How does evolutionary evaluation illuminate body size among canids?

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ABSTRACT
In this review, we examine mammalian body size as it reflects life history and genomic composition, with a primary focus on canids and the domestication of the gray wolf. The range of variation in body size is greater among Carnivora than any other terrestrial order. In the Canidae, this range is some 2 orders of magnitude. Macroevolutionary patterns (eg, Bergmann's rule and Cope's rule) that have been proposed in the past often fail to comport with modern studies on this aspect of carnivoran evolution. Clades often begin with small to medium size (mesocarnivorans) and diversify mostly in a right-skewed (larger) direction. The observed variation in body size reflects phenotypic plasticity in response to life history. As with many Mammalia, historically high gene flow (hybridization and introgression) among canid lineages has been a crucial source of genomic variation (nuclear and mitochondrial), yielding potential for high plasticity of phenotypes such as body size. In addition, epigenetic marks connect genetic expression with environmental conditions in the manifested phenotypes. Among Mammalia generally, a larger size is associated with a longer life span, reflecting the foregoing genomic composition and environmental influences over a long geological time. However, the larger modern domestic dog breeds trend toward shorter life spans. The latter appears to reflect genetically mediated phenotypes that emerged secondary to domestication but nonetheless against a background of broadly and deeply conserved developmental and physiological patterns and body plans.

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Finarelli reported that body size among canids ranges from 1 (fennec fox, Vulpes zerda) to 35 kg (gray wolf, Canis lupus lupus). However, Mech reported that adult male wolves average 41 to 45 kg (up to about 55 kg), and female adults 37 to 39 kg. Among world wolves, one of the smallest, the Arabian wolf (Canis lupus arabs), is reported to weigh 18 to 20 kg. Finarelli evaluated multiple independent trends that led to increasing canid body size across 40 million years, with new canid taxa arising in 4 episodic pulses (punctuations). Three of these pulses led to larger body size (Paleogene and Neogene Periods) and 1 to smaller size (Quaternary Period), while the probability for extinction of any single taxon remained unchanged. Large predator body size is usually associated with hypercarnivory that over geological time can become an evolutionary trap for an entire clade. However, both body size extremes (large hypercarnivorous and small hypocarnivorous) have revealed shorter extant periods pre-extinction, compared to mesocarnivores.

Domestication

Darwin noted: “Domestic breeds often have an abnormal or semimonstrous character, as amongst dogs, the Italian greyhound, bulldog, Blenheim spaniel, and bloodhound...” Ballard and Wilson suggested that smaller animal size postdomestication could be associated with niche ecology, wherein driving forces could include or exclude human interventions.

Body weight among domestic dogs ranges from 2 to 100 kg, and height at the shoulder ranges from 15 to 80 cm. Artificial selection by humans (intentional or unintentional) has established covariances among long bones, vertebrae, and skull morphology. The resulting panoply of modern dog breeds has been maintained by close inbreeding, beginning during the Victorian Period.

Macroevolutionary Patterns

More than a century of literature in paleobiology has focused on “rules” or “laws” regulating species’ adaptation over time. Body size often has been the central feature in these formulations, and size thus begs consideration in the present review.

Bergmann’s rule

Bergmann originally proposed 3 principles regarding the relationship between genus-level animal body size and climate (translation in James): 1) homeothermy depends on the balance between internal heat production and heat loss from body surfaces; 2) there are physical limitations on body surface-to-body volume ratio; and 3) smaller species in a genus should occur in warmer climates.

Regarding canids, Meiri et al examined museum skulls of 44 species of wild carnivores, using condy- lar basal length as an index of body size. All were mainland adults. Regression of measurements on latitude found that 22 species were consistent with Bergmann’s rule and 22 were not. The wild canid species in the sample (Canis aureus, Canis latrans, C lupus lupus) appeared to obey Bergmann’s rule. However, after a detailed analysis of previous studies that validated the Bergmann’s rule, the authors suggested that these earlier conclusions could be “an artefact of nonrandom sampling and submission.”

Janssens et al noted that small domestic dog size was observed well before known climate change, among specimens such as the Bonn-Oberkassel and Natufian dogs from an end-Pleistocene (late Paleolithic) human burial. On the other hand, large domestic dogs have been observed from well before the post-Victorian expansion of selective dog breeding. For example, the animal remains at the Cherokee Sewer Site (in Iowa; 7,430 to 7,020 calibrated years before the present [BP]) include 2 large domestic dogs that lived several thousand years after the probable initial gray wolf domestication (in Eurasia by circa 23,000 to 16,000 years BP). The Cherokee Site also dates several thousand years before the Victorian age. It is well recognized that, since the Victorian age, increasingly intensive human intervention has occurred via artificial breeding selection.

The foregoing observations indicate a size variability that likely occurred through conscious or unconscious selection of domestic dogs for breeding, certainly well before the Victorian period. Therefore, genomic and phenotypic plasticity that facilitated the foregoing events must have preexisted the indicated dating by a very substantial period of time.

Cope’s rule

Cope wrote: “Genera have been produced by a system of retardation and acceleration in the development of individuals; the former on preestablished, the latter on preconceived direction.” This general statement has come to be applied specifically to the evolution of mammalian lineages toward larger body size. The latter alone does not confirm long-term “mid-size” success, but the idea nonetheless is thought-provoking in that direction, given the extinction of giant hosphercyon and borophagine lineages (see below).

Additionally, there is a physiological constraint on ever smaller sizes (a “left wall”) that is more relaxed for larger sizes. Thus, while expanding genera can yield size gradients bidirectionally, body size in general may increase because there is more “room for expansion” in that direction. Stanley noted that exceptions to Cope’s rule are recognized, although the mode tends to remain constant at a modest size within the taxon.

These observations shed some light on the history of the 3 subfamilies of North American Canidae (Hesperocyoninae, Borophaginae, and Caninae) that coexisted around 25 million years ago. The former 2 trended toward increasing body size and a coevolving shift to hypercarnivory. Trophic specialization, combined with declining population density, set the stage for the ultimate extinction of both clades.

Island rule

Foster noted that small-sized island taxa (rodents and lagomorphs) are larger than mainland
populations of the same taxa, while artiodactyls and carnivores are smaller in size. This was the original form of the island rule. Lomolino22 expanded the Foster26 database, observing an insular mammalian trend ranging from gigantism (among smaller species) to dwarfism (among larger species), converging eventually on an “optimal” body plan within the ecological niche. This observation could help to explain mesocarnivoran success.

Putative mechanisms for changes in physical size within taxon include 1) less predation; 2) less competition, allowing taxa to evolve toward intermediate size; and 3) more limited resources.23 The study by Meiri et al20 used metrics that included skull (condylobasal) length, upper canine tooth maximum diameter, and lower carnassial tooth length. Average measurements from the insular population were divided by the average value of the “corresponding nearest mainland population, yielding a relative insular body size.”

By 2011, Meiri et al20 had assembled a large database of body masses, with skull and dental measurements among mammals, birds, and reptiles. Mammalian analyses were based on island and mainland paired adult populations (1,184 islands, 15 orders, 45 families, and 276 species).28,29 Among Canidae, the correlation between the size ratio of insular and mainland species and body mass was low, thus not overtly supporting the island rule, compared to earlier studies.28 However, it seems appropriate to comment that factors influencing these types of studies can include correct species identification; estimation of age at death (juvenile or adult); species-appropriate bone specimens and metrics; measurement accuracy; and expected variance among outcomes. Thus, some differences among studies are expected.

Resource rule

McNabb32 recognized that the allocation of energy for changes in patterns of growth and development can fluctuate in response to resource availability, thus accounting (at least in part) for size trends in mammalian evolution. For example, the early coexistence of South American canids evolved eventually into 3 distinct morphotypes, using skull morphometrics as a proxy for overall variation in size and shape.33 The authors stated: “Size differentiation can be interpreted as a mechanism that eventually allowed these taxa to fulfill different ecological niches.”

Thus, physiologically and ecologically driven traits do answer some questions relating to body size variation. In a recent study,34 the relationship of intraspecific variation in body size among mammals was correlated with resource availability and starvation resistance. Starvation resistance refers to larger sized animals with larger fat stores being able to withstand food shortages in highly seasonal environments. This certainly brings Bergmann’s rule into some focus, but Henry et al34 pointed out that the correlation is not strong. These findings, based as they are on real data and interpreted using rather complex mathematics, also may be relevant to interspecific body size variation. However, as Karasov and Martinez del Rio35 cautioned, one must tread carefully. Species in a clade are not “statistically independent data points.” They differ within historical constraints (channeling). Thus (again), degrees of variability are expected.

Reconsideration of Cope’s rule

Here, we might further consider Cope’s rule in its original context, known as the Cope Law of the Unspecialized, which states that “evolutionary novelties” among animal founders of a new lineage tend to be small-to-medium in size, and are unspecialized.22,36 The general observations by Marnweeck et al37 on the life history traits of small carnivorans, shed some light on their characteristics: 1) species rich and diverse; 2) occupying a wide range of niches; 3) intermediate in the trophic hierarchy; 4) short lifespan; 5) relatively high reproductive rate; 6) relatively small home ranges; and 7) relatively large population. These traits are carried forward as descendents adapt to the ecological conditions of new niches. However, as with intraspecific size variation, Raia and Fortelius36 found the increase in body size in Cope’s rule exhibited “weak directionality.” Yet again, we observe that degrees of variability, both biologically and among studies, are expected.

Longevity and related traits

Greater body size among mammals generally is accompanied by a longer lifespan. Size and life history traits are thought to be subject to the same selective forces,38 thus presenting a related macroevolutionary pattern. Jiminez39 plotted body mass against lifespan for individuals from 38 wild canid species and found a modest but statistically significant positive relationship (y = 0.2135x + 10.0289, r² = 0.1811, P < .0001). Paradoxically, the opposite is true for the domestic dog.40 Cichon41 showed that longevity is the result of a complex interaction among life history traits, including the allocation of resources to growth, reproduction, and somatic repair.

The rapid development of artificial selection for increased body size did not allow for the optimization of the complex physiological processes of reproduction and organ repair. Indeed, Kraus et al40 observed that shorter lifespan among large domestic dogs is associated with a higher rate of aging, as well as the correlated incidence of other morbidities,42–44 implying failure of cellular repair mechanisms. Relating to morbidity, rate of aging, and indirect effects on average longevity, it should be noted that the pervasive genomic effects of post-Victorian inbreeding among most 19th- to 21st-century dog breeds average about 25% (the equivalent of a full sibling).42,43 At least among the latter domestic dog populations, many outcomes have not been positive in terms of population health.42

These various macroevolutionary patterns can be summarized as environmental and ecological conditions that impose selective forces on the coevolution of both body size and the pattern of life history traits (reproduction, development, and metabolic...
pathways). It is our view that a capacity for such complexity of genomic patterns and complex phenotypic plasticity must have preexisted across taxa, over a long geological time.

**Phenotypic Plasticity**

Phenotypic plasticity refers to the presence of different phenotypes (morphology, physiology, and behavior) resulting from the same genotype, in response to changing environmental conditions. Body size among animals is a trait that commonly exhibits plasticity, especially in response to changing nutritional and thermal conditions, as predicted by the resource rule. Moreover, different genotypes can display differing capacities for plasticity in response to the same stressors.

**Domestic dog**

The modern dog is an example of intraspecific size radiation driven by domestication. Skull morphometry can supply quantitative metrics of plasticity. Among domestic dogs, the wide spectrum of skull size and shape varies on the same order of magnitude as the variation encompassing order Carnivora. Dog skull morphological patterns generally conform to those of the canid genera Canis, Cuon, and Lycaon. Morphologic variations during domestication probably arose within this conserved developmental pattern. Nonetheless, as Morey correctly observed, “For all their remarkable variability in size and form, modern dogs have not accomplished the genetic re-organization necessary to transcend a basic phylogenetic boundary.”

**Genomic Aspects**

Given the critical importance of the genomic landscape that provides for an underpinning of plasticity, an overview of relevant canid genomics is appropriate. Hypothetically, mutations in genes that regulate development and body plan could explain the rapid evolution of morphological variation among modern domestic taxa. The authors proposed a similar mechanism for generating new alleles. However, according to Fondon and Garner, typical mutation rates are insufficient to account for rapid phenotypic changes among domestic animals during artificial breeding selection.

Heterochrony, as a driver of rapid phenotypic transformation, is an acceleration or retardation of traits along an ontogenic continuum. Drake evaluated a 3-D morphometric analysis of an ontogenetic series of skulls of *C lupus lupus*, compared to skulls of adult dogs from 106 modern domestic dog breeds. There was no mathematical resemblance of any breed of domestic dog to juvenile or adult wolves, thus calling into question any simple explanation invoking heterochrony in domestic dog diversity.

Geiger compared dog cranium phenotypes from a series of juvenile to adult specimens, using geometric morphometry to elucidate patterns of 3-D change. Neomorphism (novel phenotypes) was evident in pre- and perinatal stages, while pae-domorphism (heterochrony) dominated postnatal development. The authors observed that “skull morphology is not a good indicator of domestication.”

**Nuclear DNA**

Microsatellites (or tandem repeats) in the genome have high mutation rates that can lead to high genetic diversity. Fondon and Garner examined DNA sequences from 92 dog breeds, looking at encoded transcription factors that are involved in morphological development. They found numerous tandem repeats associated with differences in skull and limb morphology.

The authors found similar coding repeats in the gray wolf (*C lupus lupus*), coyote (*C latrans*), arctic fox (*Vulpes lagopus*), and swift fox (*Vulpes velox*), perhaps relating tissue or cell type to morphological phenotype. A single allele, insulin-like growth factor 1 (IGF-1), was associated with all small domestic dog breeds that were examined by Sutter et al. The IGF-1 gene explained 50% of the variation among adult sizes. According to Gray et al., the IGF-1 gene was assimilated from the Middle Eastern gray wolf (*C lupus lupus*) fairly early in dog domestication, circa 12,000 BP.

Akey et al. reported extensive genotyping of autosomal SNPs (single nucleotide polymorphisms). The authors identified 155 of the most differentiated genomic regions in 275 dogs, representing 10 diverse modern breeds having “signatures” of recent artificial selection. These regions influenced some of the most variable phenotypic expressions, including size and skeletal morphology. Concerning size, however, Boyko et al. reported just 6 quantitative trait loci that explained most of the size variation.

In another study, Plassais et al. examined over 144 modern dog breeds, along with 54 wild canids and 100 modern village dogs. The authors identified strong impact variants associated with 16 phenotypes that together explained > 90% of dog body size variation. There were eight body size loci that each contributed 2% to 9% of the variance, while 3 loci (including IGF-1) each contributed 12% to 15% of the variance.

Ostrander et al. reviewed the genomics and demographic history of domestic dogs. Six genes (including IGF-1) were associated with 46% to 53% of the body size variation among dog breeds. Evolutionary bottlenecks were observed in wolf and dog populations, at the onset of domestication. In small bottlenecked populations, selection is weakened, leading to potentially deleterious variation.

Plassais et al. evaluated the relationship between domestic dog body size and the locus surrounding the IGF-1 gene. The authors found that a single long noncoding RNA (antisense to IGF-1 [IGF1-AS]) allele variant complexed with a protein-coding mRNA, blocking translation and thus affecting IGF-1 production. High IGF1-AS small allele (C) frequency was found in several non-wolf canids and in foxes. The observation indicated that the C allele likely is more ancestral. The T allele (large size) was segregating among gray wolves prior to 53,000 BP. It appears to
have been nearly lost and may have been “revived” in canids secondary to late human interventions. Thus, while the T allele also is “relatively” ancient, it does not appear to be foundational in terms of the size plasticity among modern domestic dogs. 62

The recognized higher frequency of the more ancestral IGF1-AS allele (C) among small dog breeds and small wild canids, and the T allele among larger breeds and modern wolves, reveals an important evolutionary contribution to the size plasticity among canids. Furthermore, Plassais et al62 also found the C allele among pandas, cats, and ferrets. The latter data further confirm that the C allele of IGF1-AS original,62 since the divergences of the multiple species evaluated extend deep into geological time (barring separate origins of IGF1-AS or convergence).

Transposable elements (TEs; transposons or jumping genes) are DNA sequences that can insert spontaneously into new positions on the chromosome, potentially rearranging the genetic architecture by causing DNA deletions, inversions, translocations, and duplications.65 The result is a change in gene expression contributing to intraspecies variation.65 TEs comprise 31% of the dog genome, and their effect on variation is breed specific.65

Mitochondrial genome (mitochondrial DNA)

Larger body size is correlated with lower basal metabolic rate that in turn reflects the density and activity of mitochondria.66 There are 1 to 10 copies of mitochondrial genome (mtDNA) in each mitochondrion, inherited maternally in a non-Mendelian fashion.66 The rate of base pair substitution in mitochondrial DNA (mtDNA) is approximately 10 times that of nuclear DNA, providing scientists with a “high resolution analysis of the evolutionary process.”67 This has been most trenchantly applied to deciphering the lineages and geographic origins of domestic animals, including the dog.68

Popadin et al69 reported that protein-coding mtDNA of larger mammals have a 43% higher rate of slightly deleterious mutations, compared to their smaller ancestors. This may explain, in part, the decline and extinction so often observed in lineages evolving ever-larger body size.

Epigenome

Epigenetics refers to variation in phenotype due to changes in gene expression (on or off or modified expression) without any change in DNA sequences.70 Epigenetic actions are a common and potent mechanism underlying an organism’s plastic response capability to novel or changing environments.71–73 Such epigenetic marks can be heritable and, in the longer term, the phenotypic changes can be followed by “genetic accommodation” via a change in allele frequencies or gene networks.72,74,75 Thus, epigenetic marks could explain the discrepancy between the prevalence and appearance of a phenotype and the results of classical genetics and genome-wide associations in the study of domestication.74

In summary, the impact of environmental conditions and resources on plasticity must be understood as a complex adaptive system involving the interaction of nuclear DNA, mtDNA, and epigenetic mechanisms.

Gene flow and hybridization

Gene flow is the movement of genes among genetically distinguishable populations, resulting in viable offspring.77,78 Introggression, in which traits are overtly altered, refers to the interspecies movement of alleles resulting from hybridization and back-crossing.79 Together, these terms describe a “fundamental force in speciation and adaptation.”79 Since hybridization is more common in nature than genetic mutation, it may constitute a much greater reservoir for adaptive variation.80 However, the outcome also can be highly deleterious, especially if the genetic exchange is unidirectional, potentially extirpating one of the species (“genetic swamping”).81,82

Using data from nuclear and mitochondrial DNA, Gopalakrishnan et al83 mapped the interspecies gene flow across Canis. The data revealed that the dog and gray wolf complex has received introgressions from golden jackal (C aureus; 2 events); golden wolf (Canis lupaster, northwestern); golden wolf (C lupaster, eastern); and an unknown “ghost” wolf lineage or basal canid. In addition, both northwestern and eastern golden wolf populations received introgression from the Ethiopian wolf (Canis simensis) that may have contributed indirectly to the dog and gray wolf complex.

Extensive hybridization has occurred between the eastern wolf (Canis lupus lycaon) and the eastern coyote (C latrans),84 resulting in introgression and fertile offspring that exhibit intermediate phenotypes in behavior and ecological niche characteristics. The altitude-adaptive gene (EPAS1) in the Tibetan gray wolf (debated taxonomy) and in the closely related Himalayan wolf (Canis himalayensis) suggests that about 39% of the genomes (including EPAS1) of these 2 wolf populations derived from an unknown ancient canid lineage.85

Among New World Canidae, hybridization has been described between the pampas fox (Lycalopex gymnocercus) and Andean fox (Lycalopex culpaeus).86 Hybridization also has been reported between the kit fox (Vulpes macrotis) and swift fox (V velox).87

Gene flow and hybridization: domestication

Hybridization is well documented in the history of the domestic dog. Darwin86 recorded anecdotal observations of dog crosses with wolf, dingo, and jackal. In other studies, investigators concluded that 11% of dingoes and 2% of dogs were hybrids,88 while Galov et al90 reported hybridization between golden jackal (C aureus) and domestic dog.

Among further examples, Kopaliani et al91 described gene flow between livestock-guarding dogs and wolves in Georgia (Caucasus): 10% of wolves and 20% of dogs were most closely related to individuals in the other population. In a central Italian agricultural landscape, approximately 50% of wild wolves (C lupus lupus) had genomic evidence of recent interbreeding with domestic dogs.92
east Eurasia, 5.5% of modern dog genomes represent introgression from a putative ancestor of the Japanese wolf (Canis lupus hodophilax).

Hybridization commonly results in genomic changes via the proliferation of TEs and promotion of speciation. Regarding epigenetics, methylation patterns differ significantly between gray wolves and domestic purebred dogs. Hypermethylation was found to be concentrated in dog TEs that govern gene function and stability. Moreover, many of these methylation marks are highly heritable. MicroRNAs can be derived from TEs, and histone modification (epigenetics) can regulate TE expression.

Gene flow in mtDNA has been documented in hybridization between the coyote (Canis latrans) and Minnesota and Canadian wolves (Canis lupus lycaon), resulting in a larger size in the coyote, with subsequent range expansion. Other examples include hybridization of the red wolf (Canis rufus) with the coyote and gray wolf, hybridization of the Ethiopian wolf (C. simensis) with the domestic dog, and recent hybridization between the wolf and the Scandinavian and Finnish Spitz breed of dog. Thus, complex genomic events over geological time have contributed substantially to the history that has led to the domestic dog.

**Conclusion**

The order Carnivora displays the largest range of body size and mass among terrestrial Mammalia. Among Canidae, body size varies by 2 orders of magnitude, but size itself is not statistically different from other carnivore families. The implication is that the genomic capacity for size variance among modern domestic dogs very likely is rooted deeply in geological time.

Early researchers proposed rules governing geographical and temporal determinants of body size, though larger systematic studies often have yielded conflicting results. Clades often begin with small to medium size (mesocarnivorans) and diversify mostly conflictive patterns differ significantly between gray wolves and domestic purebred dogs. Hypermethylation was found to be concentrated in dog TEs that govern gene function and stability. Moreover, many of these methylation marks are highly heritable. MicroRNAs can be derived from TEs, and histone modification (epigenetics) can regulate TE expression.

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Early researchers proposed rules governing geographical and temporal determinants of body size, though larger systematic studies often have yielded conflicting results. Clades often begin with small to medium size (mesocarnivorans) and diversify mostly in a right-skewed (larger) direction. Body size variation reflects phenotypic plasticity in response to life history and survival-directed adaptation. Phenotypic plasticity, in turn, reflects an underlying genomic landscape that includes dynamic interactions among nuclear DNA, mtDNA, and epigenetic mechanisms. Research into canid genomics must consider all 3 of these genetic domains, especially since gene flow permeates canid evolutionary history, and contributes to this family’s successful episodes of dispersal, colonization, and radiation into new continents.

Herein lie the roots that led to the domestic dog.

Domestication of the gray wolf and associated 19th- to 21st-century interventions by humans have resulted in intraspecific radiation of major dog phenotypes that include body size. In the modern domestic dog, body size varies within and between breeds and is accompanied by differences in longevity, morbidity, and rate of aging. These observations clearly invite further examination of the domestic dog in the context of a successful mammalian family. A focus that seems appropriate includes frequently adventitious effects related to historical phenotypic plasticity and the constraints that have resulted from recent pervasive inbreeding.

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