DO HUMAN JOINTS ADAPT TO MECHANICAL STIMULATION? PHYSICALLY ACTIVE INDIVIDUALS DISPLAY LARGER JOINT SURFACES, BUT NO ALTERATIONS IN CARTILAGE THICKNESS.

Introduction: A fundamental question in musculoskeletal research is to what extent the morphology and quality of the connective tissues are determined by a fixed genetic program, and to what extent they can be modulated by postnatal mechanical stimulation. Functional adaptation has been observed in muscle and bone tissue, immobilization or space flight leading to an immediate atrophy of the tissue, and intense physical training causing substantial increases in muscle cross sectional area and bone mineral density. However, it is currently unknown whether human joints - and specifically articular cartilage – functionally adapt to mechanical stimulation, and whether the large phenotypic variation seen in human cartilage morphology [1] can be explained based on varying levels in physical activity. Determining the physiological window within which tissue adapts to mechanical loading should permit to determine the threshold at which normal tissue adaptation is exceeded and irreversible cartilage damage occurs due to mechanical overloading, to avoid cartilage atrophy and promote tissue healing after joint injury and trauma, and to develop evidence-based concepts of preventing degenerative joint disease.

The current study was designed to test the hypothesis that the phenotypic variability of human cartilage morphology (differences in cartilage volume, thickness, and surface areas) result from differences in physical activity between individuals, and from functional adaptation of the cartilage to these mechanical stimuli.

Material and methods: We examined 36 healthy individuals (18 women and 18 men, aged 19 to 32 yrs.) without symptoms or signs of musculoskeletal disease, no history of pain, trauma, or operations of the knee, and no history of fracture or immobilization. The individuals were selected in a way, to obtain groups with maximal differences in the loading history of the knee joint (36 individuals: 18 TRI, 18 Physically inactive volunteers), and to include both men and women. The physically inactive volunteers, and the study protocol was ratified by the local ethics committee.

Sagittal magnetic resonance imaging (MRI) was performed on the right knee joint using a previously validated [2] fat-suppressed, three-dimensional gradient echo sequence (FLASH-3D: TR = 45 ms, TE = 11 ms, FA = 30°; spatial resolution 2 x 0.31 x 0.31 mm³). Written consent was obtained from all volunteers, and the study protocol was ratified by the local ethics committee. The data were transferred digitally to a workstation (Octane Duo, Silicon Graphics, Mountain View, CA) and the segmentation of the cartilage plates performed interactively [3]. Using validated in-house software [4] we determined the cartilage volume, cartilage thickness, and size of the joint surface areas after 3D reconstruction throughout all knee joint cartilage plates. Differences between groups were evaluated for statistical significance using a non-parametric test (Mann Whitney U).

Results: The total knee joint cartilage volume was 17.9 ± 2.2 ml in physically inactive women, and 23.0 ± 2.7 ml in men. The volume was not significantly higher in triathletes, with 18.9 ± 2.4 ml in women, and 25.3 ± 3.1 ml in men. Differences between groups are shown in Table I. The mean knee joint cartilage thickness in the physically inactive volunteers was 1.86 ± 0.24 mm in women, and to 2.01 ± 0.31 mm in the men, and it was not significantly different in the triathletes (1.93 ± 0.23 mm in women, and 1.99 ± 0.27 mm in men). The size of the joint surface areas of the knee joint was 88.9 ± 8.2 cm² in the physically inactive women, and 110.0 ± 5.6 cm² in the men. The values in the triathletes were significantly higher in males (120.0 ± 5.3 cm²) and were also higher in females (95.2 ± 7.3 cm²), but did only attain borderline significance (p = 0.08) (Tab. 1).

Analyzing the single surfaces, the patellar cartilage volume and joint surface areas were significantly bigger in the male triathletes (compared with the inactive volunteers (+15%; p< 0.05, and +12%; p< 0.05, respectively). The joint surface areas were significantly bigger in the lateral tibia of the male triathletes (+16%, p< 0.05), and in the medial tibia of the female triathletes (+19%; p< 0.05).

Table I: Gender differences in physically inactive volunteers (PIV), and differences of triathletes (TRI) vs. Physically inactive individuals

<table>
<thead>
<tr>
<th></th>
<th>PIV</th>
<th>Men TRI vs. PIV</th>
<th>Women TRI vs. PIV</th>
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</thead>
<tbody>
<tr>
<td>Cartilage Volume</td>
<td>+29% *</td>
<td>+6% N.S.</td>
<td>+10% N.S.</td>
</tr>
<tr>
<td>Thickness</td>
<td>+8% N.S.</td>
<td>+4% N.S.</td>
<td>-1% N.S.</td>
</tr>
<tr>
<td>Joint surface</td>
<td>+24% ***</td>
<td>+7% N.S.</td>
<td>+9% **</td>
</tr>
</tbody>
</table>

N.S. = difference not significant; *p< 0.05; **p< 0.01; ***p< 0.001

Discussion: Unexpectedly, we find no increase in cartilage thickness in healthy triathletes, but significantly larger joint surface areas. Comparing both genders, men display substantially larger surface areas than women, but not significantly thicker cartilage. Our findings do not, however, exclude the possibility that cartilage can undergo atrophic changes (thinning) when there is a lack of mechanical stimulation, and that there may be an adaptation of its biochemical composition to decreased or increased mechanical loading.

Our results suggest that adaptation of joint (cartilage) morphology may occur during growth, and that external mechanical stimuli guide the enchondral ossification process to form larger epi- and metaphyses. However, mechanical loading does not appear to be the mechanism by which enchondral ossification is stopped from reaching the articular surface and does not appear to determine cartilage thickness. These findings also refute the hypothesis that the morphology of mature cartilage can be modulated postnataley by an increase in mechanical stimulation, and they suggest that the thickness variation observed between individuals must have other sources than differences in the intensity of physical exercise. These findings may thus reveal a general principle of joint development and anatomy, species with much larger body weights also not displaying thicker knee joint cartilage than humans [5], but larger joint surface areas. The reason may be that beyond a certain thickness the nutritive situation of the cartilage (which is based on diffusion) becomes problematic, or that the tissue will be mechanically inferior when exceeding a certain thickness. This adaptive process might be recapitulated in osteoarthritis (although not functionally relevant), in which osteophytes form to increase the joint surface.

In conclusion, our findings suggest that joint size can be modulated during growth, but that (opposite to muscle and bone) mature cartilage thickness does not adapt to mechanical stimulation. This finding may reveal a general, fundamental principle in the development and functional adaptation of diarthrodial joints.

References:

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