SYNOVIAL FLUID METABOLITE PROFILES DIFFER BETWEEN OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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Abstract:
Background: Non-inflammatory osteoarthritis (OA) and inflammatory rheumatoid arthritis (RA) lead to significant disability and reduction in quality of life. Despite both these chronic conditions being typically age-related with insidious onset, their underlying aetiologies are markedly different. Synovial fluid (SF) is located within the articular joint cavity, in close contact and near proximity to numerous tissues found to be primarily altered during OA and RA. Thus this bio-fluid holds huge potential in the early diagnosis of these conditions through the identification of metabolite markers. Previous analyses have been inhibited by the low volumes of SF aspirated from human joints. Nuclear magnetic resonance (NMR) allows analysis of small volumes of SF with minimal sample preparation using non-invasive and non-destructive methods.
Methods: Following ethical approval and consent, SF was aspirated from knee joints of 10 patients with OA (mean age 67.4Y) and 14 with RA (mean age 65.4Y). 100µl of each sample was analysed by ^{1}H NMR spectroscopy using a 700 MHz Avance IIIHD Bruker NMR spectrometer equipped with a TCI cryoprobe. Chenomx, Bruker TopSpin and AMIX software were used to identify metabolites and process spectra. Statistical analysis was carried out using R and Metaboanalyst.
Results: 51 metabolites were annotated in total, including amino acids, saccharides, nucleotides and soluble lipids. PCA analysis identified separation between non-inflammatory arthritis (OA) and inflammatory arthritis (RA) cohorts. 32 metabolites were significantly different between OA and RA SF, including citrate, creatinine, glucose, glutamine, glycerol, pyruvate and taurine which were higher in OA . 3-hydroxybutyrate, acetate, isoleucine, leucine, sarcosine and threonine were higher in RA. Pathway analysis revealed that the metabolic pathways most impacted were aminoacyl-tRNA biosynthesis, nitrogen metabolism, valine, leucine and isoleucine biosynthesis, glycine, serine and threonine metabolism and taurine and hypotaurine metabolism (FDR<0.05).
Conclusion: Relatively low volumes of SF aspirated from human joints have previously been prohibitive to metabolomic analysis. We have demonstrated NMR spectroscopy can be utilized to produce analysable spectra from a low volume of SF taken in a clinical environment, which may prove beneficial in aiding clinical diagnosis. We have identified quantifiable differences in metabolite abundances between non-inflammatory arthritis (OA) and inflammatory arthritis (RA), which may prove valuable as a diagnostic aid as well as improving our understanding of the pathogenesis of these conditions.
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