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Evaluating Genetic Analysis and Neuroimaging Tools in Pain Research

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Magnetic Resonance Imaging (MRI) and genomic technologies offer non-invasive means of investigating the mechanisms underlying pain and nociception. In search of such mechanisms, this thesis investigated the effects of third molar extraction surgery on blood perfusion in pain-related brain areas, as well as gene expression levels in peripheral whole blood. It also investigated the effect of a common genetic variation -SNP rs1799971- in mu-opioid receptor 1 (OPRM1) on brain grey matter density in patients suffering from unspecified low-back pain and fibromyalgia syndrome. A cohort of 20 patients underwent MRI arterial spin labeling scans before and after TME and also provided concurrent peripheral whole blood samples for investigation of changes in perfusion and gene expression between the pain-free and painful condition. Reliable changes in blood-perfusion emerged in pain-relevant brain regions, which corresponded to self-reported pain ratings of the patients indicating utility of arterial spin labeling as a viable biomarker of prolonged pain states with high sensitivity and specificity. Gene expression analysis revealed 837 probe sets with significant differential expression, out of which eight of the top 20 genes had explicit associations with various pain phenotypes. Gene Set Enrichment Analysis revealed significant enrichment of 280 pathways out of which pathways for osteoclast differentiation, MAP Kinase signalling and inflammatory mediators of TRP channels represented the most plausible pathways in the context of postsurgical pain. A voxel-based morphometry analysis of an additional cohort of 22 female patients with chronic musculoskeletal pain dependent upon OPRM1 genotype did not reveal any differences between the two different patient groups and AA- vs. AG-carriers with regard to pain intensity ratings. However, the data revealed significant grey matter density decreases in carriers of the G-allele in the right inferior frontal gyrus pars opercularis at the whole brain level uncorrected for age and duration of pain. When corrected for age and pain duration additional grey matter decreases emerged in G-allele carriers compared to A-allele carriers in bilateral posterior insula, left amygdala, posterior cingulate and parahippocampus. Correlations with selected pain-relevant regions of interest revealed negative correlations for AA-carriers between sensory and affective pain scores and GM density in two structures of the basal ganglia and posterior and paracingulate cortex. Negative correlations between grey matter density and sensory scores in the amygdala and affective scores in the left caudate were found in AG carriers. While grey matter decreases have strong associations with increased levels of reported pain, the absence of differences in pain ratings between genotypes, in spite of greater grey matter decreases in AG-carriers, suggested an inherent risk of relative hypertrophy, which might represent a compensatory response to genotype-specific impairment of endorphine-mediated analgesia. MRI and genomic technologies display great utility in exploring mechanisms of pain and nociception.