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Acute changes in knee cartilage transverse relaxation time after running and bicycling

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ABSTRACT

Purpose: To compare the acute effect of running and bicycling of an equivalent cumulative load on knee cartilage composition and morphometry in healthy young men. A secondary analysis investigated the relationship between activity history and the change in cartilage composition after activity.
Methods: In fifteen men (25.8 ± 4.2 years), the vertical ground reaction force was measured to determine the cumulative load exposure of a 15-min run. The vertical pedal reaction force was recorded during bicycling to define the bicycling duration of an equivalent cumulative load. On separate visits that were spaced on average 17 days apart, participants completed these running and bicycling bouts. Mean cartilage transverse relaxation times (T_2) were determined for cartilage on the tibia and weight-bearing femur before and after each exercise. T_2 was measured using a multi-echo spin-echo sequence and 3T MRI. Cartilage of the weight bearing femur and tibia was segmented using a highly-automated segmentation algorithm. Activity history was captured using the International Physical Activity Questionnaire.
Results: The response of T_2 to bicycling and running was different ($p=0.019$; mean T_2: pre-running=34.27 ms, pre-bicycling=32.93 ms, post-running=31.82 ms, post-bicycling=32.36 ms). While bicycling produced no change (-1.7%, $p=0.300$), running shortened T_2 (-7.1%, $p<0.001$). Greater activity history predicted smaller changes in tibial, but not femoral, T_2.
Conclusions: Changes in knee cartilage vary based on activity type, independent of total load exposure, in healthy young men. Smaller changes in T_2 were observed after bicycling relative to running. Activity history was inversely related to tibial T_2, suggesting cartilage conditioning.

1. Introduction

Understanding the acute changes of cartilage in response to different mechanical loads is fundamental in identifying the optimal amount and type of loading that promotes cartilage health (Bennell et al., 2011; Hinterwimmer et al., 2004; Van Ginckel et al., 2010). Magnetic resonance imaging (MRI) studies have compared the morphometric changes to cartilage in response to different types of activity (Eckstein et al., 1999, 2000; Eckstein, 2005; Kessler, 2005). In all morphometric MRI investigations comparing different types of loading, the amount of loading exposure was not standardized between activities.

Morphometric studies do not provide insight into the mechanisms underlying the acute response of cartilage to different loads. Mechanical testing and modelling indicates that the viscoelastic responses of articular cartilage to loading is caused by fluid flow (Lu and Mow, 2008; Nordin and Frankel, 2012). Spin-spin relaxation time (T_2) as well as spin-lattice relaxation time in the spinning reference frame ($T1\rho$) provide insight into these mechanisms (Choi and Gold, 2011). T_2 is positively correlated with free water, and is sensitive to collagen fiber organization and alignment, and potentially collagen abundance (Choi and Gold, 2011; Palmer et al., 2013). $T1\rho$ is inversely related to proteoglycan abundance within cartilage (Choi and Gold, 2011; Palmer et al., 2013). T_2 and $T1\rho$ have been used in *ex vivo* investigations, where,

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T_2 alone was related to histological degradation of cartilage (Nebelung et al., 2016a) and $T1\rho$ showed greater response to uniaxial loading (Nebelung et al., 2016b).

In vivo investigations have also explored the acute response of cartilage composition to physical activity. Loading shortens T_2 and $T1\rho$ (Choi and Gold, 2011), indicating a decrease in free water content and increased collagen anisotropy (T_2), and an increase in proteoglycan concentration ($T1\rho$). Running causes the greatest reduction in superficial cartilage T_2 compared to other sub-layers (Cha et al., 2012; Mosher et al., 2010). No data compare compositional changes in knee cartilage after different activities. In such a comparison, cumulative exposure to mechanical load must be equivalent between activities to conclude that differences are the result of activity type.

The purpose of this study was to investigate, in healthy men, (i) whether running and bicycling change knee cartilage T_2; (ii) whether there are differences in T_2 change between running and bicycling of equal cumulative load; and (iii) the relationship between activity history and T_2 change. Secondary analyses explored sub-regional changes in cartilage T_2 and morphometry. It was hypothesized that (i) running and bicycling would shorten T_2; (ii) sustained loads during bicycling would cause greater cartilage deformation and shortening of T_2 than high impact loads during running, and (iii) there would be an inverse relationship between activity history and T_2 change.

2. Methods

2.1. Protocol

Participants attended one visit to McMaster University (Hamilton, Ontario, Canada) for biomechanical analyses and two visits to St. Joseph's Healthcare Imaging Research Center (Hamilton, Ontario, Canada) to obtain MRI scans preceding and following running and bicycling protocols. Data collection took place between February and July of 2015. Mean time between MRI visits was 17 days (range 1–79 days). One long delay (79 days) occurred because of re-scheduling for MRI maintenance. This participant reported no injuries, adverse events, or changes in physical activity over this 79-day period. For MRI visits, activity order was arbitrarily assigned based on scheduling feasibility (5/15 participants performed running first). Before study initiation, approval was obtained from the Hamilton Integrated Research Ethics Board. All participants provided written informed consent.

2.2. Participants

Healthy men (18–35 years) were recruited from the McMaster and Hamilton communities using laboratory and McMaster social media and postering. All data reflect the right knee. Exclusion criteria were self-reports of leg injury within the past 3-months; history of orthopedic surgery to the limb of interest; symptomatic knee OA according to the American College of Rheumatology Clinical Criteria (Altman et al., 1986); Lower Extremity Functional Scale (LEFS) score <74 (Wang et al., 2009); answering "Yes" to a question on the Physical Activity Readiness Questionnaire (Canadian Society for Exercise Physiology, 2004); or body mass >200 lbs (to accommodate the imaging coil). Participants were screened for contraindications to MRI, including vascular stents, aneurysm clip(s), or cochlear implants. Participant demographics are presented in Table 1. All participants met the inclusion and exclusion criteria.

Table 1
Participant Demographics. Mean, standard deviation (SD), minimum, and maximum values of demographics of 15 participants.

	Mean	SD	Minimum	Maximum
Age (y)	25.8	4.2	20	33
Height (m)	1.79	0.06	1.70	1.89
Body Mass (kg)	75.8	9.7	59.5	93.5
Body Mass Index (kg/m^2)	23.71	2.62	18.53	27.16
Activity History (Metabolic min/week)	6570.6	4158.7	924	17287.5
Lower Extremity Functional Scale (/80)	79.8	0.6	78	80

2.3. Biomechanics

2.3.1. Running

Force measurements were collected to calculate the vertical ground reaction force (vGRF) impulse of one running stride. Participants completed a 5-min run on a commercial treadmill (5.1AT, Advanced Fitness Group, USA) to determine their self-selected moderate running speed and mean step-count per minute using an accelerometer placed at the centre of mass on the shank (GTX3, Actigraph, FL, USA) (Gatti et al., 2015). Then, participants performed five practice trials of over-ground running along a laboratory runway (11.9 m). The runway was equipped with three floor-embedded force platforms (OR6-7, AMTI, MA, USA) sampling at 1000 Hz. Biomechanics were collected over-ground while running at the MRI was performed on a treadmill. While the anterior–posterior and medial-lateral ground reaction forces are different between running over-ground versus running on a treadmill, the vGRF is not different between these conditions (Riley et al., 2008). After practice, participants completed at least five successful trials (right foot planted on one force platform for the entire stance phase at a running speed within $\pm 5\%$ of self-selected moderate).

The vGRF signals from successful trials were filtered using a dual-pass, second-order, low-pass Butterworth filter at 20 Hz. This cut-off was determined using residual analysis (Winter, 2005) (Matlab Version 2014a, Mathworks, Natick MA). Impulse was calculated using the trapezoidal method (Maly et al., 2013). The mean impulse of five trials was calculated.

2.3.2. Bicycling

Force measurements were collected to calculate the vertical pedal reaction force (vPRF) impulse of a bicycle pedal revolution. Participants were fitted to a cycle-ergometer (Excalibur, Lode, NL) using anthropometric-based road bicycle fitting guidelines (Bowen, 2011). Pedal reaction forces were collected using a pedal fitted with a bi-axial load-measuring device (Novatech, UK). Vertical and anterior/posterior forces were sampled at 1000 Hz and an electromagnetic switch identified pedaling frequency. Participants first bicycled for 5-min to determine self-selected moderate power output when pedaling at 80 revolutions per minute (RPM). Participants then completed a 5-min trial, at 80 RPM and their self-selected power, during which data were collected.

The vPRF data was filtered the same as for running, but with a cutoff of 10 Hz. The bicycling vPRF data were divided into individual revolutions using the electromagnetic switch. Data during acceleration (first 25 revolutions) were removed and the vPRF impulses of the remaining revolutions were calculated. The mean of the vPRF impulses was calculated.

2.4. Equivalent cumulative loads

Force and repetition data from the running and bicycling bouts were used to normalize cumulative loads to a 15-min run using Eq. (1);

$$C_L = R \cdot I \cdot t \tag{1}$$

where C_L is cumulative load, R is repetitions (steps/pedal revolutions) per minute, I is impulse per repetition and t is time (in minutes). The C_L determined the duration that participants would bicycle based on Eq. (2);

$$D_t = \frac{C_L}{R \cdot I} \tag{2}$$

where the duration of cycling (D_t) is determined by C_L (from running), R and I. Data were also collected at the MRI visits to refine the activity duration performed at the second MRI visit. For running, repetitions were recorded using an accelerometer. For bicycling, vPRF and repetitions were recorded using the same load measuring pedal and electromagnetic switch.

2.5. Magnetic resonance imaging data acquisition

MR images were acquired using a 3-Tesla GE Discovery MR750 (GE Healthcare, Milwaukee WI), with a dedicated transmit and 8-channel receive knee coil array (Invivo Corp). To ensure participants had healthy knees, three clinical scans [sagittal proton density (PD) weighted, coronal PD and axial T2-weighted/fat saturated (FS)] were reviewed by a radiologist (ST) with >25 years of clinical experience. No abnormalities were noted. Imaging parameters are detailed in Table 2. The clinical scans were acquired pre-activity on one visit.

All imaging was performed in the morning (Mosher et al., 2010) and each participant lay supine for 30-min before the protocol (Subburaj et al., 2012). After, participants were transported to the MRI via a wheelchair. The knee was marked with a permanent marker whilst within the knee coil to standardize positioning. After activity, participants immediately walked into the MRI room (<3 m) and lay on the MRI for repositioning and collection; post-activity scanning commenced within $\sim$3-min of activity cessation. Two sequences were used (Table 2). Sagittal multi-echo spin echo (MESE) images were acquired with the CartiGram T_2-mapping sequence (GE Healthcare, Milwaukee WI) (Bining et al., 2009; Dautry et al., 2014; Kai et al., 2011; Kijowski et al., 2013), that was designed for the calculation of

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