECT scores and MD values detected a tendency (p<0.07, TFCE, corrected for multiple comparisons) for negative correlation between MD and painDETECT scores in an area within the left hemisphere, marginally involving the ACC and the insula.

Fig.1: (A) Axial slice showing the region with positive correlation between MD and pain duration (bright green). (B) Axial slices through the thalamus, including the divisions described by Behrens et al and (C) the overlay (green) of the significant cluster.

Discussion: Higher mean diffusivity implies less structural density and therefore our findings suggest that as pain progresses there may be a reduction in projections and density of neural fibres in these thalamic regions. The observation that this was also found in thalamic divisions connected to posterior parietal regions is in accordance with cortical thinning findings within the precuneus and parietal regions on chronic OA pain and may be due to the chronic engagement of the pain processing networks. We could not replicate results from previous DTI studies reporting ultrastructural fibre abnormalities in pain patients compared to investigated neuropathic types of chronic pain. In fact, when exploring interrelations between MD and neuropathic-like symptoms as measured by painDETECT, we found a tendency for negative interrelation.

Conclusions: Taken together our findings suggest that microstructural abnormalities in OA pain, a primary nociceptive condition, are a feature of pain chronification. They seem to develop after several years of persistent pain probably preferentially in patients with more neuropathic-like symptoms.

References:
8. Altshuff et al. (2013). EFIC.