High Investment in Reproduction Is Associated with Reduced Life Span in Dogs

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ABSTRACT: Prominent differences in aging among and within species present an evolutionary puzzle. The theories proposed to explain evolutionary differences in aging are based on the axiom that selection maximizes fitness, not necessarily life span. This implies trade-offs between investment in self-maintenance and investment in reproduction, where high investments in growth and current reproduction are associated with short life spans. Fast growth and large adult size are related to shorter life spans in the domestic dog, a bourgeoning model in aging research; however, whether reproduction influences life span in this system remains unknown. Here we test the relationship between reproduction and differences in life span among dog breeds, simultaneously controlling for shared ancestry and recent gene flow. We found that shared ancestry explains a higher proportion of the among-breed variation in life history traits, in comparison with recent gene flow. Our results also show that reproductive investment negatively impacts life span, and more strongly so in large breeds, an effect that is not merely a correlated response of adult size. These results suggest that basic life history trade-offs are apparent in a domestic animal whose diversity is the result of artificial selection and that among-breed differences in life span are due to a combination of size and reproduction.

Keywords: aging, reproduction, growth, trade-off, domestic dog.

Introduction

Aging is the result of physiological deterioration of an organism, which increases the probability of death. Across vertebrates there are striking differences in aging, resulting in very different life spans (Jones et al. 2014). For instance, the Greenland shark (*Somniosus microcephalus*) approaches 400 years and reaches sexual maturity at about 150 years (Nielsen et al. 2016). At the other extreme, the turquoise killifish (*Nothobranchius furzeri*) has a median life span of up to 7 months and can reach sexual maturity in 3–4 weeks in captivity (Kim et al. 2016). Although aging is ubiquitous, the prominent differences among species present an evolutionary puzzle. The theories proposed to explain evolutionary differences in aging are all solidly based on the axiom that selection maximizes fitness (i.e., survival and reproduction), not necessarily life span (reviewed in Maklakov and Chapman 2019). As a result, the strength of selection on a trait declines after sexual maturation and with advancing age, resulting in Haldane's famous "selection shadow" (Haldane 1941; Hamilton 1966; Maklakov and Chapman 2019). Selection can thus favor traits that bestow benefits in early life, even if these same traits incur costs later in life, particularly so if costs are apparent only toward the end of the reproductive life span (Medawar 1952). Such late-life detrimental effects can result from antagonistic pleiotropic effects, where an allele has beneficial effects in early life but has detrimental effects in late life (Williams 1957), or from trade-offs in resource allocation (e.g., if fast growth compromises life span; Kirkwood 1977). These two hypotheses to explain evolution of aging are not mutually exclusive.

Because animals have a limited energy budget, energetically demanding activities, such as growth or reproduction, inevitably consume resources that will no longer be available for other energetically demanding activities, such as somatic maintenance, resulting in faster physiological deterioration and reduced longevity (Kirkwood 1977; Kirkwood and Holliday 1979; Kirkwood and Rose 1991; Chen et al. 2020). Such trade-offs between growth, development, reproduction, and somatic maintenance underlie life history theory (Kirkwood and Austad 2000; Jones et al. 2008; Kaplan and Robson 2009; Healy et al. 2019).

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Fast growth and high investment per reproductive event compromise individual life span (Metcalfe and Monaghan 2003; Austad 2010). At a within-species level, studies on mice, rats, and dogs selected for fast growth or large body size found that they exhibit reduced longevity (Patronek et al. 1997; Miller et al. 2000; Bartke et al. 2001*a*; Rollo 2002). Long-lived mutants, on the other hand, exhibit major reductions in growth rate and adult body size (Miller et al. 2000; Bartke 2017). Experimental evolution studies have demonstrated negative associations between early-life fitness and longevity in *Drosophila* and other invertebrates (Rose and Charlesworth 1980; Travers et al. 2015). At an among-species level, fast-growing species show short life spans compared with slow-growing ones (Bielby et al. 2007; Jones et al. 2008). Furthermore, a recent review that surveyed 26 studies involving 24 different species of bird, mammal, and reptile found only five studies that did not detect a trade-off between early- and late-life fitness (Lemaître et al. 2015), indicating that high investment in early reproduction has detrimental effects in late-life fitness. The fact that most studies of natural populations were able to detect the predicted trade-offs is surprising, as selective mortality acting on poor-condition individuals could remove them from the population, thus reducing the signal for low early-life reproductive effort, masking the existence of a trade-off. Greater understanding of the trade-offs that drive differences in longevity require disentangling the effects of growth and reproduction, ideally in a setting where the potential confounding effects of extrinsic mortality and individual differences in resource acquisition (van Noordwijk and de Jong 1986) are minimized.

The domestic dog represents a unique animal model, as its biology has several distinctive aspects that are relevant for aging studies. Because of selective breeding, there are almost 20-fold variations in body size and more than twofold differences in life span. This striking phenotypic diversity among dog breeds has been generated under circumstances where persistence is ensured despite potential fitness costs associated with the selected traits, which presents an excellent opportunity to gain greater understanding of the potential life history trade-offs. Dogs and humans have coevolved and share recent evolutionary selection processes, such as adaptation to digestion of starch-rich diets (Axelsson et al. 2013), and there are clear signs of convergent evolution in the human and dog genomes (Theofanopoulou et al. 2017). Purebred dogs can also be considered to be freed of extrinsic mortality, owing to the absence of predators, and have general access to sufficient resources as well as often high-quality health care. Finally, unlike laboratory animals, dogs share the human environment and lifestyle and are exposed to the same pollutants (Gilmore and Greer 2015). Dogs present an extraordinary level of phenotypic variation in skeletal structure, including overall size, leg length, and variants of skull shape, even in comparison with all canids (Drake and Klingenberg 2010). The largest dog breeds are more than one order of magnitude heavier than the smallest breeds, and litter sizes show fivefold variation, while longevity differs more than twofold among breeds (see the supplemental PDF). Previous studies have documented a decrease in life span with increasing body size across breeds (Speakman et al. 2003; Fleming et al. 2011; Greer et al. 2011; Selman et al. 2013), contrary to what is observed when comparing between mammalian species but in accordance with comparisons of individuals from the same species from laboratory strains of mice and rats (Miller et al. 2000, 2002; Rollo 2002), comparisons among horses or humans (Masoro and Austad 2010; Tapprest et al. 2017), and comparisons across evolutionarily divergent populations of garter snake (*Thamnophis elegans*; Bronikowski and Vleck 2010). The negative correlation between body size and life span in dogs has been attributed to fast growth (Kraus et al. 2013). However, it is unclear whether reproductive investment differences among dog breeds also influence life span when controlling for body size, reflecting the expected trade-off between reproduction and longevity.

Dog breeds present both an analytical challenge and an opportunity. The more than 400 described dog breeds can be considered closed populations, with many breeds having been developed mainly during the past 200 years as a result of artificial selection, reproductive separation, migration, and hybridization (Parker et al. 2004; Spady and Ostrander 2008). Gene flow has been suggested to play a particularly important role in the immense phenotypic variation observed among breeds, occurring during natural hybridization between gray wolves and dogs, between so-called local breeds from different geographic origin and with influence of different wolf populations, and within major clades of modern dogs (Vilà et al. 1997; Parker et al. 2004; Franz et al. 2016; Bergström et al. 2020). The aforementioned gene flow means that the relationships between dog breeds are unlikely to be treelike; thus, there is no appropriate phylogeny to represent their relationships, and typical comparative approaches to control for nonindependence of observations are unsuitable (Stone et al. 2011). Genomic analyses have allowed to disentangle the signatures of ancient shared ancestry and those of recent hybridization events, revealing the evolutionary history of dog breeds (Lindblad-Toh et al. 2005; Parker et al. 2017). This novel genomic information also allows detailed analyses accounting for the potential confounding effects of both shared ancestry and gene flow, both of which violate the assumption of independence of observations (and residuals in linear models; Felsenstein 2002; Stone et al. 2011). In addition, recent genomic information allows analyses of the contribution of shared ancestry and recent gene flow in shaping key phenotypic traits of dog breeds (e.g., Garamszegi et al. 2020).

Here we aim to gain greater understanding of the life history trade-offs associated with the strong artificial selection on body size across dog breeds. More specifically, we aim to test whether the life history trade-off between reproductive investment and life span is observed across dog breeds. We hypothesize that breeds with high reproductive investment (i.e., litter size multiplied by neonate weight) present reduced life span, when controlling for adult weight. We employ a mixed model approach, following Garamszegi et al. (2020), which allows us to simultaneously account for nonindependence due to shared ancestry and recent gene flow involved in the creation of new breeds (Felsenstein 2002; Stone et al. 2011; Larson et al. 2012; Parker et al. 2017). Using this modeling approach, we were also able to explore the influence of shared ancestry, which mostly represents the ancient origin of main breed types, versus recent hybridization events, occurring mostly during the past centuries, on key life history traits among dog breeds (Parker et al. 2017; Garamszegi et al. 2020).

Methods

We collected data on life span (years), mean adult weight (kg, as an estimate of body size), mean neonate weight (kg), and mean litter size for as many dog breeds as possible from the published literature. Given the different sources from which we obtained data and the risk that criteria for data collection differed among sources, we first carefully checked the degree to which data from different sources were comparable according to the degree to which information from different sources for the same trait was correlated. We discarded sources when the correlation with other sources was $r < 0.6$ so that we used only sources that show high correlations with each other.

Life Span

We collected life span information from the American Kennel Club's (AKC) official website (https://www.akc.org) and other published sources (Michell 1999; Bell et al. 2012; O'Neill et al. 2013; Leroy et al. 2015; table S1). Life span represents expected longevity of individuals of a given breed. Data were collected from various sources that differ in how the information was obtained (e.g., using clinical health data from veterinarians [O'Neill et al. 2013], dog owner questionnaires [Michell 1999], or information from kennel clubs [Leroy et al. 2015]). When a range of values was given, we used the midpoint of said range. When life span data were available from different sources, to ensure consistency, we first tested the correlation among data sources for breeds for which we had information from more than one source. We discarded sources when the correlation with other sources was $r < 0.6$ so that we used only sources that show high correlations with each other, including the data from AKC, and calculated an average for each breed. Following this approach, we were able to collect information on longevity for 277 dog breeds. The sources from which we obtained information on life span do not indicate whether neutered individuals were excluded from their samples. However, within-breed differences in life span as a result of neutering vary among studies, breeds, and the sex of individuals (see Michell 1999; Moore et al. 2001; O'Neill 2013). Furthermore, reported differences are small (<2 years) compared with among-breed differences in life span (e.g., a Saint Bernard lives 6.4 years, whereas a Coton de Tuléar lives 17 years). Ideally, we would have used sex-specific data on life span, but such information is simply not available for a large enough sample of breeds.

Adult Weight

We collected mean adult weight, combining male and female weights (or using the mean breed-specific weight), as life span data for most breeds was not sex specific (table S2). Since only recognized breeds are included (according to the criteria of the AKC), adult weight is expected to present limited variation among sources because it is highly related to pedigree parameters on which there is strong artificial selection, such as height (weight and height correlation, $r = 0.85$). Although we acknowledge that there is sexual size dimorphism in many breeds (more notably so in larger ones), such dimorphism is small compared with among-breed differences in size, so it is highly unlikely to affect our results. Given the high correlation among adult weights from different sources ($r > 0.94$; see table S2), we chose to use weights from the official AKC database. We collected information on adult weight for 253 dog breeds.

Neonate Weight and Litter Size

Because of the scarcity of information from different published sources for the same breed for mean neonate weight and litter size, it was not possible to test the correlations in these variables among different sources. Nonetheless, as an approximation we compared data collected from primary publications with data obtained from compendia to verify whether values are comparable. For neonate weight the correlation between articles and compendia was $r = 0.84$, while the correlation for litter size was $r = 0.83$. We thus combined information from articles and compendia to maximize the sample size and calculated an average when we had more than one value for the same breed. Data for neonate weight came from seven different sources and covered 281 breeds (table S3). Data for litter size were obtained from 20 different sources (table S4). In addition, for 13 breeds (Picardy sheepdog, curly coated retriever, Coton

de Tuléar, field spaniel, Great Pyrenees, Irish water spaniel, komondor, Kuvasz, miniature bull terrier, otterhound, pharaoh hound, Chinese shar-pei, and schipperke), the litter sizes were obtained from two specialized websites (table S4), as they were not available from other published sources. Litter sizes from the aforementioned websites were within the expected range for both breeds and adult weights, and both websites reported similar values, which gives us additional confidence that these are unlikely to be biased. We collected information on litter sizes for 253 breeds. Finally, we calculated total reproductive investment as the product of breed-specific litter size and neonate weights.

Growth

Previous work suggests that growth may compromise longevity in dogs (Galis et al. 2007; Kraus et al. 2013; Fan et al. 2016). Therefore, as a proxy for total investment in growth, we subtracted the adult weight from the neonate weight and divided the result by the neonate weight to estimate how much a newborn individual must grow to reach average adult weight for each breed. Following this approach, we collected information on growth for 124 breeds. Previous studies followed individuals from 16 different breeds during their lifetimes, weighing them at different ages, and estimated growth curves by plotting mean body weight against age, fitting a logistic equation (Hawthorne et al. 2004; Posada et al. 2014). This approximation was not possible, since such information does not exist for most breeds and would not be strictly comparable among different studies. Nonetheless, our estimate of growth is correlated with the estimated time to reach 99% of adult size (weeks) obtained from the available logistic growth curves (Hawthorne et al. 2004; Posada et al. 2014; $r = 0.66$, $n = 16$ breeds). On the other hand, the exponent of the rapid-growth phase of the growth curves shows a low correlation with our estimate of growth ($r = 0.28$, $n = 16$). Finally, mean adult size is more strongly correlated with the time to reach 99% of adult size ($r = 0.64$, $n = 16$) than it is with the exponent of the rapid-growth phase of the growth curves ($r = 0.27$, $n = 16$), which suggests that larger breeds take longer to reach adult size rather than grow faster.

Because our estimate of growth does not consider the time taken to reach adult size, following reviewer suggestions we obtained information on the onset of puberty, that is, the average age at which females have their first estrus (Johnston et al. 2002). This is the best proxy we could find for age at maturity, and we assumed that it reflected the age at which juveniles reached adult size. As an admittedly somewhat rough proxy for growth rate, we divided the difference between adult size (kg) and neonate weight (kg) by the age at onset of puberty. We were thus able to obtain a proxy for growth rate for 34 of the breeds for which we had data on other life history traits and life span.

Shared Ancestry and Recent Gene Flow

To estimate the influence of shared ancestry versus recent gene flow on differences in life history traits among breeds, as well as to control for statistical nonindependence of observations due to the aforementioned factors (Felsenstein 2002; Stone et al. 2011), we used novel genomic information (Parker et al. 2017) following Garamszegi et al. (2020). We built two matrices that reflected expected similarity in phenotypic traits as a result of shared ancestry and recent gene flow. Said matrices are akin to covariance matrices used to control for phylogenetic nonindependence or spatial correlation, among others, and were included in the linear models as random factors. For both matrices, we used information from 150,067 informative single-nucleotide polymorphisms (SNPs), from which the origin of major clades of dog breeds can be reliably resolved (Parker et al. 2017). Degree of shared ancestry was based on distance data based on the proportion of allele comparisons that are not identical by descent, where breeds with a more distant common ancestor are expected to present a higher proportion than breeds sharing a more recent common ancestor. Garamszegi et al. (2020) have shown that such estimates are repeatable when multiple estimates for each pairwise between-breed comparison are obtained on the basis of different pairs of individuals. We created a matrix where the off-diagonals represent median distances between breeds (where longer distances indicate a more distant shared ancestor and thus lower expected covariance, and shorter distances indicate the opposite) and the diagonal, representing comparisons within breeds, was filled with zero. Since analyses require a matrix describing expected covariances among breeds owing to shared ancestry (Felsenstein 2002; Stone et al. 2011), we subtracted each value from one to obtain an expected similarity value (see Garamszegi et al. 2020).

To estimate of the influence of the homogenizing effect of gene flow on life history traits, we used identical-by-descent haplotype sharing estimated by 100-SNP windows (Parker et al. 2017). Haplotype sharing between breeds provides reliable information on recent genetic admixture, as the length of haplotype sharing between breeds reflects the history of between-breed crosses because recombination events following admixture will slowly decay the length of such shared haplotypes. As for the SNP data above, Garamszegi et al. (2020) have shown that shared haplotype data reliably estimate between-breed similarities, as they are significantly repeatable when estimated according to information from different individuals of the same breed. Using estimates of haplotype sharing from Parker et al. (2017), we created a matrix of haplotype sharing filling the off-diagonals

with the medians of the pairwise between-breed haplotype sharing and the diagonals with the medians of the within-breed haplotype sharing. To scale the matrix so that estimates of haplotype sharing varied between zero and one, we recalculated each off-diagonal cell relative to the respective within-breed haplotype-sharing values (Garamszegi et al. 2020). Both matrices were included in Bayesian mixed models as random factors, enabling us to partition variance into variation explained by shared ancestry, variation explained by hybridization, and unexplained variation (see below).

We combined the available genomic data from Parker et al. (2017) with our database of life history traits, which included data on life span, adult weight, neonate weight, litter size, reproductive investment, and growth rates. We obtained a final complete data set (i.e., without any missing data) for a total of 92 different breeds, which was used for all subsequent analyses.

Statistical Analyses

We used a Bayesian mixed modeling approach (Hadfield and Nakagawa 2010), which allowed us to partition among-breed variation in life history traits into variance components of evolutionary importance and control for nonindependence of observations. First, we ran univariate models, with the aim of estimating the influence of shared ancestry and gene flow on key life history traits. We ran models where the life history trait of interest was the response variable, without any fixed effects, and our estimates of shared ancestry and gene flow were included as random factors, enabling us to partition variation around the estimated mean value of the life history trait (intercept) into effects of shared ancestry and gene flow. Because we did not have repeated samples from a sufficient number of individuals within each breed, we did not include estimates of within-breed variation. We also used Bayesian mixed models, including shared ancestry and gene flow as random factors, for all analyses of the relationships between life history traits and life span. For these models, we first standardized all variables for ease of interpretation, as some models included interaction terms (Schielzeth 2010). We fitted all models using the MCMCglmm package (Hadfield 2010) in R (R Development Core Team 2020). Before entering the matrices of expected similarity owing to shared ancestry or gene flow, we applied single-value decomposition on each matrix, as required to include the matrices as random factors in the Bayesian mixed models (see Hadfield course notes; Hadfield 2010). We defined weakly informative priors for all models (G: $V = 1, \nu = 1$; R: $V = 1, \nu = 0.002$; Hadfield and Nakagawa 2010; Garamszegi et al. 2020). We ran models for 400,000 iterations, with a thinning interval of 50, and discarded the first 70,000 iterations as burn-in. The trace and distribution of all parameters were checked visually. For all analyses, we had effective sample sizes ranging between 5,600 and 7,281. Adult weight, neonate weight, and reproductive investment values were square root transformed for normality.

Results

Influence of Shared Ancestry and Hybridization on Life History Traits

The univariate mixed models indicated that most of the variation in key life history traits among dog breeds is the result of common ancestry (estimated by shared SNPs), which explained 74.7%–97.2% of the among-breed variation. In contrast, recent gene flow (estimated by haplotype sharing) explained 2.6%–24.2% of the variation (see table 1). Life span and adult weight showed the highest influence of shared ancestry (95.36%–97.15%), while neonate weight showed the lowest (74.67%).

Life Span and Weight

We confirmed the previously reported negative relationship between weight and life span across dog breeds, even when accounting for shared ancestry and recent gene flow (see table S5). Our results indicate that most of the variance within the relationship between adult weight and longevity is explained by common ancestry (73.1%) compared with the influence of recent gene flow (25.2%).

Life Span and Reproductive Investment

Life span decreases with higher reproductive investment (product of litter size and neonate weight; see table S6). However, because of the high correlation between neonate weight and adult weight ($r = 0.87$, without controlling for nonindependence of observations), we cannot rule out that we are detecting an effect of weight on longevity, if larger breeds also invest more in reproduction. Therefore, to disentangle the effect of size on longevity from the effect of reproductive investment on life span, we tested the relationship between reproductive investment and life span, controlling for adult body weight, and included an interaction between adult weight and reproductive investment. We found a significant interaction between reproductive investment and adult weight affecting life span, indicating that the reduction in life span resulting from higher reproductive investment is dependent on adult weight (see table 2), with larger breeds showing a higher reduction in life span with increased reproductive investment compared with smaller breeds. Most of the variance in life span is explained by shared ancestry compared with recent gene flow in this model.

Table 1: Bayesian mixed models on life span, weight, litter size, and neonate weight

	Eff.samp	Post.mean	95% CI	% variance explained	pMCMC
Life span:					
Random effect:					
Shared ancestry	5,645	17.41	11.14–24.19	97.15	…
Gene flow	5,380	.47	.08–.98	2.61	…
Residual variance	1,440	.04	.00–.19	.24	…
Fixed effect:					
Intercept	6,600	9.32	2.53–15.99	…	.008**
Weight:					
Random effect:					
Shared ancestry	6,019	12.58	7.17–18.79	95.36	…
Gene flow	5,387	.56	.12–1.11	4.27	…
Residual variance	1,510	.05	.00–.19	.36	…
Fixed effect:					
Intercept	6,600	5.75	.07–11.43	…	.04*
Litter size:					
Random effect:					
Shared ancestry	1,932	7.80	.08–18.24	79.69	…
Gene flow	2,033	1.92	.60–3.25	19.68	…
Residual variance	1,386	.062	.00–.28	.64	…
Fixed effect:					
Intercept	6,600	5.34	.34–10.32	…	.047*
Neonate weight:					
Random effect:					
Shared ancestry	6,600	.07	.03–.10	74.67	…
Gene flow	6,600	.02	.01–.02	24.15	…
Residual variance	5,917	.00	.00–.00	1.18	…
Fixed effect:					
Intercept	6,600	.62	.13–1.03	…	.006**

Note: Estimates of shared ancestry (based on shared single-nucleotide polymorphisms) and recent gene flow (based on haplotype sharing) were included as random effects. Shown are the effective sample sizes (eff.samp) for all parameters, their posterior means (post.mean), the 95% credibility intervals (95% CI), and the proportion of the variance partitioned among the random effects and the residual variance (% variance explained). For the fixed effects (intercept), estimates of the *P* values (pMCMC) are shown.

* $P < .05$.

** $P < .01$.

Life Span, Growth, and Reproductive Investment

Because both growth and reproduction may influence life span (Stearns et al. 2000; Metcalfe and Monaghan 2003), we carried out a final model to test the relationships between life span, growth, and reproductive investment and the interaction between growth and reproductive investment affecting life span. The interaction between growth and reproductive investment was statistically significant (table 3), indicating that breeds that grow a lot suffer greater reduction in life span with higher reproductive investment than breeds that require less growth to reach adult body size (table 3). As in previous models, most of the variance in life span is explained by shared ancestry compared with gene flow. The results are qualitatively the same if we repeat the analysis using our proxy for growth rate (instead of growth; see table S7).

Discussion

We found that among-breed variation in key life history traits is mainly explained by shared ancestry (range: 75%–92% of the variance), as measured by SNPs that are identical by descent, a measure of overall genetic similarity. On the other hand, recent gene flow, measured according to shared haplotypes, had a more reduced influence (range: 3%–24%). Adult body weight and life span showed the highest influence of shared ancestry, while litter size showed the lowest. Our results further indicate that reproductive investment influences life span, but the effect is dependent on breed weight and growth. Larger breeds that invest more in reproduction pay a higher price in reduced life span than smaller breeds. To illustrate, a 65.7-kg Saint Bernard has on average 9.4 pups per litter, with neonates that weigh

Table 2: Bayesian mixed model of the relationship between adult weight (square root transformed), reproductive investment (rep invest), and life span among dog breeds

	Eff.samp	Post.mean	95% CI	% variance explained
Random effect:				
Shared ancestry	4,685	.79	.10 to 1.5	75.55
Gene flow	3,740	.22	.11 to .35	21.8
Residual variance	1,677	.02	.00 to .10	2.65
				pMCMC
Fixed effect:				
Intercept	5,000	−.41	−2.17 to 1.12	.63
Weight	5,000	−.99	−1.30 to −.69	<2e−04***
Rep invest	4,799	.27	−.008 to .57	.068
Weight × rep invest	4,740	−.27	−.41 to −.13	<2e−04***

Note: Adult weight and reproductive investment are fixed effects, and their interactive effect on life span was also tested. Estimates of shared ancestry (based on shared single-nucleotide polymorphisms) and recent gene flow (based on haplotype sharing) were included as random effects. Shown are the effective sample sizes (eff.samp) for all parameters, their posterior means (post.mean), the 95% credibility intervals (95% CI), and the proportion of the variance partitioned among the random effects and the residual variance (% variance explained). For the fixed effects, estimates of the *P* values (pMCMC) are shown.

*** $P < .001$.

0.468 kg (~0.7% of adult body weight), and lives an average of 6.4 years, while a 2.2-kg toy poodle has ~2.2 pups per litter, with neonates that weigh 0.117 kg (already ~5.3% of adult body weight), and lives an average of 14.7 years.

Shared ancestry, reflecting the ancient evolutionary history of dog breeds through processes of artificial selection or neutral processes, plays a more important role in explaining the interbreed variation in key life history traits compared with recent events of admixture. These results are in line with Garamszegi et al. (2020), who studied a behavioral trait and found that common ancestry has a considerable role on the among-breed variance in human-directed play behavior (~80%) compared with relatively recent gene flow (~18%).

The apparent minor influence of admixture could seem surprising, as gene flow in purebred dogs reflects artificial selection directed by humans to obtain or refine specific desired phenotypes, resulting in different breeds. Thus, it would be reasonable to expect some degree of homogenization of particular phenotypic traits as a result of such admixture among breeds. It is possible that crosses among different breeds involved differences in specific phenotypic traits breeders wanted to incorporate into the newly created breeds, but they seem to have involved more minor differences in life history traits, such as neonate weight, for example,

Table 3: Bayesian mixed model of the relationship between growth and reproductive investment among dog breeds

	Eff.samp	Post.mean	95% CI	% variance explained
Random effect:				
Shared ancestry	5,808	.88	.11 to 1.67	75.07
Gene flow	4,470	.26	.10 to .37	22.07
Residual variance	2,261	.03	.00 to .09	2.85
				pMCMC
Fixed effect:				
Intercept	5,400	−.50	−2.25 to 1.17	.56
Growth	7,281	−.43	−.62 to −.24	<2e−04***
Rep invest	6,777	−.32	−.52 to −.13	.001**
Growth × rep invest	6,330	−.32	−.48 to −.16	<2e−04***

Note: Growth and reproductive investment (rep invest) are fixed effects, and their interaction was also tested. Estimates of shared ancestry (based on shared single-nucleotide polymorphisms) and recent gene flow (based on haplotype sharing) were included as random effects. Shown are the effective sample sizes (eff.samp) for all parameters, their posterior means (post.mean), the 95% credibility intervals (95% CI), and the proportion of the variance partitioned among the random effects and the residual variance (% variance explained). For the fixed effects, estimates of the *P* values (pMCMC) are shown.

** $P < .01$.

*** $P < .001$.

as more pronounced differences in such traits could lead to problems. Evidence from whole-genome scans for selection across 10 phenotypically diverse breeds found several genomic regions with evidence of selection, which include candidate genes for phenotypic differences, such as size, coat color or texture, behavior, skeletal morphology, and physiology (Akey et al. 2010). Finally, it is also possible that interbreed crosses that occurred more distantly in the past become harder to identify, and thus we observe the effects of only more recent crosses (Parker et al. 2017), diluting potential effects on life history traits. For example, breeds with a more recent history share a larger proportion of haplotypes, such as the bullmastiff with the mastiff and bulldog, the golden retriever with both the flat-coated retriever and the Irish water spaniel, or the Chinook with the German shepherd and Greenland sled dog (Parker et al. 2017).

The difference in the relative magnitude of the influence of recent gene flow on the amount of among-breed variation in life span and adult weight (2.6% and 4.3%, respectively) in comparison with litter size and neonate weight (19.7% and 24.1%, respectively) is interesting. This difference suggests that admixture had a stronger influence on traits related to reproduction compared with adult body weight or life span. It is possible that life span is more strongly correlated with adult weight than litter size or neonate weight and thus more closely reflects the artificial selection imposed on adult weight. It is also possible that directed hybridization in the formation of modern breeds involved crosses between breeds of similar size to avoid "mechanical" problems associated with large size differences, whereas other traits had larger differences. Besides artificial selection directed by humans, a comparison of the effects of shared ancestry and recent gene flow could be useful in future studies to trace the evolution of specific traits that are correlated or interact with each other, as predicted by the domestication syndrome (Wilkins et al. 2014; Theofanopoulou et al. 2017).

We found a negative association between reproduction and life span among dog breeds. We first confirmed the previously reported negative association between life span and adult body size (Speakman et al. 2003; Fleming et al. 2011; Greer et al. 2011; Selman et al. 2013), even when controlling for the confounding effects of shared ancestry and gene flow. We then tested the association between life span and reproductive investment, including adult body mass as a covariate. We found a significant interaction between reproductive investment and adult body mass, indicating that high reproductive investment reduces life span but more so in larger breeds. In other words, larger breeds with higher reproductive investment, such as Saint Bernard or Great Dane, show a steeper decrease in life span compared with small breeds with lower reproductive investment, such as the Griffon Bruxellois or miniature pinscher. These results indicate that basic life history trade-offs, such as between reproduction and life span, are also apparent in domestic dogs, whose striking diversity is the result of artificial selection. Our results are also in line with predictions from the disposable soma theory of aging (Kirkwood 2017), although they could also be explained by antagonistic pleiotropic effects (Williams 1957).

Previous work suggested that the negative association between adult weight and longevity is a result of the increased growth that large breeds require to reach adult weight, which might have led to shorter life spans owing to specific developmental diseases or faster aging processes (Galis et al. 2007; Kraus et al. 2013). The lower ratio between neonate weight relative to adult weight of large breeds, in comparison with smaller ones, means that more energy needs to be invested in growth to reach adult size, which leads to lower investment in somatic maintenance, thus reducing life span (Fan et al. 2016). On the basis of these previous results, we also included a final model to test whether the observed relationship between reproductive investment and life span holds when including a proxy for amount of growth (the ratio between neonate and adult body weight) instead of adult weight. We again found that higher reproductive investment is associated with reduced life span, but the effect depended on our proxy for growth, where breeds that must grow a lot, such as the Saint Bernard or rottweiler, showed a steeper decline in life span with greater reproductive investment compared with breeds that grow less, such as the Coton de Tuléar or papillon. It is worth noting that our results indicating a reduction in life span associated with reproduction are in line with evidence that sterilization increases life span by 13.8% in male dogs and by 26.3% in female dogs (Hoffman et al. 2013).

According to the disposable soma theory, aging is the result of the trade-off in the allocation of limited resources between two competing functions: reproduction and somatic maintenance. Organisms are not immortal because investing in error-proof somatic maintenance is wasteful and not an evolutionarily stable strategy, as extrinsic mortality can terminate even intrinsically immortal organisms (Maklakov and Immler 2016). Physiological deterioration is accelerated by fast growth and high investment in reproduction, resulting in reduced life span. There is ample evidence for the detrimental effects of fast growth and development on life span. For example, artificial selection for fast growth in fruit flies (*Drosophila melanogaster*) and mice (*Mus musculus*) results in decreased life span (Miller 2000; Stearns et al. 2000), and increased embryo growth rates are associated with shorter life spans in birds and mammals (Ricklefs 2006). Differences in life span across dog breeds were also found to be associated with differences in growth rate (Kraus et al. 2013). On the other hand, the costs of reproduction involve not only investment in gamete production but also the wear and tear of tissues, DNA damage from free

radicals, and accumulation of toxic waste products in the cells (reviewed in Maklakov and Immler 2016). Our results suggest that high investment in reproduction can explain among-breed differences in life span, as higher reproductive investment is associated with reduced life span, with larger breeds showing a steeper trade-off between reproductive investment and life span compared with smaller breeds, even when controlling for shared ancestry and gene flow. Why do we observe an interaction with adult weight rather than merely additive effects? It is possible that greater reproductive investment imposes a steeper trade-off with life span in larger breeds because individuals from such breeds have already traded off self-maintenance with growth early in their lifetimes or because the cost of reproduction is compounded with developmental diseases that result from high growth (Fleming et al. 2011; Kraus et al. 2013; Farrell et al. 2015).

Conclusion

In sum, our results indicate that shared ancestry, estimated as SNPs that are identical by descent, explains a higher proportion of the among-breed variation in key life history traits, in comparison with recent gene flow, estimated as haplotype sharing. These results suggest that recent crosses between preexisting breeds (Parker et al. 2017) have left a minor imprint on life history traits. Interestingly, litter size and neonate weight showed a much higher influence (>4 times higher) of hybridization compared with adult body weight and life span. Our results also show that investment in reproduction negatively impacts life span and more strongly so in large breeds. The interaction between adult weight, or growth, and reproduction on life span suggests that the effect is not merely a correlated response of the effect of adult weight on life span. These results are in line with predictions from the disposable soma theory for the evolution of aging and suggest that among-breed differences in life span are due to a combination of body weight and investment in reproduction. The precise mechanisms involved require further investigation.

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Statement of Authorship

A.G.-V. conceived the study; I.B.-G., A.G.-V., and C.V. designed the study; I.B.-G. collected the data; I.B.-G. and A.G.-V. analyzed the data; I.B.-G., A.G.-V., and C.V. interpreted the results; I.B.-G. wrote the first draft of the manuscript; and A.G.-V. and C.V. provided comments and edited the final version.

Data and Code Availability

All data and code to reproduce the results of this work are available in the Dryad Digital Repository (https://doi.org/10.5061/dryad.1g1jwsv0s; Bargas-Galarraga et al. 2022).

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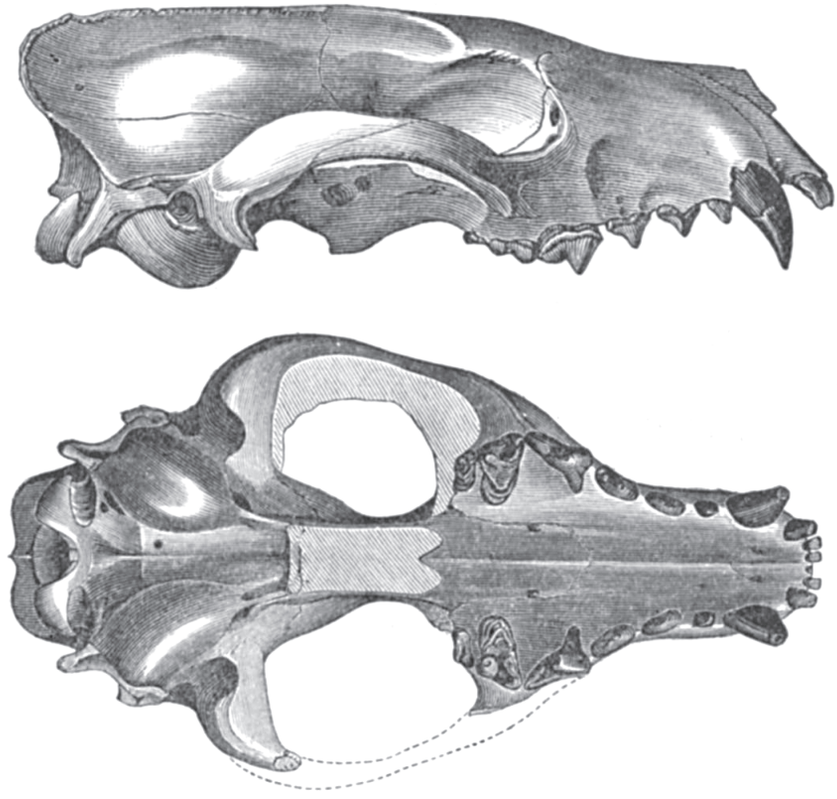

"Three American species certainly belong to Temnocyon. . . . *T. coryphæus* [figured] is as large as the coyote, and was very abundant during the John Day epoch in Oregon." From "On the Extinct Dogs of North America" by E. D. Cope (*The American Naturalist*, 1883, 17:235–249).