AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY 116:266–277 (2001)

Articular Area Responses to Mechanical Loading: Effects of Exercise, Age, and Skeletal Location

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KEY WORDS epiphyses; articular surface area; mechanical loading; exercise; sheep; body mass

ABSTRACT How reliable are reconstructions of body mass and joint function based on articular surface areas? While the dynamic relationship between mechanical loading and cross-sectional geometry in long bones is well-established, the effect of loading on the subchondral articular surface area of epiphyses (hereafter, articular surface area, or ASA) has not been experimentally tested. The degree to which ASA can change in size and shape is important, because articular dimensions are frequently used to estimate body mass and positional behavior in fossil species. This study tests the hypothesis that mechanical loading influences ASA by comparing epiphyses of exercised and sedentary sheep from three age categories: juvenile, subadult, and adult (n = 44). ASA was measured on latex molds of subchondral articular surfaces of 10 epiphyses from each sheep. Areas were standardized by body mass, and compared to diaphyseal cross-sectional geometrical data. Nonparametric statistical comparisons of exercised and control individuals found no increases in ASA in response to mechanical loading in any age group. In contrast, significant differences in diaphyseal cross-sectional geometry were detected between exercised and control groups, but mostly in juveniles. The conservatism of ASA supports the hypothesis that ASA is ontogenetically constrained, and related to locomotor behavior at the species level and to body mass at the individual level, while variations in diaphyseal cross-sectional geometry are more appropriate proxies for individual variations in activity level. Am J Phys Anthropol 116:266–277, 2001.

Wolff's law, that bone macrostructure and microstructure adapt to their mechanical environments, is a long-held yet sometimes controversial principle of bone biology (reviews in Currey, 1984; Lanyon and Rubin, 1985; Martin and Burr, 1989; Bertram and Swartz, 1991; Lieberman and Crompton, 1998; Martin et al., 1998). Osteogenic responses to mechanical loading have mostly been documented in compact bone in diaphyseal cross sections and in trabecular bone in epiphyses (e.g., Pauwels, 1976; Radin et al., 1982; Currey, 1984; Lanyon and Rubin, 1985; Martin and Burr, 1989; Hou et al., 1990; Gross et al. 1997; Lieberman and Crompton, 1998; Martin et al., 1998). Little is known, however, about the degree of phenotypic plasticity that characterizes the subchondral articular surface area of epiphyses (hereafter referred to as articular surface area, or ASA) during ontogeny in response to mechanical stimuli (Ruff, 1988).

We examine here subchondral ASA responses to loading, which we compare to data on midshaft diaphyseal responses to loading. While ASA plasticity in response to loading must be mediated in part through changes in chondral growth (reviews in Frost, 1979; Carter and Wong, 1988; Herring, 1993; Martin et al., 1998), we examine ASA rather than chondral responses to loading for several reasons. First, most of the primate skeletal biology and paleontology literature on epiphyses in relation to body mass and loading focuses on ASA, and not on chondral surfaces, largely because cartilage does not fossilize or preserve. Changes in ASA in response to exercise are therefore of interest, regardless of how imposed loads affect the cartilagenous growth that influences the size of the subchondral bone in the joints. Second, ASA plasticity in response to loading is biomechanically important because it is well-established that joints undergo considerable loading, which can result in osteoarthritis and other forms of deterioration, not only in the chondral surface of the joint (Mankin et al., 1986; Jurmain, 1999), but also in the subchondral bone of the epiphysis (Bridges, 1991; Spector et al., 1996; Jurmain, 1999).

Despite the importance of mechanical loading in joints, most researchers assume that ASA and subchondral surface morphologies are fairly conservative, either because they are highly genetically canalized, and/or because they are functionally constrained by the need to fit precisely with one

Grant sponsor: National Science Foundation; Grant number: IBN 96-03833; Grant sponsor: American Federation of Aging Research.

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Received 21 June 2000; accepted 2 August 2001.

another (Pauwels, 1976; Ruff and Runestad, 1992; Ruff et al., 1993). Support for the hypothesis that articular surfaces are not phenotypically plastic in response to loading comes from several studies, most of which examine correlations between femoral head size and body mass (Jungers, 1988; Ruff, 1988, 1990; Godfrey et al., 1991). In a study of age-related changes in ASA and diaphyseal cross sections in humans from Pecos Pueblo, Ruff (1988) found that while the cross-sectional area of the femoral midshaft increased significantly over time, the size of the femoral head did not. Ruff et al. (1991) also demonstrated that femoral head size in adult Americans (mean age, 52) correlates most strongly with body mass at age 18 (the approximate age of skeletal maturity), while femoral shaft cross-sectional areas correlate best with body mass at the time of the study. Ruff et al. (1991), however, had no data to correct for the potential effects of different activity levels, and used uniplanar (radiographic) measurements of femoral head and shaft size.

Despite these indications of phenotypic stability, there is reason to ask if ASA evinces some degree of phenotypic plasticity in response to mechanical loading, especially to stresses applied during ontogeny, before epiphyses have reached their final adult size. Articular stress is primarily a function of the force applied to a joint relative to its surface area. One would therefore predict a close relationship between loading and joint size in order to avoid the generation of high stress concentrations, which can damage not only articular cartilage but also osseous components of the epiphysis, diminish function through loss of congruence, and lead to various types of joint disease (Radin et al., 1982; Currey, 1984; Jungers, 1988; Kamibayashi et al., 1995). Alexander (1980) reasoned that maximum joint stresses should be constant regardless of body mass, suggesting that articular surface areas should scale with geometric similarity to body mass (to the 0.67 power). Comparative analyses have largely supported this prediction (e.g., Godfrey et al., 1995), but with some interesting exceptions. Although interspecific studies among primates have shown that joint surface area tends to scale isometrically with body mass (Ruff, 1988), the pattern of variation is complex. Godfrey et al. (1991) showed that joint surface dimensions in primates scale for the most part with geometric similarity in hindlimbs and with positive allometry in forelimbs. In addition, joint surfaces of mammals who leap habitually tend to have high positive residuals with respect to the general scaling relationship among mammals against body mass (Godfrey et al., 1995; Runestad, 1997; Runestad Connour et al., 2000), and this scaling relationship is positively allometric in bipedal hominids whose hindlimb joint dimensions are significantly larger than those predicted by interspecific primate allometries (Jungers, 1988, 1991; Ruff, 1988, 1990; Ruff and Runestad, 1992). From an interspecific perspective, the mechanical effect of loading on any given joint is likely to be complex and influenced by variations in the shape of the joint and the range of excursion through which the joint is loaded (Ruff and Runestad, 1992; Rafferty and Ruff, 1994; Runestad, 1997). However, a likely explanation for these observations is that larger joint surface areas are an adaptation for resisting larger loads, so it follows that, within a single species, such adaptations may occur in vivo to some extent.

Phenotypic plasticity in ASA has been suggested by a number of researchers, but has proven difficult to study. One reason for hypothesizing ASA lability is that cartilage, which covers much of the overlying chondral portions of joints, has been shown to be highly responsive to compressive loading (Meikle, 1975; Hall, 1978; Amprino, 1985; Frost, 1986; Herring, 1993). The mandibular condyle, for example, which is loaded under compression in mammals (Hylander, 1979, 1985; Demes, 1985; Thomason et al., 1990; Liu and Herring, 2000), has been shown to grow significantly wider and longer ($P < 0.01$) in growing rats fed hard diets compared to controls fed on soft foods (Bouvier and Zimny, 1987). With respect to ASA, Ruff et al. (1994), in a reanalysis of data from Jones et al. (1977), showed that bilateral asymmetry in radial head breadth (a good linear approximation of the size of the articular surface) in professional tennis players averaged 5.6% ($P < 0.001$). Measurements of distal humeral articular breadth in Neanderthals reveal a similar degree (less than 5%) of bilateral asymmetry (Trinkaus et al., 1994), substantially less than the high degree of asymmetry measured in the humeral diaphysis of these groups. In addition, clinical studies have shown that other aspects of subchondral epiphysis morphology, including subchondral bone thickness, Haversian remodeling, trabecular connectivity, trabecular thickness, and trabecular orientation, are responsive to exercise (Radin et al., 1982; Parfitt et al., 1983; Hou et al., 1990; Teng et al., 1997).

The degree to which ASAs are phenotypically plastic adaptations to their mechanical environment merits further testing for both clinical and biological reasons. Because bone presumably grows and changes in response to the loading it experiences, changes in ASA during growth may be important for assessing the effects of behavioral variations on load-induced degeneration of the joints (Bridges, 1991; Spector et al., 1996; Kerrigan et al., 1998). From a paleontological perspective, articular surface area and size, and typically femoral head size, are frequently used to estimate body mass in fossils (e.g., Jungers, 1988; McHenry, 1991, 1992; Grine et al., 1995; Ruff et al., 1997). Therefore, if ASA is phenotypically plastic in response to mechanical loading, differences in loading unrelated to body mass, such as variation in activity levels, have the potential to bias body-mass estimates based on articular and/or epiphyseal dimensions (Jungers, 1988; Ruff, 1990; McHenry, 1991, 1992). Interspecific differences in ASA relative to body size have been used to make contrasting inferences about locomotor behavior in hominids, especially australo-

TABLE 1. Experiments reported

Experiment	Age (days)	N (control/treatment)	Duration	Treatment[1]
Juvenile	40	11 (5/6)	89 days	$\hat{u}$ = 0.5, 60 min/day
Subadult	270	10 (4/6)	90 days	$\hat{u}$ = 0.5, 60 min/day
Adult	400–430	16 (8/8)	90 days	$\hat{u}$ = 0.5, 60 min/day

[1] $\hat{u}$ = Froude speed, $v \cdot g^{0.5} \cdot h$, where v = speed (m/s), g = acceleration constant, and h = hindlimb length (cm) (Alexander, 1977).

pithecines (e.g., Jungers, 1988; Ruff, 1988), and in other primates (Godfrey et al. 1995). Finally, if ASA is highly conservative and genetically canalized, then variations in ASA and possibly articular surface shape have the potential to be useful morphological characters for phylogenetic analysis (Lieberman, 1997).

HYPOTHESES TO BE TESTED

This paper uses an explicitly experimental approach to test several hypotheses about ASA changes in response to mechanical loading. As noted above, we focus solely on subchondral ASA, and not on chondral or articular surface shape responses to loading. The general hypothesis is that animals which experience higher levels of load-bearing activity are predicted to have larger ASAs relative to body mass, tested against the null hypothesis that ASAs are conservative and do not exhibit any substantial degree of phenotypic plasticity. This general hypothesis, however, is broken down into two more specific hypotheses that examine potential additional sources of variation due to intraskeletal location and ontogenetic variation. First, within a skeleton, one might expect a higher degree of phenotypic plasticity in response to mechanical loads in certain epiphyses. In static loading (without acceleration), muscles crossing a joint contribute to a large proportion of compressive forces in the joint, leading one to predict that higher forces act on more muscled joints (Pauwels, 1980). However, during dynamic loading, accelerations of body mass generate very high compressive forces in a joint (proportional to the product of body mass times acceleration) that can act on large moment arms, and which have to be countered by muscles and other connective tissues (review in LeVeau, 1992). Since joint surface areas tend to be smaller in distal elements in most mammals, it is reasonable to hypothesize that articular surfaces of distal elements must counteract more compressive stress (force per unit area) than those of more proximal elements. In sheep, for example, the surface area of the proximal femur is 19% larger than that of the proximal tibia, which is 63% larger than that of the proximal metatarsal (see below). Consequently, smaller ASAs relative to body mass might be expected to be more phenotypically plastic than larger ASAs in response to dynamic mechanical loads. In a similar fashion, stresses are expected to be higher on the smaller of two paired joints (e.g., the glenoid fossa compared to the proximal humerus).

A second source of variation examined here is ontogenetic. Osteogenic responses to loading (mostly measured in vivo as bone mineral density) are known to be much greater in juveniles than in adults (Kannus et al., 1995; Haapasalo et al., 1996, 1998; Vuori, 1996), in large part because osteoprogenitor cells senesce dramatically after adolescence (Nishida et al., 1999). In addition, ASA is likely to be related to osteogenic activity in secondary growth centers, which fuse during adolescence. Although cartilage above the subchondral bone surface can grow interstitially and apositionally throughout life (Williams et al., 1985), one might expect mechanical loading to exert a greater effect on ASA relative to body mass in juveniles than in skeletally mature adults.

This paper investigates these issues by examining measurements of joint surface areas. It is also possible that joints may respond to loading by growth and remodeling which alter their shapes. However, an investigation of shape changes in response to differences in loading lies beyond the scope of this paper, and the data presented here pertain to the issue of changes in gross size alone.

MATERIALS AND METHODS

Subjects and exercise training

We report here the result of three experiments, summarized in Table 1, using male sheep (*Ovis aries*; Dorset). These experiments compared exercise and control animals at three different ages: juveniles, who were 40 days old at the start of the experiment and experiencing rapid skeletal growth; subadults, who were between 265–275 days old at the start of the experiment; and skeletally mature, castrated adults[1] who were between 400–430 days old at the start of the experiment. All treatment periods lasted 90 days. For 1 week prior to treatment, the exercise-group animals were habituated to running in an enclosed box on a Marquette 1800 treadmill. During the treatment period, exercise group animals ran every day at a horizontal inclination for 60 min at a Froude speed, $\hat{u}$, of 0.5 (approximately 4 Kph), which resulted in approximately 6,000 loading cycles per day per limb. At this speed,

[1]On the basis of laboratory studies of animals, the decreased level of androgens that result from castration is likely to cause increased bone turnover, loss of trabecular and cortical bone, and decreased proliferation of osteoprogenitor cells (reviewed in Ousler et al., 1996). In humans, castration, decreased testicular function, and hypogonadism are all associated with an increased risk of osteoporosis (Ousler et al., 1996; Dequeker and Guesens, 1985). It is therefore possible that castrated adult sheep might be less capable of producing a pronounced osteogenic response to exercise than uncastrated adult rams. As we argue in the Discussion, however, the effect of castration on bone modeling in adult sheep is apparently small and mirrors the pattern present in uncastrated subadult animals.

which is well below maximum running speed, the sheep's gait is at a moderate trot. At all other times, loading activity was restricted to minor locomotor activity and sedentary weight support by housing the animals in raised 1-m^2 cages. All animals were fed the same quantity of food per day and water ad libitum. Body mass was measured each week on a digital scale.

Measurements

At the end of the experiment, the animals were euthanized, and their limb bones removed and defleshed. The two articulating surfaces in a joint are expected to be closely correlated in size. Thus for most joints, only 1 of the 2 articulating epiphyseal surfaces was measured in order to reduce redundancy within data. Subchondral ASAs of the following joints were measured: distal scapula, distal humerus, proximal femur, proximal tibia, anterior astragalus, posterior astragalus, proximal metacarpal, distal metacarpal, proximal metatarsal, and distal metatarsal. Some metacarpals were not available in the juvenile sample. ASAs were measured using a latex cast method, modified after Godfrey et al. (1995). The subchondral bone of each articular surface was first outlined in pencil. The surface was then dusted with talcum powder, and two coats of Poly Latex 60 (Polytek, Easton, PA) were applied with a small brush, with 3 hr of drying after each coat. The dried molds were removed from the joints, and the edges trimmed with a scalpel following the pencil outline of the subchondral articular surface, which transfers onto the latex. To ensure flatness during measurement, the molds were scored and/or cut into multiple sections. The latex, which is naturally beige in color, was blackened using a permanent marker to enhance contrast.

The latex molds were flattened on the glass of an Arcus II transparency scanner (AGFA, Inc.) and scanned at 1,800 dpi. Mold areas were measured using the thresholding function in NIH Image 1.62. The replicability of the molding technique was assessed by making four molds of one flat joint, the proximal metacarpal, and four molds of one very irregularly shaped joint, the distal metacarpal. Measurement error (expressed as the area difference between the smallest mold and each of the other three) in the proximal metacarpal ranged from 2.76–3.34% (mean, 3.10%), while error in the distal metacarpal was between 1.03–4.35% (mean, 2.36%). A correction factor to compensate for shrinkage in the latex was calculated by making several models of a coin of known diameter and comparing this diameter with the mold diameters. The resulting average linear shrinkage was 3.54%, corresponding to an average shrinkage in area of 6.4%. Therefore, each measurement of latex mold area was multiplied by 1.064 to obtain the corrected area.

We also include data on diaphyseal cross-sectional properties for all hindlimb bones, with the exception of the astragalus. Cross-sectional measurements were obtained by cutting 2-cm sections from the midshaft of the left femur, tibia, and metatarsal. The proximal 1 cm of each section was fixed and dehydrated in 100% ethanol. Samples were embedded in Poly-methyl methacrylate (Osteobed™, Polysciences, Inc., Warrington, PA). Two sections were cut from each sample using an Isomet™ 1000 low-speed saw (Buehler Ltd., Lake Bluff, IL), affixed to glass slides using Epotek™ 301 epoxy (Epoxy Technology, Inc., Billerica, MA), ground to a thickness of 100 μm with a Hillquist™ 1005 thin-section machine (Hillquist, Inc., Fall City, WA), polished on a Hillquist™ 900 grinder, and coverslipped.

The midshaft cross sections were analyzed using an Olympus™ SZH 10 stereozoom microscope (Olympus America, Melville, NY). Images were captured using a SPOT 1.3.0 digital camera (Diagnostic Instruments, Sterling Heights, MI). Cortical area, maximum and minimum second moments of area (I_{max} and I_{min}), and the polar second moment of area (J) were calculated using NIH Image, version 1.61, running a macro written by M. Warfel (Cornell University). Measurements were averaged from both sections of each midshaft.

Since diaphyseal cross-sectional second moments of area need to be standardized to element length and body mass (Ruff, 2000), the length of each bone was measured using digital calipers (accurate to 0.01 mm). Femoral length was measured from the most proximal point on the femoral head to the line connecting the two distal condyles; tibial length was measured from the center of the lateral condylar surface to the center of the distal articular surface; and metatarsal length was measured from the center of the proximal articular surface to the most distal point of the distal articular surface.

Analysis

All statistical analysis was performed using Statview 4.5 (Abacus Concepts, Berkeley, CA). ASA was standardized in two ways. First, ASA was standardized by body mass, following the expectation that compressive stresses during locomotion are mostly proportional to body mass (see above); however, since ASA may scale isometrically with body mass (Alexander, 1980), ASA was also standardized by body $mass^{0.67}$. Second moments of area were standardized by the product of element length and mean body mass (see Polk et al., 2000). In all cases, mean body mass was averaged for the final 3 weeks of treatment. Because of small sample sizes, and to avoid assuming normal distribution of the data, all tests of significance between elements and between groups were calculated using nonparametric methods (in most cases, Mann-Whitney U test).

RESULTS

Articular surface area

Table 2 presents mean articular surface areas, standardized for body mass, of exercised and control sheep in the juvenile, subadult, and adult age groups. There were no significant differences in body

TABLE 2. Articular surface areas/body mass

	Juveniles				Subadults				Adults			
	Controls (N = 5), mean ± 1 SD	Exercised (N = 6), mean ± 1 SD	Difference	*P* value[1]	Controls (N = 4), mean ± 1 SD	Exercised (N = 6), mean ± 1 SD	Difference	*P* value[1]	Controls (N = 8), mean ± 1 SD	Exercised (N = 8), mean ± 1 SD	Difference	*P* value[1]
Body mass (kg)	38.56 ± 3.50	38.83 ± 1.97	0.70%	0.584	44.23 ± 2.91	43.37 ± 2.10	−1.94%	0.670	63.25 ± 6.52	57.38 ± 8.30	−9.29%	0.128
Glenoid fossa (mm^2/kg)	12.57 ± 1.53	13.98 ± 1.17	11.22%	0.100	15.04 ± 1.09	14.31 ± 0.60	−4.85%	0.394	10.281 ± 1.20	10.48 ± 2.08	1.95%	0.753
Glenoid fossa (mm^2/kg^0.67)	41.88 ± 4.99	46.70 ± 3.32	11.51%	0.068	52.49 ± 4.00	49.63 ± 2.09	−5.45%	0.201	65.01 ± 7.38	64.53 ± 11.63	−0.74%	0.600
Distal humerus (mm^2/kg)	30.34 ± 2.69	31.34 ± 2.78	3.30%	0.715	33.37 ± 1.52	31.17 ± 1.94	−6.59%	0.088	24.42 ± 2.69	25.73 ± 6.67	5.36%	0.916
Distal humerus (mm^2/kg^0.67)	101.16 ± 9.08	104.75 ± 8.55	3.55%	0.465	116.42 ± 3.78	108.13 ± 7.14	−7.12%	0.055	95.60 ± 7.53	96.89 ± 20.41	1.35%	0.529
Proximal metacarpal (mm^2/kg)	8.71[2]	8.57 ± 1.16	−1.58%	0.655	8.44 ± 1.54	8.27 ± 0.91	−2.01%	0.831	6.67 ± 0.71	6.93 ± 1.50	3.85%	0.834
Proximal metacarpal (mm^2/kg^0.67)	28.92[2]	28.30 ± 4.33	−2.14%	0.655	29.52 ± 5.84	28.67 ± 3.18	−2.88%	0.831	26.14 ± 2.40	26.14 ± 4.65	0.00%	0.529
Distal metacarpal (mm^2/kg)	20.4[2]	18.48 ± 2.19	−9.41%	0.655	20.67 ± 1.58	20.37 ± 1.34	−1.45%	0.522	16.11 ± 1.91	17.24 ± 4.60	7.01%	0.753
Distal metacarpal (mm^2/kg^0.67)	67.77[2]	61.04 ± 8.11	−9.93%	0.655	72.2 ± 6.56	70.64 ± 4.75	−2.16%	0.670	63.06 ± 5.79	64.86 ± 13.70	2.85%	0.834
Femoral head (mm^2/kg)	25.10 ± 1.82	25.92 ± 3.73	3.27%	0.584	29.75 ± 1.98	27.66 ± 1.48	−7.03%	0.055	22.12 ± 1.84	24.51 ± 5.27	10.80%	0.294
Femoral head (mm^2/kg^0.67)	83.68 ± 5.83	86.58 ± 11.76	3.47%	0.584	103.83 ± 7.02	95.95 ± 5.04	−7.59%	0.055	86.67 ± 5.09	92.31 ± 14.66	6.51%	0.753
Proximal tibia (mm^2/kg)	19.72 ± 1.77	21.38 ± 2.97	8.42%	0.361	23.03 ± 2.51	24.15 ± 2.49	4.86%	0.394	17.34 ± 1.57	18.00 ± 3.74	3.81%	0.916
Proximal tibia (mm^2/kg^0.67)	65.67 ± 4.51	71.43 ± 9.24	8.77%	0.273	80.39 ± 9.14	83.75 ± 8.23	4.18%	0.522	67.95 ± 4.87	67.86 ± 10.61	−0.13%	0.462
Posterior astragalus (mm^2/kg)	18.65 ± 0.85	19.78 ± 2.50	6.06%	0.361	22.52 ± 0.58	21.00 ± 1.72	−6.75%	0.088	16.58 ± 1.98	17.11 ± 3.83	3.20%	0.916
Posterior astragalus (mm^2/kg^0.67)	62.15 ± 2.24	66.07 ± 7.73	6.31%	0.361	78.60 ± 1.97	72.84 ± 5.88	−7.33%	0.055	95.60 ± 7.53	96.89 ± 20.41	1.35%	0.529
Anterior astragalus (mm^2/kg)	15.60 ± 1.22	17.23 ± 3.02	10.45%	0.361	19.29 ± 1.69	17.95 ± 1.77	−6.95%	0.286	13.30 ± 1.59	14.32 ± 4.24	7.67%	0.753
Anterior astragalus (mm^2/kg^0.67)	51.97 ± 3.55	57.50 ± 9.41	10.64%	0.465	67.29 ± 6.06	62.26 ± 6.03	−7.48%	0.201	40.26 ± 3.90	39.52 ± 5.99	−1.84%	0.674
Proximal metatarsal (mm^2/kg)	6.98 ± 0.54	8.03 ± 1.20	15.04%	0.100	9.14 ± 0.69	8.51 ± 0.81	−6.89%	0.201	6.11 ± 0.70	6.44 ± 1.93	5.40%	0.834
Proximal metatarsal (mm^2/kg^0.67)	23.30 ± 2.05	26.82 ± 3.68	15.11%	0.100	31.91 ± 2.82	29.50 ± 2.68	−7.55%	0.136	23.94 ± 2.20	24.27 ± 6.31	1.38%	0.834
Distal metatarsal (mm^2/kg)	17.88 ± 1.58	19.55 ± 2.93	9.34%	0.251	20.46 ± 1.58	20.37 ± 1.39	−0.44%	0.522	14.42 ± 1.45	15.30 ± 4.50	6.10%	0.753
Distal metatarsal (mm^2/kg^0.67)	59.57 ± 4.70	65.13 ± 10.84	9.33%	0.251	71.44 ± 4.27	70.66 ± 4.95	−1.09%	0.831	56.47 ± 4.25	57.52 ± 13.69	1.86%	0.600

[1] Calculated using Mann-Whitney U test.
[2] N = 1 for this element.

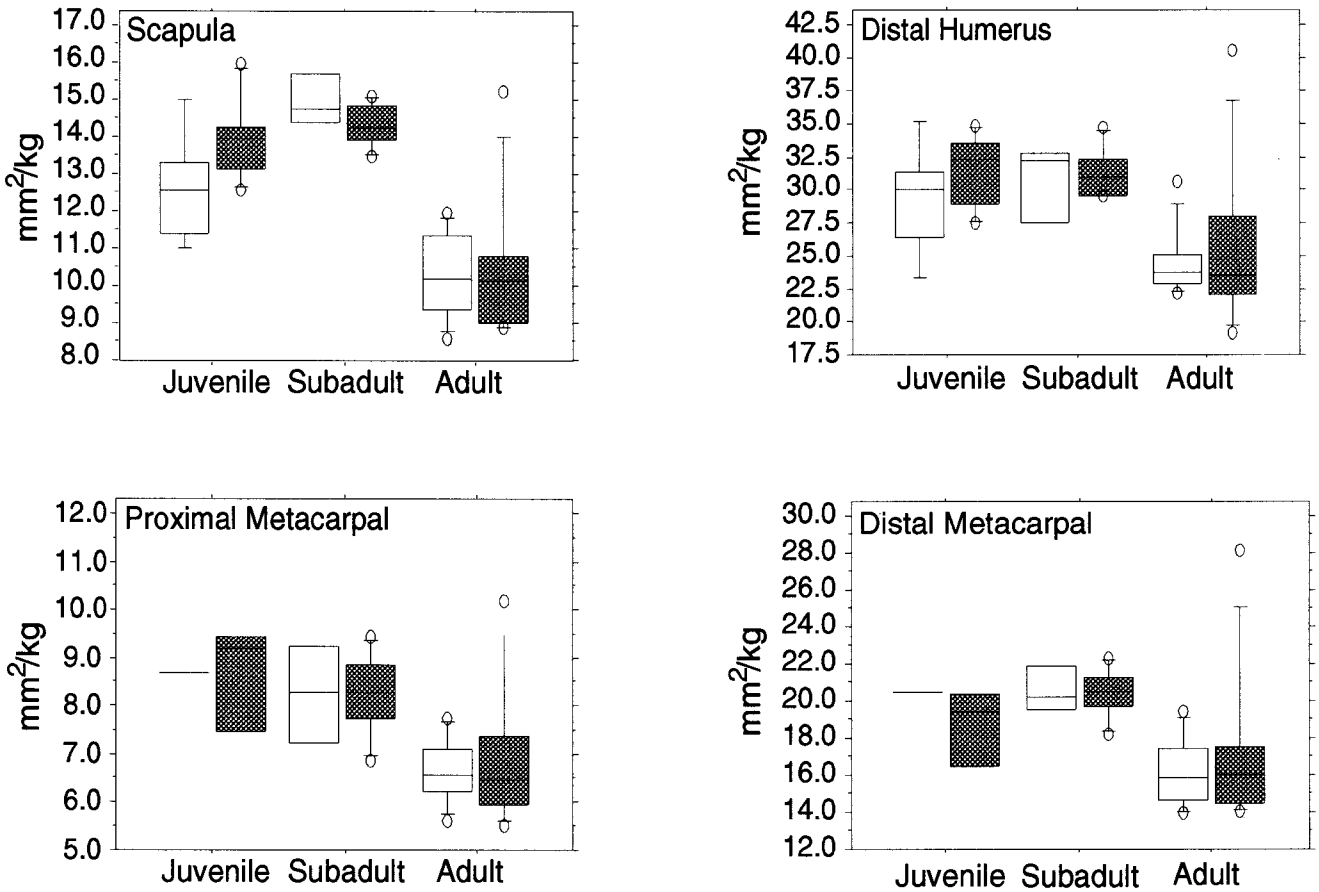

Fig. 1. Forelimb articular surface areas (mm^2), standardized by body mass (kg). Shaded bars represent exercised animals, and clear bars represent control animals. Box and whiskers represent ±1 SD and ±2 standard deviations around the mean, respectively; circles represent total range. None of the differences between exercised and controls groups are statistically significant, based on a Mann-Whitney U-test. For the metacarpal bone in the juvenile group, n = 1.

mass between runners and controls within each age group. Juvenile runners weighed 0.70% more (P = 0.58) than controls, subadult runners weighed 1.94% less (P = 0.67) than controls, and adult runners weighed 9.29% less than controls (P = 0.13).

In the forelimb, which includes the articular surfaces of the glenoid fossa, distal humerus, and proximal and distal metacarpal, there are no significant differences in articular surface area between exercised and control individuals in any age group (Fig. 1). In the juvenile sample, the articular surfaces of exercised animals are modestly larger than those of the controls, although never significantly (Table 2). ASAs are 3–11% larger in runners than controls for all bones except the metacarpal, which may reflect the small sample size for this element (control N = 1, runner N = 4). In the subadult sample, the articular surface areas of exercised animals are 1.5–7% smaller than those of controls in the forelimb (Fig. 1, Table 2). In skeletally mature adults, the articular surfaces of exercised animals are 2–7% larger than those of controls, but none of the increases are statistically significant (Fig. 1, Table 2).

Comparisons of articular surfaces in the hindlimb between treatment groups are similar to those for the forelimb. The articular surface areas of exercised juveniles and skeletally mature adults are 3–13% larger than those of controls, but these differences are not statistically significant (Fig. 2, Table 2). In subadults, the articular surfaces of exercised animals are 0.5–7.5% smaller than those of controls, with the exception of the tibia. The difference in ASA of one joint, the subadult proximal femur, does approach significance (P = 0.055; Fig. 2, Table 2). However, the surface area of the femur is 8% smaller, not larger, in the exercised group.

When ASAs are scaled by body $mass^{0.67}$, however, several differences between the exercised and control groups approach statistical significance. In juveniles, the ASA of the glenoid fossa is 11.5% larger in the exercised group (P = 0.07). In subadults, the distal humerus is 7.0% smaller (P = 0.055), the femoral head is 7.6% smaller (P = 0.055), and the posterior surface of the astragalus is 7.3% smaller (P = 0.055) in the exercised group than in the control group.

While there are no significant within-group differences between runners and controls for comparisons of articular surface area, there are some significant differences in body mass and ASA between sheep of different age categories (pooled runners and controls). The subadults weighed 12.9% more (P =

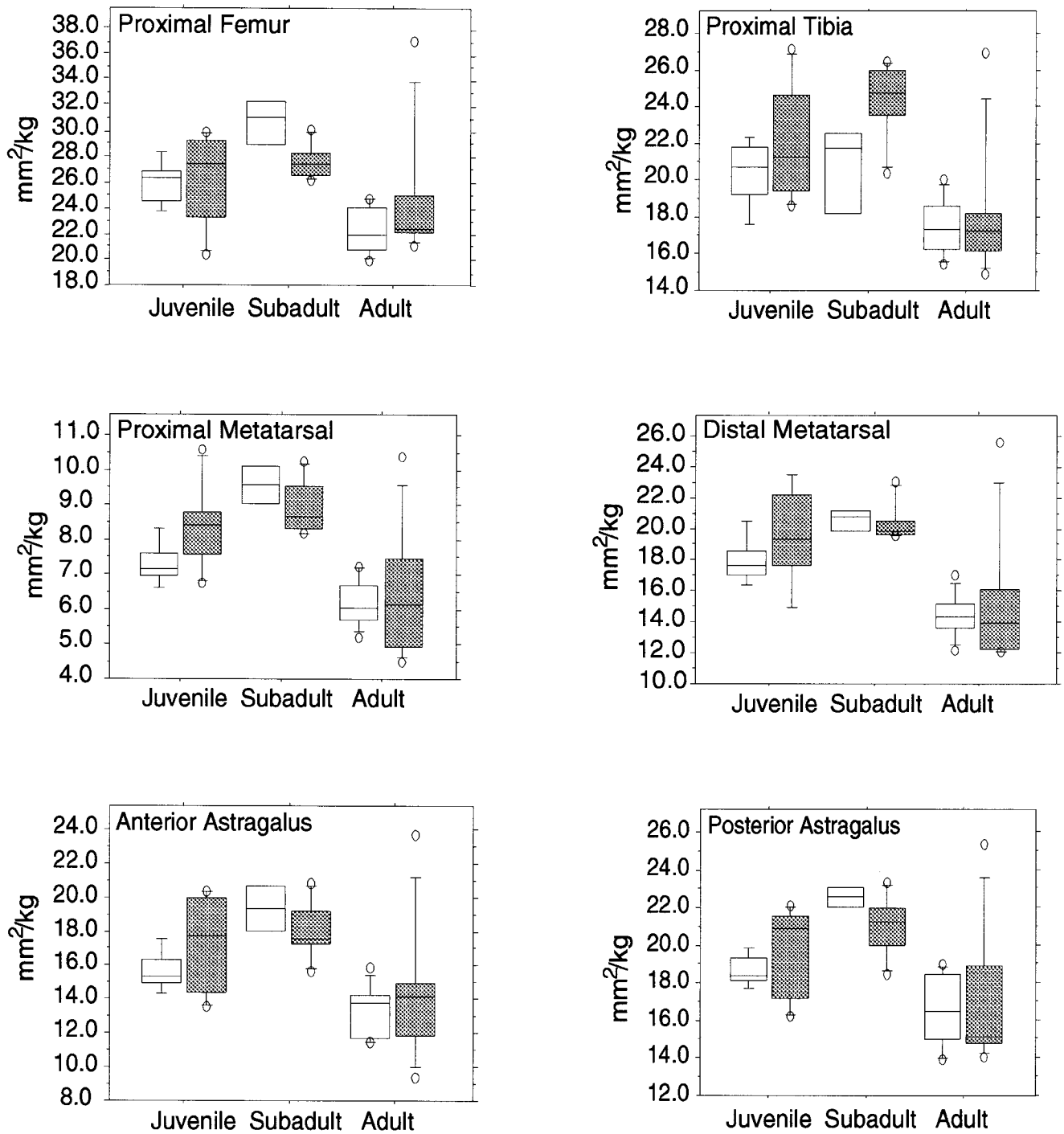

Fig. 2. Hindlimb articular surface areas (mm^2), standardized by body mass (kg). Shaded bars represent exercised animals, and clear bars represent control animals. Box and whiskers represent ±1 SD and ±2 standard deviations around the mean, respectively; circles represent total range. None of the differences between exercised and controls groups are statistically significant, based on a Mann-Whitney U-test.

0.012) than the juveniles. Six of the 10 ASAs examined were significantly larger in subadults than in juveniles ($P < 0.05$), when standardized by body mass: the proximal metatarsal, the glenoid fossa of the scapula, the femoral head, the proximal tibia, and the anterior and posterior surfaces of the astragalus. The skeletally mature adults weighed 55.8% more than the juveniles ($P < 0.0001$), and 38.0% more than the subadults ($P = 0.0002$). However, perhaps because of their larger body mass relative to the younger sheep, the articular surfaces of adults are actually 9–26% smaller relative to body mass than the articular surfaces of juveniles, and this difference is highly significant for all joints but the distal metacarpal, in which there is not a significant difference, and the glenoid fossa and the proximal femur, in which the adults have significantly larger ASAs relative to mass than the juveniles do (Table 3).

TABLE 3. Ontogenetic differences in articular surface areas scaled by body mass and body mass$^{0.67}$

	Juveniles (n = 11)	Subadults (n = 10)	Adults (n = 16)						
	Mean SD	Mean SD	Mean SD	Subadult-juvenile % difference[2]	P-value[1]	Adult-subadult % difference[3]	P-value[1]	Juvenile-adult % difference[4]	P-value[1]
Body mass	38.71 ± 2.62	43.71 ± 2.34	60.32 ± 7.82	12.9	0.0012	38.0	0.0002	55.8	<0.0001
Glenoid fossa (mm^2/kg)	13.34 ± 1.47	14.6 ± 0.86	16.85 ± 2.96	9.4	0.0411	15.4	0.0153	26.3	0.0007
Glenoid fossa ($mm^2/kg^{0.67}$)	44.51 ± 4.67	50.77 ± 3.15	64.77 ± 9.41	14.1	0.0039	27.6	<0.0001	45.5	<0.0001
Distal humerus (mm^2/kg)	30.88 ± 2.65	32.05 ± 2.04	25.07 ± 4.96	3.8	0.3242	−21.8	<0.0001	−18.8	<0.0001
Distal humerus ($mm^2/kg^{0.67}$)	103.12 ± 8.55	111.45 ± 7.17	53.05 ± 10.07	8.1	0.0242	−52.4	<0.0001	−48.6	<0.0001
Proximal metacarpal (mm^2/kg)	8.61 ± 1.16	8.34 ± 1.12	6.8 ± 1.14	−3.1	0.4795	−18.5	0.0019	−21.0	0.0182
Proximal metacarpal ($mm^2/kg^{0.67}$)	28.46 ± 3.55	29.01 ± 4.15	26.14 ± 3.57	1.9	0.7773	−9.9	0.0917	−8.2	0.1564
Distal metacarpal (mm^2/kg)	18.96 ± 2.39	20.49 ± 1.39	16.67 ± 3.45	8.1	0.2579	−18.6	0.0003	−12.1	0.0588
Distal metacarpal ($mm^2/kg^{0.67}$)	62.72 ± 7.43	71.26 ± 5.25	63.96 ± 10.20	13.6	0.0897	−10.2	0.0084	2.0	0.9247
Femoral head (mm^2/kg)	25.55 ± 2.91	28.5 ± 1.92	23.32 ± 4.01	11.5	0.0290	−18.2	0.0002	−8.7	0.0204
Femoral head ($mm^2/kg^{0.67}$)	85.26 ± 9.22	99.1 ± 6.86	89.49 ± 11.00	16.2	0.0031	−9.7	0.0022	5.0	0.4592
Proximal tibia (mm^2/kg)	20.63 ± 2.54	23.7 ± 2.43	17.67 ± 2.80	14.9	0.0242	−25.4	0.0002	−14.3	0.0016
Proximal tibia ($mm^2/kg^{0.67}$)	68.81 ± 7.74	82.4 ± 8.29	67.91 ± 7.98	19.8	0.0019	−17.6	0.0006	−1.3	0.6930
Posterior astragalus (mm^2/kg)	19.26 ± 1.94	21.61 ± 1.54	25.07 ± 4.96	12.2	0.0060	16.0	0.0084	30.2	0.0001
Posterior astragalus ($mm^2/kg^{0.67}$)	64.28 ± 6.01	75.15 ± 5.42	96.24 ± 14.88	16.9	0.0015	28.1	0.0001	49.7	<0.0001
Anterior astragalus (mm^2/kg)	16.49 ± 2.43	18.48 ± 1.78	10.38 ± 1.64	12.1	0.0486	−43.8	<0.0001	−37.1	<0.0001
Anterior astragalus ($mm^2/kg^{0.67}$)	54.99 ± 7.59	64.28 ± 6.26	39.89 ± 4.90	16.9	0.0112	−37.9	<0.0001	−27.5	<0.0001
Proximal metatarsal (mm^2/kg)	7.56 ± 1.07	8.76 ± 0.79	6.28 ± 1.42	15.9	0.0137	−28.3	0.0002	−16.9	0.0057
Proximal metatarsal ($mm^2/kg^{0.67}$)	25.22 ± 3.44	30.47 ± 2.86	24.1 ± 4.57	20.8	0.0012	−20.9	0.0016	−4.4	0.5537
Distal metatarsal (mm^2/kg)	18.72 ± 2.58	20.4 ± 1.14	14.86 ± 3.26	9.0	0.0696	−27.2	0.0002	−20.6	0.0009
Distal metatarsal ($mm^2/kg^{0.67}$)	62.35 ± 8.40	70.97 ± 4.46	56.99 ± 9.81	13.8	0.0191	−19.7	0.0002	−8.6	0.0651

[1] Probability from a Mann-Whitney U test.
[2] Calculated as 100*((subadult mean − juvenile mean)/juvenile mean).
[3] Calculated as 100*((adult mean − subadult mean)/subadult mean).
[4] Calculated as 100*((adult mean − juvenile mean)/juvenile mean).

When ASA is standardized by mass$^{0.67}$, different patterns emerge (Table 3). The difference in scaled mass diminishes so that the adults have only a 23.9% ($P = 0.0002$) larger scaled mass than the subadults and a 34.4% ($P < 0.0001$) greater scaled mass than the juveniles. Rather than having smaller scaled ASAs than juveniles, the adults have ASAs that range in size from 48.6% ($P < 0.0001$) smaller to 49.7% ($P < 0.0001$) larger than those of juveniles. As before with standardization by body mass, when scaled by mass$^{0.67}$, most of the subadult ASAs are larger than those of the juveniles ($P < 0.05$). Likewise, the adults have ASAs scaled by mass that fall between 52.4% ($P < 0.0001$) smaller and 28.1% ($P = 0.0001$) larger than those of subadults. These results illustrate the profound changes in proportions that occur during growth which greatly alter the size of ASAs relative to the mechanical demands placed on them by body weight. For the purposes of this study, it is important to note that when viewed against this background of normal ontogenetic alterations of body proportions, it is all the more remarkable how little the mass-adjusted ASA dimensions change within each age group in response to exercise.

Cross-sectional geometry

Table 4 summarizes the differences in size-standardized cortical area, I_{max}, I_{min}, J, and I_{max}/I_{min}, between exercised and control animals in each age group. In contrast to the articular surfaces, there are some significant differences in the cross-sectional geometry of the midshafts between exercised and control animals, mostly in more distal hindlimb elements during the juvenile period. In the juvenile exercised group, I_{max} in the tibia is 28.67% higher ($P = 0.02$) than in the control group, and I_{max} in the metatarsal is 20.72% higher ($P = 0.04$) than in the control group. Also, J in the tibia is 25.49% higher ($P = 0.02$), and J in the metatarsal is 21.28% higher ($P = 0.07$) in exercised vs. sedentary groups. Among adult treatment groups, cortical area in the metatarsal is 16.34% greater ($P = 0.01$), and adjusted I_{min} in the metatarsal is 16.59% greater ($P = 0.04$) in exercised sheep than in sedentary controls. Exercise also produced a few significant differences in the distributions of mass (I_{max}/I_{min}) in long bone cross sections in subadults and adults, but not in juveniles. Among subadults, I_{max}/I_{min} in the tibia is 10.58% lower in the exercised group than in sedentary controls ($P = 0.02$). Among adults, I_{max}/I_{min} in the femur is 11.32% lower ($P = 0.07$) than in the exercised group than in sedentary controls.

DISCUSSION

The results from this study indicate that the effects of mechanical loading from moderate exercise are not only complex but also differ substantially in diaphyses and the subchondral articular surfaces of epiphyses. Most importantly, the levels of mechanical loading experienced by sheep in this study had

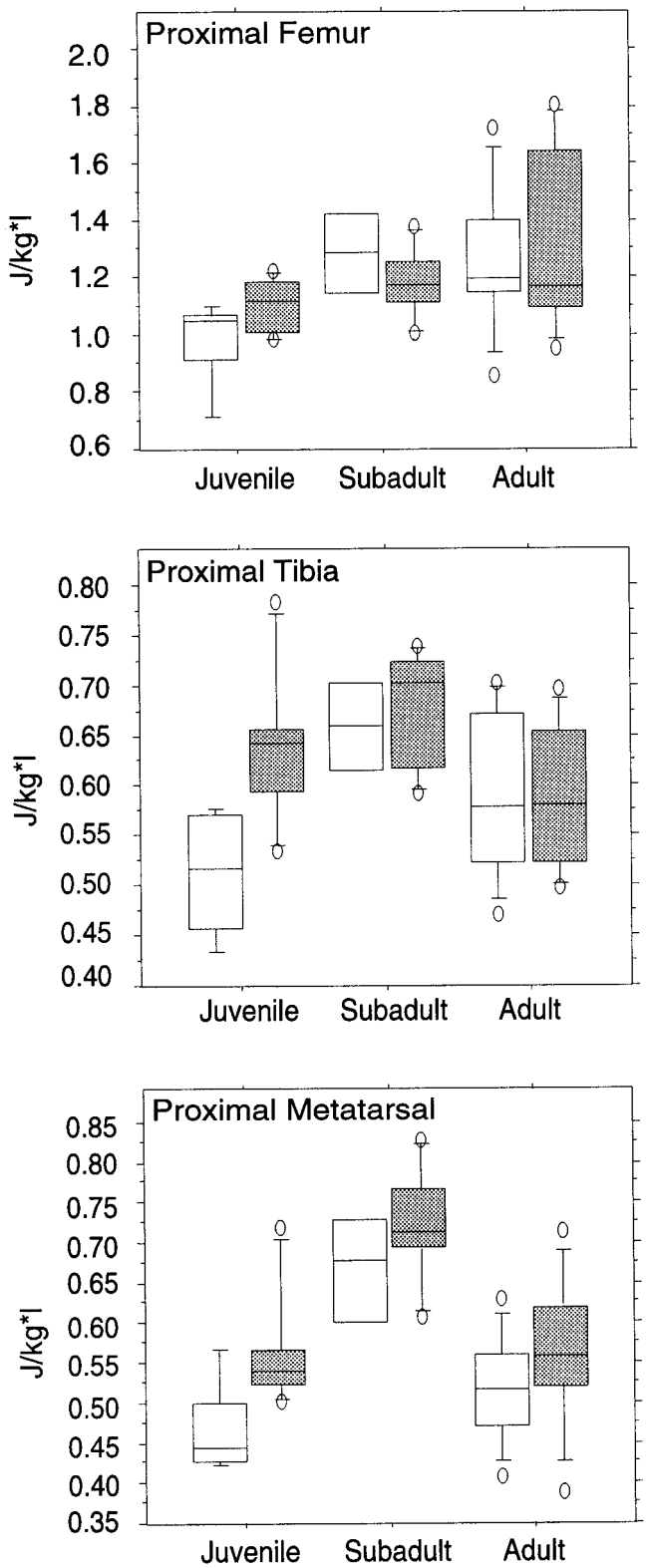

Fig. 3. Hindlimb polar second moment of area (J/kg · 1). Shaded bars represent exercised animals, and clear bars represent control animals. Box and whiskers represent ±1 SD and ±2 standard deviations around the mean, respectively; circles represent total range. The difference between juvenile exercised and control groups in the tibia is statistically significant ($P = 0.02$), and in the metatarsal approaches significance ($P = 0.07$); none of the other differences are statistically significant.

TABLE 4. Hindlimb diaphyseal cross-sectional geometry

	Juveniles				Subadults				Adults			
Cortical area (CA/kg)	Controls (N = 5)	Runners (N = 6)	Difference	P value[1]	Controls (N = 4)	Exercised (N = 6)	Difference	P value[1]	Controls (N = 8)	Exercised (N = 8)	Difference	P value[1]
Femur	3.45 ± 0.42	3.52 ± 0.21	2.03%	>0.9999	3.69 ± 0.46	3.66 ± 0.26	−0.81%	0.6698	3.19 ± 0.59	3.54 ± 0.31	10.97%	0.2076
Tibia	3.69 ± 0.46	3.46 ± 0.36	−6.23%	0.1441	3.30 ± 0.29	3.41 ± 0.16	3.33%	0.3938	2.77 ± 0.32	2.90 ± 0.22	4.69%	0.5283
Metatarsal	2.50 ± 0.26	2.63 ± 0.25	5.20%	0.2012	2.49 ± 0.25	2.56 ± 0.13	2.81%	0.5224	2.02 ± 0.23	2.35 ± 0.23	16.34%	0.0063
Imax/kg												
Femur	0.56 ± 0.09	0.63 ± 0.07	13.51%	0.3613	0.74 ± 0.12	0.67 ± 0.08	−9.84%	0.3938	0.76 ± 0.11	0.73 ± 0.19	−3.84%	0.3446
Tibia	0.29 ± 0.04	0.38 ± 0.05	28.67%	0.0176	0.38 ± 0.03	0.37 ± 0.04	−0.80%	>0.9999	0.35 ± 0.05	0.34 ± 0.06	−2.29%	0.9164
Metatarsal	0.25 ± 0.03	0.30 ± 0.04	20.72%	0.0446	0.37 ± 0.06	0.40 ± 0.05	7.77%	0.5224	0.29 ± 0.04	0.32 ± 0.06	10.14%	0.2076
Imin/kg												
Femur	0.43 ± 0.07	0.47 ± 0.04	11.29%	0.2733	0.54 ± 0.05	0.51 ± 0.06	−4.28%	0.5224	0.53 ± 0.09	0.56 ± 0.14	8.90%	0.7527
Tibia	0.22 ± 0.03	0.26 ± 0.04	21.30%	0.0679	0.28 ± 0.03	0.30 ± 0.02	10.55%	0.1356	0.24 ± 0.04	0.25 ± 0.04	4.66%	0.5286
Metatarsal	0.22 ± 0.03	0.26 ± 0.04	20.00%	0.0446	0.30 ± 0.03	0.32 ± 0.03	9.49%	0.2008	0.22 ± 0.03	0.25 ± 0.04	16.59%	0.0357
Imax/Imin												
Femur	1.31 ± 0.09	1.33 ± 0.07	1.83%	0.4652	1.38 ± 0.12	1.30 ± 0.09	−5.31%	0.2008	1.44 ± 0.13	1.28 ± 0.20	−11.32%	0.0742
Tibia	1.36 ± 0.06	1.45 ± 0.13	6.40%	0.3613	1.37 ± 0.06	1.23 ± 0.07	−10.58%	0.0190	1.49 ± 0.13	1.39 ± 0.20	−6.65%	0.3446
Metatarsal	1.14 ± 0.05	1.15 ± 0.07	0.53%	0.8551	1.26 ± 0.13	1.24 ± 0.08	−1.66%	0.8312	1.32 ± 0.09	1.25 ± 0.15	−5.39%	0.248
Polar moment of area (J/kg*I)												
Femur	0.98 ± 0.15	1.10 ± 0.10	12.24%	0.1441	1.28 ± 0.16	1.18 ± 0.13	−7.81%	0.3938	1.26 ± 0.26	1.32 ± 0.33	4.76%	0.4622
Tibia	0.51 ± 0.06	0.64 ± 0.08	25.49%	0.0176	0.65 ± 0.06	0.68 ± 0.06	4.62%	0.3938	0.59 ± 0.09	0.59 ± 0.08	0.00%	0.9164
Metatarsal	0.47 ± 0.06	0.57 ± 0.08	21.28%	0.0679	0.67 ± 0.08	0.72 ± 0.07	7.46%	0.3938	0.52 ± 0.07	0.57 ± 0.10	9.62%	0.1415

[1] Calculated using Mann-Whitney U test.

no statistically significant effect on ASAs in juvenile, subadult, or adult animals. While the ASAs of runners tended to be slightly larger than those of controls, the size differences were not statistically significant in any joint. Consequently, the null hypothesis that ASAs are conservative and do not exhibit any substantial degree of phenotypic plasticity in response to mechanical loading is not rejected. Moreover, this study found no effect of location or age on ASA responses to loading. There was no trend for distal ASAs to be any more phenotypically plastic than proximal ASAs. In addition, ASA differences between exercise and control groups were not higher in the juveniles than in subadults or adults.

The midshaft diaphyseal responses to loading documented in this experiment were less exaggerated than those documented in other studies that measured effects of longer periods of exercise or which induced higher levels of loading (reviewed in Martin et al., 1998). In general, the exercise-induced mechanical loading studied here caused significant changes mostly in the cross-sectional properties of the distal hindlimb elements (the tibia and metatarsal) of the juvenile sheep, but not in the more proximal femur (Fig. 3). In addition, and with few exceptions, the most pronounced changes are in juveniles, with no significant changes in standardized measurements of I_{max} or J in subadults or adults. One potential problem with these data is that the adult sheep were castrated, which can decrease bone growth through lower levels of circulating androgens (Ousler et al., 1996). However, the similar degree of plasticity in subadults and adults suggests that any decreased osteogenic effects from castration were probably negligible in this study. These data therefore indicate that efforts to reconstruct loading history from cross-sectional properties may be more sensitive when derived from distal elements, and mostly reflect differences that occur prior to skeletal maturity. We do not have enough data to determine the extent to which longer durations and/or higher intensities of exercise cause changes in diaphyseal cross-sectional properties in subadults or adults, but previous studies show that exercise in older individuals mostly influences endosteal rather than periosteal dimensions (Woo et al., 1981; Ruff et al, 1994). Since second moments of area are a fourth power function, changes in endosteal shape have generally minor effects on bone strength in resistance to bending or twisting. In addition, the larger adjusted I_{max} and I_{min} in the lower limb elements of exercised juveniles compared to controls, in combination with stability in the ratio of I_{max}/I_{min}, suggests that during locomotion, juvenile limb bones are being bent in both anteroposterior and mediolateral directions, and that exercise-imposed increases in bending stresses remain proportional in the anteroposterior and mediolateral planes.

The experimental data reported here therefore agree with comparative studies that indicate that ASAs are highly constrained (Ruff, 1988; Ruff et al., 1991). In addition, it is reasonable to conclude that diaphyseal second moments of area are more labile than ASAs in juveniles, but not in adults. However, additional experiments are necessary to test more completely the hypothesis that ASAs have little or no phenotypic plasticity because of functional or genetic constraints. It is possible, for example, that the magnitudes and number of loading events in this study were insufficient to elicit any appreciable growth response. As noted above, Ruff et al. (1994) found that radial head breath in professional tennis players was 5.6% greater in the racket-holding vs. nonracket-holding arm. One possibility for the discrepancy between this study and that of Ruff et al. (1994) is that the asymmetries in mechanical loading which young tennis players place on their elbows are far more extreme in terms of stress magnitude, number of loading events, and possibly duration of loading events than measured by this study, as well as by most experimental and comparative studies. Further experimental research is necessary to quantify how much and what kinds of loading are necessary to induce changes in articular surface area.

Although ASA appears to be highly conservative, it is well-known that bone in epiphyses does respond to loading through other mechanisms such as changes in trabecular orientation, trabecular thickness, trabecular connectivity, Haversian remodeling, and subchondral bone thickness (Radin et al., 1982; Parfitt et al., 1983; Hou et al., 1990; Rafferty and Ruff, 1994; Kamibayashi et al., 1995; Pidaparti and Turner, 1997; Teng et al., 1997). For example, Rafferty and Ruff (1994) showed that, in primate femoral and humeral heads, trabecular mass correlates with joint reaction forces, whereas subarticular surface area correlates with variations in joint mobility. These apparently decoupled subchondral osseous responses to loading are advantageous from a functional perspective, because they allow joints to respond to their mechanical environment without altering articular morphology and risking loss of congruence. These various osseous responses, however, most likely vary in part as a function of articular surface size. In most mammals, distal elements tend to be more diminutive than proximal elements (see Hildebrand, 1985; Myers and Steudel, 1985; Lieberman and Pearson, 2001). Since total compressive forces during dynamic loading are probably similar in proximal and distal joints (see above), then the stresses experienced by more distal articular surfaces are likely to be considerably higher than those experienced by proximal joints. As a result, if distal and proximal articular surfaces are similarly conservative in response to mechanical loading, then one would predict distal joints to be more phenotypically plastic in response to mechanical loading in terms of subchondral bone thickness and trabecular architecture. Further study of these alternative mechanisms of adaptation is necessary, particularly in relation to chondral responses to loading, which must play a key role in subchondral epiphyseal

growth and shape (see Martin et al., 1998; Frost, 1999).

Finally, the stability of ASA throughout ontogeny, in contrast to the higher plasticity of diaphyseal cross-sectional properties, suggests that joint size and shaft dimensions should not be considered to be equivalently reliable when making behavioral and taxonomic inferences from fossils. In terms of estimating body mass *at the species level*, the results presented here suggest that, on a priori grounds, body mass estimates based on articular dimensions (Jungers, 1988; McHenry, 1992; Hartwig-Scherer, 1994) are likely to be more accurate than estimates of body mass based on shaft size (i.e., Aiello, 1981; Rightmire, 1986; McHenry, 1988; Hartwig-Scherer, 1994). As noted above, articular dimensions are not independent of locomotor modes (Godfrey et al., 1991), but they are independent of intraspecific variation in activity levels. In contrast, diaphyseal dimensions are not independent of intraspecific variation in activity levels. This difference may explain why body mass estimates for australopithecines based on femoral shaft measurements (e.g., Jungers, 1988; McHenry, 1992) are typically higher than estimates based on joint size (McHenry, 1988). This potential disparity may characterize the upper limb bones of *Australopithecus afarensis*, including the robust and ruggedly modeled ulna A.L. 438-1a, and humeri A.L. 137-50 and MAK-VP-1/3 (Kimbel et al., 1994; White et al., 1993). Based on a great ape model, it would not be surprising if the midshaft dimensions of these bones predicted higher body masses than those predicted by their epiphyses (when present) or their length. However, for more recent fossil species, joint size and shaft dimensions produce very similar body mass estimates (Jungers, 1988). In order to make inferences about the behavior and body mass of individuals for a given species, it may be more appropriate to use diaphyseal area, which is sensitive to changes in both body mass and activity level throughout life (Ruff et al., 1991).

ACKNOWLEDGMENTS

We thank R. Bernstein, A.W. Crompton, B. Demes, M. Okalita, K. Rafferty, L. Tuanquin, M. Toscano, and F. Weidemann for assistance with experiments and preparation of specimens. Three anonymous reviewers' comments helped improve the manuscript, and we are grateful for their input. This research was supported by National Science Foundation grant IBN 96-03833 to D.E.L.

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