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Variation in mammalian proximal femoral development: comparative analysis of two distinct ossification patterns

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Abstract

The developmental anatomy of the proximal femur is complex. In some mammals, including humans, the femoral head and greater trochanter emerge as separate ossification centres within a common chondroepiphysis and remain separate throughout ontogeny. In other species, these secondary centres coalesce within the chondroepiphysis to form a single osseous epiphysis much like the proximal humerus. These differences in femoral ontogeny have not been previously addressed, yet are critical to an understanding of femoral mineralization and architecture across a wide range of mammals and may have key implications for understanding and treating hip abnormalities in humans. We evaluated femora from 70 mammalian species and categorized each according to the presence of a 'separate' or 'coalesced' proximal epiphysis based on visual assessment. We found that ossification type varies widely among mammals: taxa in the 'coalesced' group include marsupials, artiodactyls, perissodactyls, bats, carnivores and several primates, while the 'separate' group includes hominoids, many rodents, tree shrews and several marine species. There was no clear relationship to body size, phylogeny or locomotion, but qualitative and quantitative differences between the groups suggest that ossification type may be primarily an artefact of femoral shape and neck length. As some osseous abnormalities of the human hip appear to mimic the normal morphology of species with coalesced epiphyses, these results may provide insight into the aetiology and treatment of human hip disorders such as femoroacetabular impingement and early-onset osteoarthritis.

Key words chondroepiphysis; epiphysis; femur; hip development; morphology; ossification.

Introduction

The proximal femur has received much attention in the bone biology literature because it exhibits a high incidence of pathology and debilitating injury in humans, especially among the elderly. The femoral neck is a common site of fracture and bone loss, and deformities in hip geometry and development are known to be associated with osteoarthritis in young men and women (Stulberg et al. 1975; Harris, 1986; Ganz et al. 2003; Siebenrock et al. 2004; Tanzer & Noiseux, 2004). Many therapeutic strategies (including hip replacement) have been developed using a variety of animals (i.e. rats, rabbits, sheep, dogs and primates) (Bergmann et al. 1984; Sumner et al. 1990; Bagi et al. 1997; Bergmann et al. 1999; Kuo et al. 1998; Kim et al. 2001); however, there are potential differences between laboratory models and their clinical application. In the current study, we report variation in femoral neck ossification among mammals that may affect the outcomes of comparisons using diverse species.

The mammalian femur is distinguished from other long bones by its complex developmental history. The entire proximal end originates as a single chondroepiphysis in which secondary ossification centres for the femoral head and greater trochanter emerge separately (Fig. 1A) (Ogden, 1981). In some mammals (including humans) these remain distinct throughout growth and are connected only by a thin bridge of cartilage. This 'intra-epiphyseal' region initially develops as a thick layer of cartilage covering the superior femoral neck (Fig. 1A), but gradually narrows and thins as the neck elongates, resulting in discrete capital and trochanteric

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growth centres (Figs 1B and 2A) (Ogden, 1981, 1983). In other species, however, these secondary centres coalesce to form a single osseous epiphysis that covers the entire end of the bone, similar to the head and tubercles of the proximal humerus (Fig. 2B). Although first noted by Lütken (1961) over four decades ago, these differences in femoral ossification have remained largely unrecognized and the extent to which femoral development varies among mammals has not been investigated. As a consequence, differences in femoral ontogeny have not been acknowledged in previous analyses of the femoral neck and may have key implications for understanding and treating human hip abnormalities. The purpose of this study is two-fold: (1) to document variation in proximal femoral ossification among broad mammalian groups, and (2) to assess the impact of body size and locomotion on these variants of femoral development. We then discuss their aetiology and relevance with special reference to the pathophysiology of the human hip.

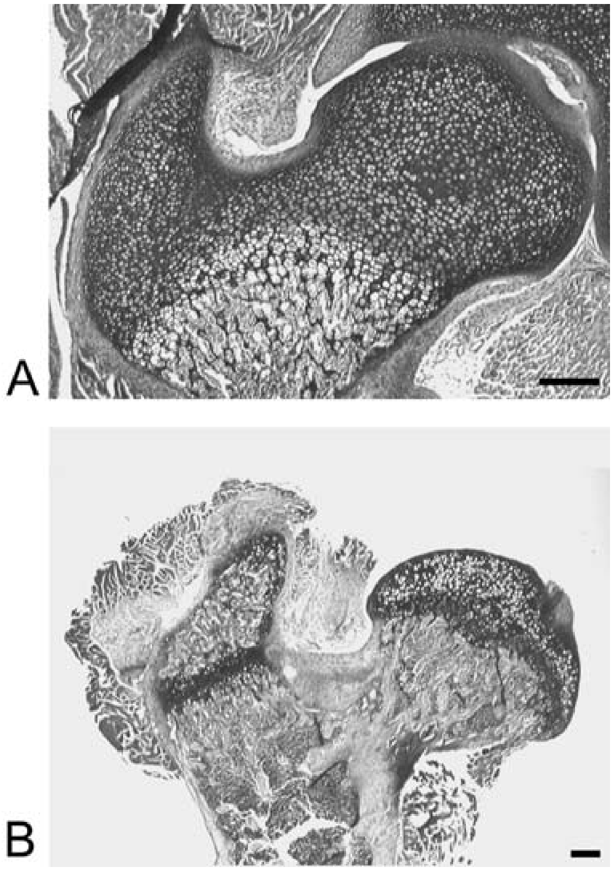

Fig. 1 Histological sections of proximal femora from (A) 7-day-old and (B) 28-day-old C57BL/6J mice. During early postnatal development, the entire end of the femur consists of a single chondroepiphysis (A). Clear separation of the head and trochanter becomes evident later in ontogeny and the two epiphyses remain discrete throughout the rest of the growth period (B). Scale bar = 200 μm.

Materials and methods

Sample

We examined dried femora (n = 266) from 70 mammalian species representative of 39 families and 15 orders from osteological collections (Table 1). Specimens are housed in the Laboratories of Physical Anthropology and Vertebrate Zoology, Cleveland Museum of Natural History, and the Division of Mammals, National Museum of Natural History, Smithsonian Institution. The sample is restricted to subadults (adulthood defined on the basis of epiphyseal closure) and is of mixed sex.

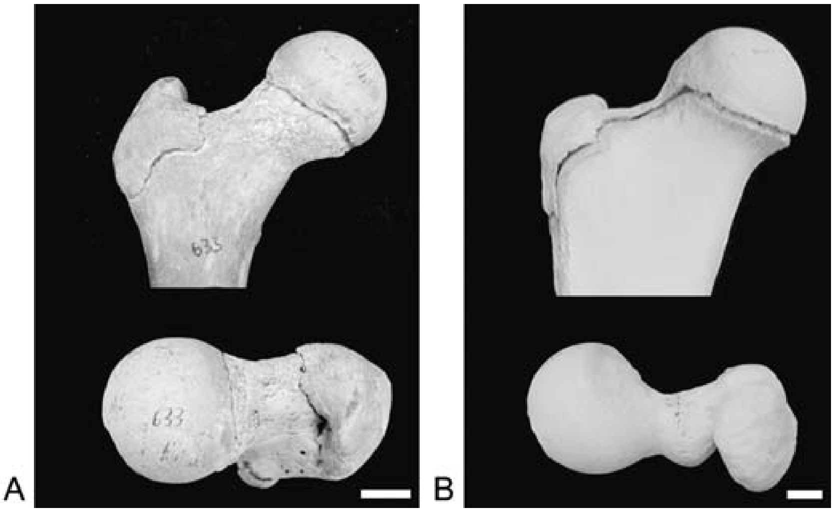

Fig. 2 Examples of separate and coalesced ossification. Proximal femora from a modern human (A) and polar bear (*Ursus maritimus*) (B) illustrate the two very different patterns of ossification described here. Top: anterior views; bottom: superior view, anterior is up. There is an observable distance between the femoral head and greater trochanter in the human (A), while the entire proximal end of the polar bear femur (B) is occupied by a single osseous epiphysis as is typical of most other long bones. Scale bar = 10 mm.

Table 1 Classification of ossification type, mode of locomotion and body size for all mammals* surveyed

Taxon	Common name	Specimens observed	Ossification type	Locomotor category	Adult body size†	References‡
Artiodactyla						
Antidorcas marsupialis	springbok	4	coalesced	cursorial	30–48 kg	1
Antilope cervicapra	blackbuck	3	coalesced	cursorial	38.5 kg	1,2
Bison bison	American bison	4	coalesced	cursorial	350–1000 kg	1
Bos taurus	domestic cattle	3	coalesced	cursorial	800–1000 kg	1
Gazella dorcas	gazelle	3	coalesced	cursorial	12–85 kg	1
Camelus dromedarius	Arabian camel	3	coalesced	cursorial	300–690 kg	1
Lama guanicoe	guanaco	3	coalesced	cursorial	100–120 kg	1
Odocoileus virginianus	white-tailed deer	5	coalesced	cursorial	75–100 kg	1
Giraffa camelopardalis	giraffe	3	coalesced	cursorial	800 kg	1
Sus barbatus	bearded pig	5	coalesced	cursorial	50–350 kg	1
Phacochoerus aethiopicus	wart hog	2	coalesced	cursorial	50–150 kg	1
Tragulus napu	mouse deer	3	coalesced	cursorial	0.7–8 kg	1
Perissodactyla						
Equus burchelli	Burchell's zebra	3	coalesced	cursorial	175–385 kg	1
Equus caballus	horse	3	coalesced	cursorial	484 kg	1,2
Tapiris indicus	Asian tapir	3	coalesced	cursorial	225 kg	1,2
Carnivora						
Canis lupus	gray wolf	6	coalesced	cursorial	37–40 kg	1
Lycaon pictus	African hunting dog	4	coalesced	cursorial	17–36 kg	1
Urocyon cinereoargenateus	grey fox	4	coalesced	cursorial (climbing)	2.5–7 kg	1
Vulpes vulpes	red fox	3	coalesced	cursorial	6 kg	1,2
Felis catus	domestic cat	4	coalesced	cursorial	2.5 kg	1,2
Felis concolor	puma	4	coalesced	cursorial	36–103 kg	1
Felis pardalis	ocelot	3	coalesced	cursorial	11.3–15.8 kg	1
Lynx canadensis	Canada lynx	2	coalesced	cursorial	12 kg	1,2
Neofelix nebulosa	clouded leopard	3	coalesced	cursorial	16–23 kg	1
Panthera leo	lion	7	coalesced	cursorial	120–250 kg	1
Panthera pardus	leopard	4	coalesced	cursorial	46.3 kg	1,2
Mustela frenata	long-tailed weasel	3	coalesced	cursorial	85–340 g	1,3
Mustela vison	American mink	2	coalesced	amphibious	1217 g	1
Procyon lotor	raccoon	7	coalesced	ambulatory (climbing)	2–12 kg	1,2,3
Ursus americanus	black bear	7	coalesced	ambulatory (climbing)	92–270 kg	1,3
Ursus maritimus	polar bear	4	coalesced	amphibious	150–500 kg	1,2,3
Zalophus californianus	California sea lion	3	separate	aquatic	50–400 kg	1
Phoca vitulina	harbour seal	2	separate	aquatic	50–150 kg	1
Chiroptera						
Pteropus alecto	flying fox	3	coalesced	volant	–	1
Pteropus mariannus	flying fox	3	coalesced	volant	–	1
Pteropus poliocephalus	flying fox	2	coalesced	volant	–	1
Rousettus madagascariensis	rousette fruit bat	6	coalesced	volant	50–100 g	1
Lipotyphla						
Erinaceus europaeus	Eurasian hedgehog	5	coalesced	ambulatory	928 g	1,2
Rodentia						
Capromys pilorides	Cuban hutia	4	separate	climbing	0.5–7 kg	1
Myocastor coypus	nutria	3	separate	amphibious	5–10 kg	1
Castor canadensis	beaver	3	separate	amphibious	20 kg	1,2
Erethizon dorsatum	common porcupine	3	variable	climbing	3.5–7 kg	1
Hystrix cristata	African porcupine	3	separate	fossorial	11.3 kg	1,2
Rattus rattus	black rat	4	separate	climbing	77–108 g	1
Marmota monax	woodchuck	5	separate	fossorial	3–7.5 kg	1
Tamias striatus	chipmunk	3	separate	fossorial	70–124 g	1

Table 1 *Continued*

Taxon	Common name	Specimens observed	Ossification type	Locomotor category	Adult body size†	References‡
Lagomorpha						
Lepus europus	brown hare	8	coalesced	saltatorial	1350–7000 g	1,3
Lepus townsendii	white-tailed jack rabbit	5	coalesced	saltatorial	1350–7000 g	1,3
Scandentia						
Tupaia tana	tree shrew	4	separate	climbing	150 g	1,2
Primates						
Lemur catta	ring-tailed lemur	3	coalesced	saltatorial	2678–2705 g	4
Otolemur crassicaudatus	greater bush baby	3	coalesced	saltatorial	1242–1495 g	4
Chlorocebus aethiops	vervet monkey	3	coalesced	ambulatory (climbing)	3257–4582 g	4
Theropithecus gelada	gelada baboon	3	coalesced	ambulatory (climbing)	11.7–20 kg	1,4,5
Presbytis frontata	white-fronted langur	3	coalesced	climbing (suspensory)	5–5.6 kg	1,5
Trachypithecus pileatus	capped langur	3	coalesced	climbing (suspensory)	10–12.8 kg	1,4
Hylobates sp.	gibbon	3	separate	suspensory	5–7.5 kg	1,4
Pongo pygmaeus	orangutan	3	separate	suspensory (ambulatory)	37–77.5 kg	1,4
Pan troglodytes	chimpanzee	8	separate	ambulatory (suspensory)	32–60 kg	1,4
Gorilla gorilla	gorilla	7	separate	ambulatory (suspensory)	70–175 kg	1,4
Homo sapiens	human	10	separate	bipedal	55–68 kg	1,4
Xenarthra						
Dasypus novemcinctus	long-nosed armadillo	3	coalesced	fossorial	3.7 kg	1,2
Cyclopes didactylus	silky anteater	3	coalesced	climbing	175–357 g	1
Tenrecoidea						
Tenrec ecuadatus	tenrec	3	coalesced	fossorial	1.6–2.4 kg	1
Macroscelidea						
Petrodromus tetradactylus	forest elephant shrew	3	separate	fossorial	160–280 g	1,3
Hyracoidea						
Procavia capensis	hyrax	2	coalesced	ambulatory	3.8 kg	1,2,3
Proboscidea						
Loxodonta africana	African elephant	3	coalesced	graviportal	2750 kg	1,2,3
Marsupialia						
Caluromys derbianus	wooly opossum	3	coalesced	climbing	200–500 g	1,3
Chironectes minimus	water opossum	3	coalesced	amphibious	604–970 g	1,3
Didelphis albiventris	American opossum	2	coalesced	ambulatory	2.5–5 kg	1,3
Didelphis virginiana	Virginia opossum	6	coalesced	ambulatory	2.5–5 kg	1,3

*Arranged phylogenetically by order after Archibald (2003).

†Based on reported ranges.

‡References for size and locomotion data: (1) Nowak (1991); (2) Sacher & Staffeldt (1974); (3) Vaughn (1986); (4) Rowe (1996); (5) Napier & Napier (1994).

Designation of ossification type

Two operational classes of proximal femoral ossification were defined: (1) a 'separate' pattern in which the femoral head and greater trochanter remain functionally separate throughout ontogeny as described above for humans (Fig. 2A), and (2) a 'coalesced' pattern in which the capital and trochanteric ossification centres coalesce into a single osseous epiphysis that spans the entire proximal end of the femur just as it does in many other long bones (Fig. 2B). Species were considered to display the 'coalesced' pattern if the ossification centres of the femoral head and greater trochanter made actual contact at any point along the femoral neck and/or fused to form a single structure prior to epiphyseal closure. Species were considered to display 'separate' ossification if the two bony epiphyses maintained at least some spatial separation until adulthood (epiphyseal closure). As the femoral head and greater trochanter both originate separately within a common chondroepiphysis (and thus always initially show some degree of separation early in ontogeny), these designations required that individuals of multiple ages be available for examination so as to reconstruct reliably the progression of ossification for each species. Isolated specimens were thus not suitable for classification because contact between the femoral head and trochanter, or lack thereof, was often not obvious until late in ontogeny. A single individual preserves only the stage of development it had reached at the time of death and is alone an insufficient indicator of the dynamic growth processes of its species. Given that species with 'separate' ossification were more difficult to identify, it is important to acknowledge the possibility that these taxa may be underrepresented in the present sample. Nevertheless, both patterns occur within diverse groups of species and so the effects of any sampling bias are assumed to be minor.

Body size and locomotion

We compiled body size and locomotion data from the literature (Table 1) in order to determine whether femoral ossification pattern might simply reflect body size and/or locomotor style. Body mass data were used to place species into six categories defined by increasing orders of magnitude: $10^1/10^2$ = species with body mass between 10 and 99 g; $10^2/10^3$ = 100–999 g; $10^3/10^4$ = 1000–9999 g; $10^4/10^5$ = 10 000–99 999 g; $10^5/10^6$ = 100 000–999 999 g; $10^6/10^7$ = 1000 000–9999 999 g. Locomotor habit was broadly defined following Feldhamer et al. (2004) using 11 categories: cursorial (running); ambulatory (walking); graviportal (heavy-bodied); climbing; suspensory; bipedal; saltatorial (jumping and leaping); fossorial (burrowing); amphibious (terrestrial and aquatic); aquatic (most of time spent in water); and volant (flying). Although underestimating the size variation and locomotor specializations of certain taxa, these general classifications functionally comprise all species in this analysis.

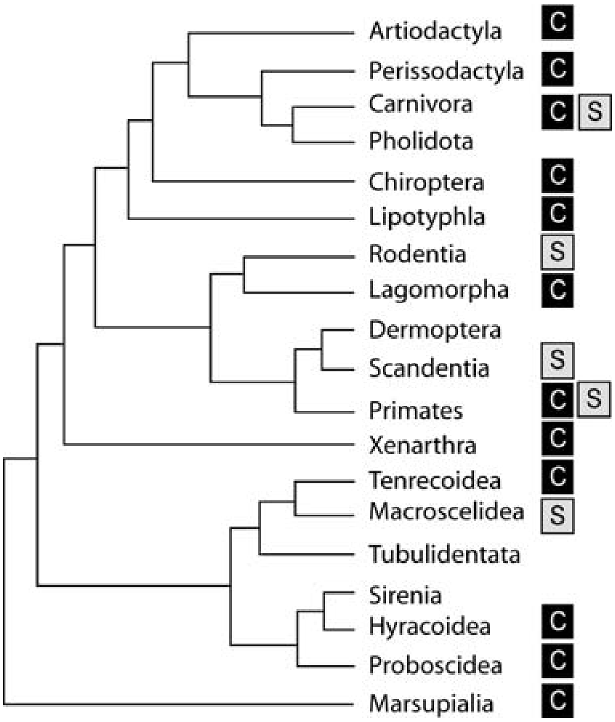

Fig. 3 Phylogenetic tree depicting higher-level relationships among mammalian groups (after Archibald, 2003); C = coalesced, S = separate. All major taxa are included in the tree, but ossification data were not available for Pholidota, Dermoptera, Tubulidentata and Sirena. Note the predominance of coalesced taxa and the appearance of separate ossification in divergent lineages. A test of phylogenetic independence conducted at the ordinal level (Reeve & Abouheif, 2003) confirms that ossification type is not significantly correlated with phylogenetic history at this level ($P > 0.20$). These results contradict a straightforward phylogenetic explanation for the emergence of the two ossification types in such diverse orders. Note also that both patterns of ossification are seen in carnivores and primates (see Table 1 for details), necessitating their analysis at the infra-order level to allow for variation in the character state.

Results

Ossification type

Ossification type varied considerably among mammals (Table 1, Fig. 3) and the classification of taxa was demonstrably independent of phylogeny in terms of higher-level relationships. When mapped onto a phylogenetic tree (Fig. 3), ossification type appears highly conserved within individual orders. However, Figure 3 clearly illustrates that although there is a general predominance toward the 'coalesced' pattern of ossification, 'separate' epiphyses are observed in diverse and distantly related lineages, making a straightforward phylogenetic argument for the development of the separate pattern unsatisfactory. Indeed, a test of phylogenetic independence (Reeve & Abouheif, 2003) reveals that ossification pattern is not significantly correlated with phylogeny at the ordinal level ($P > 0.20$). Although the lack of within-order variation suggests that phylogenetic history may explain the emergence and/or persistence of ossification type as families and species diverge within particular orders, there is clearly some other factor driving the initial evolution of these character states among distantly related lineages. For example, taxa in the coalesced group include marsupials, artiodactyls (including both the large white-tailed deer and the small mouse deer), perissodactyls, bats, carnivores and several primates (e.g. langurs, baboons, lemurs and galagos). The separate group includes hominoids, many rodents, tree shrews and marine mammals. Interestingly, hominoids and rodents are considered to be on opposite ends of a continuum with regard to growth, body size, reproduction, longevity, mortality and age at sexual maturity (Pianka, 2000), making it also unlikely that the different ossification patterns described here can be linked to a particular life-history variable. With the exception of one rodent species noted in Table 1 (*Erethizon dorsatum*), we did not observe within-species variation in either group.

Body size

Except for the largest size category (occupied only by the African elephant), there is nearly equal representation of coalesced and separate species across all six size classes, indicating no relationship between body size and mode of ossification (Fig. 4). For example, humans and apes share a similar (separate) ossification pattern with rodents, tree shrews and marine mammals. These species vary by several orders of magnitude in body mass, making it unlikely that the different ossification patterns can be ascribed to size.

Locomotion

Species were assigned to discrete locomotor categories in order to assess any association between ossification type and mode of locomotion (Fig. 5). The cursorial group includes only coalesced species and seems to dominate the graph in Figure 5(A). However, this results largely from the unusually large number of species in this single category (artiodactyls and carnivores are disproportionately represented; see Discussion and Table 1). If this group is removed (Fig. 5B), a better view of the ossification type in each remaining category is obtained, and there appears to be no consistent association between femoral development and locomotion.

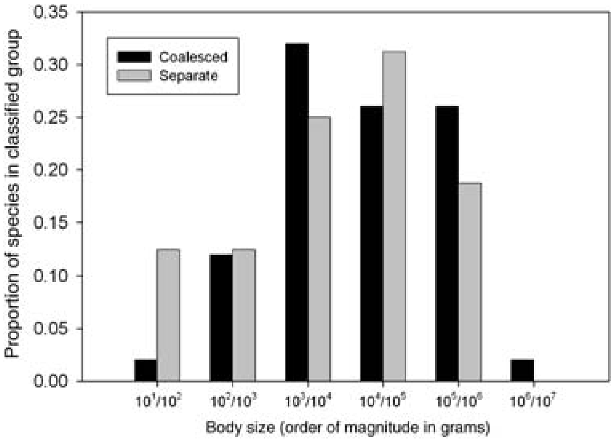

Fig. 4 Bar graph comparing the distribution (frequencies) of coalesced and separate species among the body mass categories (see text for size classifications). For each ossification class, the vertical axis is the proportion of total species represented in each mass category (e.g. number of coalesced species in $10^1/10^2$ size class/total number of coalesced species). There is no detectable relationship between ossification pattern and body mass.

Discussion

This study represents the first attempt to classify femoral ossification patterns in a wide range of mammals, documents previously unrecognized variation in a region of the skeleton central to bone biology research, and provides a framework for investigating the developmental basis of femoral architecture and mineralization. We found that pattern of femoral ossification varied considerably among mammalian taxa, and somewhat surprisingly, that it appeared to be independent of overall body size and locomotion. These results are difficult to interpret as the functional demands of the femur do differ across species. However, our sample covers a broad taxonomic range and we therefore suspect that there may be too much variation in locomotor style within orders to identify underlying relationships. For example, chimpanzees and humans both have separate femoral head and trochanteric epiphyses yet employ very different modes of locomotion (knuckle-walking vs. bipedalism). Interestingly, despite noted differences in femoral morphology between

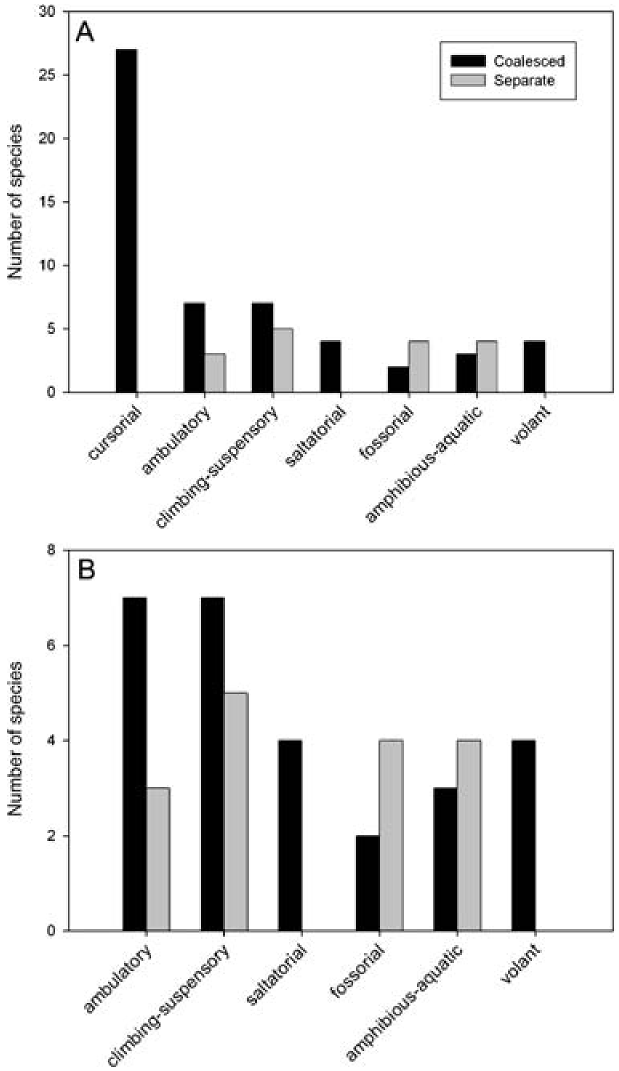

Fig. 5 Number of classified species in each locomotor category. Similar categories were combined to facilitate graphical representation. Ambulatory includes bipedal and graviportal species. (A) The two main cursorial groups (artiodactyls and carnivores) are disproportionately represented in the sample (see Table 1), which complicates interpretation of the remaining species. (B) Removal of the cursorial group provides a clearer view of the distribution of ossification type in the remaining locomotor categories. Representative species of both ossification types occupy a wide range of locomotor modes.

chimpanzees and humans (both macro- and microscopically; Kalmey & Lovejoy, 2002; Lovejoy et al. 2002; Lovejoy, 2005), both species have femora that are substantially more mobile and similar to one another when compared with those from cursorial carnivores and artiodactyls in which limb motion is much more stereotyped (habitual protraction and retraction). It is noteworthy that all cursorial species have both coalesced femora and limited hip mobility. There may therefore be a 'threshold' effect whereby the locomotor demands of a species require increased femoral mobility and neck length associated with 'separate' morphology (discussed below), but once such a shape is established, secondarily derived differences in femoral anatomy readily occur with increasing locomotor diversity.

Evolutionary implications

A coalesced epiphysis may represent the primitive condition for the mammalian proximal femur, with separate ossification being a novel acquisition in a number of derived lineages. This idea is supported from a phylogenetic perspective (Fig. 3), as well as by consideration of general trends in mammalian evolution. For example, the proximal femur in *Didelphis* (opossum) develops from a single cartilaginous cap without secondary ossification in the femoral head (Nesslinger, 1956). This genus belongs to the oldest and most generalized family of marsupials (Vaughan, 1986) and is likely to have preserved the primitive mammalian condition of femoral ossification. With the exception of some bipedal dinosaurs in which the femoral head is offset from the shaft, the femur of primitive reptiles is cylindrical and its proximal articular surface is aligned with the long axis of the shaft (Romer, 1956). Mammals differ from their reptilian ancestors by having increased flexibility of the axial skeleton and greater range of motion of the limbs (Vaughan, 1986). This difference is much more pronounced in the hindlimb than in the forelimb because of the latter's flexibility as provided by its synsarcotic fixation to the thorax. In many mammals, the femoral head has become offset from the shaft allowing greater flexibility at the more restrictive acetabulum (Carroll, 1988). Thus, the constant coalescence of all osteogenic centres as in the proximal humerus may represent the primitive condition, with displacement of the femoral head from its shaft requiring a more complex developmental process in some species that necessitate increased hip mobility (i.e. rodents, hominoids, pinnipeds) relative to those characterized by more stereotyped limb movements (i.e. carnivores and artiodactyls). We therefore hypothesize that geometry, rather than size, is the principal determinant of proximal femoral ossification pattern. Specimens exhibiting separate ossification appear to have longer, more constricted and well-defined femoral necks than do those with coalesced ossification. The latter appear to have

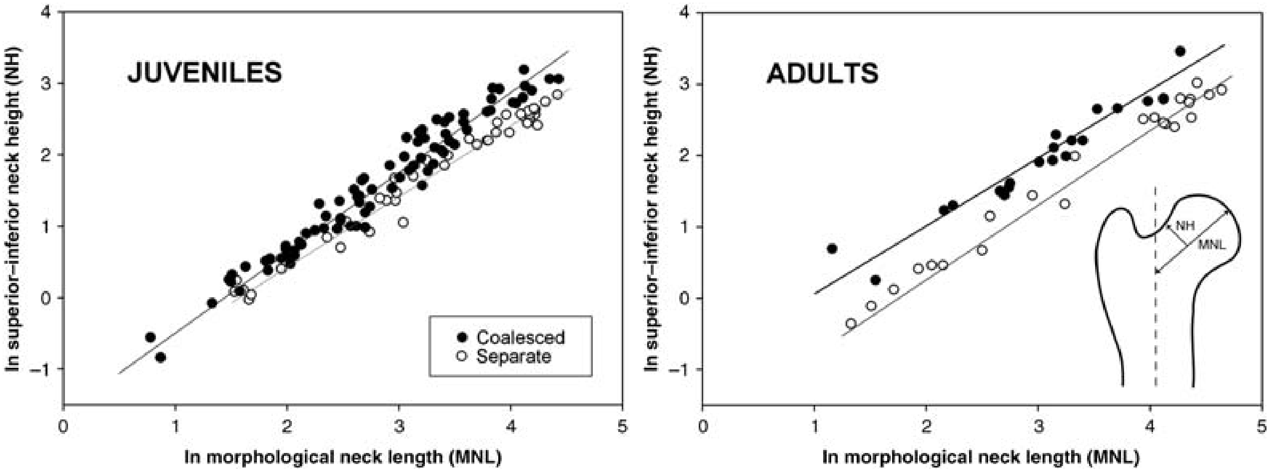

Fig. 6 Comparison of femoral neck length vs. superior–inferior neck height in juvenile (left) and adult (right) mammals classified according to ossification type. Each point represents a single individual for which metric data were available, and all major taxa are represented. Data were measured in millimetres and natural-log transformed to facilitate graphical representation due to the large size range present in the sample. Individuals with separate epiphyses have longer and more constrained femoral necks (i.e. smaller neck height) relative to those demonstrating the coalesced pattern. Analysis of covariance (ANCOVA) reveals a significant difference in least-squares slopes between separate and coalesced taxa in juveniles ($P < 0.01$) and a significant difference in elevation between the groups in adults ($P < 0.001$). Although such morphometric differences in the adults are clear, the distinction evident in the juvenile sample (encompassing a vast age and size range) further supports the link between femoral geometry and pattern of growth.

more humerus-like femoral dimensions. Figure 6 illustrates a simple comparison of femoral neck length and height (i.e. constriction) demonstrating narrower and more elongated femoral necks in individuals with a separate ossification pattern. These differences, although apparent in the juvenile sample representing a broad range of size and ages, are most pronounced in adults, suggesting a strong link between femoral shape and pattern of growth/ossification. Analysis of covariance (ANCOVA) confirms that there is a significant difference in least-squares slopes between separate and coalesced taxa in juveniles ($P < 0.01$) and a significant difference in elevation between the groups in adults ($P < 0.001$; Fig. 6). A more comprehensive multivariate analysis using additional femoral metrics is currently underway but these preliminary data suggest that the head and trochanter may remain separate in mammals with long and distinct femoral necks simply as a consequence of their increased spatial separation. Therefore, geometric changes, be they due to functional demands of loading and/or phylogenetic constraint, are probably the basis for the differences in femoral ossification pattern described here. This could explain why separate ossification appears in divergent mammalian lineages such as hominoids and rodents if these taxa did indeed evolve similarly shaped femora to enhance hip mobility.

Human hip pathology

The variation in ossification of the proximal femur is particularly interesting with regard to known pathologies of the human hip joint. A generally flattened and non-spherical femoral head (often termed 'pistol grip' deformity; Stulberg et al. 1975), resulting from such disorders as Legg–Calve–Perthes disease or a slipped capital epiphysis, is associated with mild to severe growth disturbances and reduced hip mobility (Tanzer & Noiseux, 2004). These conditions are often characterized by a shortened femoral neck with atypical contact of the head and greater trochanteric epiphyses (Edgren, 1965) much like the normal coalesced pattern described for many of the mammals studied here. Indeed, these human pathologies putatively stem from an abnormal connection of the head and trochanter within the initial chondroepiphysis (Siebenrock et al. 2004, and references therein). Such deformities not only disrupt growth and impair mobility, but also are associated with femoroacetabular impingement (inadequate clearance between the femoral neck and acetabulum; Murphy et al. 2004), and as a direct consequence, early-onset osteoarthritis (Harris, 1986; Ganz et al. 2003). From our observations of published radiographs of patients suffering from such disorders (Edgren, 1965), we note that their femoral morphology is remarkably similar to that of a normal coalesced species. This further suggests that femoral morphology is directly related to the behavioir of its epiphyses.

Concluding remarks

Differences in femoral ossification should be duly considered when comparing hip anatomy and architecture across a wide range of mammals. This is especially important when using animal models to understand human pathologies, as many commonly used laboratory species do not share the human developmental pattern. Kuo et al. (1998) recognized differences in femoral morphology between chimpanzees, dogs and humans, and noted that this should be taken into account when using animals to infer function and loading in human hip replacement designs. Indeed, we further emphasize this point as the three species also differ in their femoral ossification patterns. Until this variation is better understood, we would stress that analyses of femoral morphology should preferentially restrict comparisons to only mammals with similar patterns of ossification.

Our future research is focused on understanding the developmental basis of these differences in femoral ossification. By determining the molecular mechanisms that produce coalesced vs. separate epiphyses within an initially similar chondroepiphysis, it may be possible to identify therapeutic targets for the treatment and prevention of human hip disorders such as femoroacetabular impingement and early-onset osteoarthritis.

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