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PROINFLAMMATORY ENVIRONMENT IN RA AND OA STRONGLY INFLUENCES ADIPOSE TISSUE ACTIVITY

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Introduction Rheumatoid arthritis (RA) and osteoarthritis (OA) are inflammatory diseases leading to joint destruction and disability. Apart from joint inflammation they are characterised by high-grade (RA) or low-grade (OA) systemic inflammation. Thus, it is possible that proinflammatory environment affect not only articular (AAT), but also subcutaneous adipose tissue (ScAT) activity.

Objectives The aim of present work was to compare reactivity of AAT and ScAT from RA and OA patients to proinflammatory stimulus.

Methods AAT and ScAT explants, obtained from OA (n=44) and RA (n=43) patients during knee joint replacement surgery, were cultured (100 mg/ml) for 24 hours in medium (DMEM) alone or in the presence of proinflammatory IL-1 β (1 ng/ml), known to be overproduced in inflamed joint. Concentrations of cytokines (proinflammatory IL-6 and TNF, anti-inflammatory IL-1Ra, IL-10, TGF β), chemokines (CCL2, CCL5) and metalloproteinase MMP-3 were measured in culture supernatants by ELISA. OA patients were treated with non-steroidal anti-inflammatory drugs while RA patients were given disease modifying drugs and/or glucocorticosteroids. Data were analysed as stimulation to control ratio (IS, index of stimulation) using Mann-Whitney U test and are expressed as median.

Results In OA the levels of secreted factors were usually significantly higher in AAT, but ScAT was characterised by significantly higher increase of IL-6 (IS=16.4), TGF β (IS=2.0), CCL2 (IS=1.8), and MMP-3 (IS=9.9) production than AAT (IS=70.3; 1.3; 1.3; 2.4 respectively). The up-regulation of other cytokines was similar in both tissues. By contrast, in AAT and ScAT from RA patients IL-1b-triggered increase of all tested factors secretion was similar. Moreover, upon IL-1b treatment the up-regulation of IL-6 (IS=13188) and MMP-3 (IS=9,1) in AAT of RA patients as well as of CCL2 from rheumatoid AAT (IS=3.2) and ScAT (IS=3.7) was significantly higher than in OA tissues (IS=70.3; 2.4; 1.3; 1.8 respectively).

References We report that in OA ScAT, exposed *in vivo* to low-grade inflammation, retains higher reactivity to proinflammatory stimulus than AAT located in chronic high-grade inflammation. In RA, however, reactivity of both adipose tissue is rather similar but in the case of secretion of some factors (CCL2 and/or IL-6, MMP-3) higher than in OA, reflecting more destructive character of this disease.

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Disclosure of interest None declared

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ABSTRACT WITHDRAWN

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ADIPOCYTOKINES LINKING OBESITY AND OSTEOARTHRITIS

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Introduction In the Western society, obesity and the resulting metabolic changes are an increasing field of medical research. Both conditions alter the expression of adipokines such as adiponectin, visfatin or leptin, which can modulate key pathways of the immune system or the progress of osteoarthritis (OA).

Objectives To evaluate cross-linking influences of the above-mentioned comorbidities, we combined a high-fat diet (HFD) with the DMM osteoarthritis mouse model (Destabilisation of the Medial Meniscus). The serologic as well as local tissue effects of HFD at different stages of OA development were correlated to the local and systemic adipokine expression.

Methods ND (normal diet) and HFD were fed to C57Bl/6 mice over a period of 3 months followed by surgical OA induction (time point 0). Tissues and sera were collected 4, 6, and 8 weeks after surgery. Serum levels of adipokines were measured by ELISA. Liver fat was scored to evaluate metabolic changes. Arthritis progression was scored and quantified based on histologic stainings of the joints (H/E, safranin O, Pappenheim and Masson-Goldner's trichrome). Immunohistochemical stainings of the joints were performed to evaluate local distribution of adipokine positive cells. Metabolic parameters were correlated to the progression of OA.

Results At all time points, OA could be induced in all settings, especially when combined with HFD (e.g.: OA score at 6 weeks HFD 3.7 vs. ND 1.4). Systemically, leptin levels were significantly higher in HFD compared to ND, suggesting a leptin and established insulin resistance. However, DMM led to decreased leptin levels at all time points, independent from diet (e.g. 4 weeks: HFD healthy 18.4 ng/ml vs. HFD DMM 3.7 ng/ml). Systemic leptin levels and fatty-liver score were positively correlated. Interestingly, the systemic increase of adiponectin mediated by DMM was only visible at week 8 (HFD healthy 5176 ng/ml vs. HFD DMM 6149 ng/ml). HFD, DMM or the combination of both did not show significant effects on serum levels of adiponectin, visfatin or IL-6. The local adipokine distribution in the joints was independent from systemic parameters.

Conclusions Our data show that similar to observations in humans, OA is deteriorated by HFD. This is reflected by increased numbers of adipokine positive cells in areas of destruction. This phenomenon appears to be based on local