Cranial Suture Closure in Domestic Dog Breeds and Its Relationships to Skull Morphology

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ABSTRACT

Bulldog-type brachycephalic domestic dog breeds are characterized by a relatively short and broad skull with a dorsally rotated rostrum (airorhynchy). Not much is known about the association between a bulldog-type skull conformation and peculiar patterns of suture and synchondrosis closure in domestic dogs. In this study, we aim to explore breed-specific patterns of cranial suture and synchondrosis closure in relation to the prebasial angle (proxy for airorhynchy and thus bulldog-type skull conformation) in domestic dogs. For this purpose, we coded closure of 18 sutures and synchondroses in 26 wolves, that is, the wild ancestor of all domestic dogs, and 134 domestic dogs comprising 11 breeds. Comparisons of the relative amount of closing and closed sutures and synchondroses (closure scores) in adult individuals showed that bulldog-type breeds have significantly higher closure scores than non-bulldog-type breeds and that domestic dogs have significantly higher closure scores than the wolf. We further found that the prebasial angle is significantly positively correlated with the amount of closure of the basispheno-presphenoid synchondrosis and sutures of the nose (premaxillo-nasal and maxillo-nasal) and the palate (premaxillo-maxillary and interpalatine). Our results show that there is a correlation between patterns of suture and synchondrosis closure and skull shape in domestic dogs, although the causal relationships remain elusive. Anat Rec, 299:412–420, 2016. © 2016 Wiley Periodicals, Inc.

Key words: wolf; synchondroses; fusion; brachycephaly; airorhynchy

INTRODUCTION

One of the most striking peculiarities of domestic dogs is their disparity of skull shape. Much of this disparity among breeds can be characterized by variation in the relative length of the rostrum and breadth of the skull as well as by the angulation of the rostrum relative to the cranial base (Rosenberg, 1966; Lüps, 1974; Nussbaumer, 1982; Brehm et al., 1985; Herre and Röhrs, 1990; Evans, 1993; Drake and Klingenberg, 2010). The most derived skull form is the bulldog-type skull conformation, traditionally referred to as brachycephaly (short head). Typical bulldog-type brachycephalic domestic dog breeds are French and English bulldog, boxer, pug, and Pekingese. Brachycephaly is characterized by a set of peculiarities, including relatively wide zygomatic arches, a relatively short rostrum, and airorhynchy (Table 1). Airorhynchy describes a dorsal rotation of the rostrum at the plane of the palate relative to the cranial base (prebasial angle $> 180°$). In most canids, including the

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TABLE 1. Skull characteristics of bulldog-type brachycephalic domestic dog breeds

Widened skull with wide zygomatic arches
Spherical skull vault[a]
Rounded and protruding forehead[a]
Increased skull height
Two temporal lines instead of a sagittal crest[a,b]
Hypoplasia of the bones of the rostrum and retrognathic upper jaw
Protruding mandible and prognathic lower jaw[b]
Shallow orbits, ocular proptosis, and widely placed orbits[b]
Up-turned nasal tip
Flat or convex (rather than concave) oral surface of the palate
Short basicranium
Persistent ventral foramen magnum[b]
Wide spread of incisors
Crowded premolars
Marked angle between molar and premolar region

See Stockard (1941), Brehm et al. (1985), Evans (1993), Turner (2008), Martin (2009), and Schoenebeck and Ostrander (2013).
[a]Probably a consequence of small body size in many brachycephalic breeds (Klatt, 1913).
[b]Not always observed and not in all breeds.

TABLE 2. Number of specimens (*n*), mean age, mean prebasial angle according to Nussbaumer (1982), and associated standard deviations (SD) of domestic dog breeds used in this study

Group	*n*	Mean age (years)	SD (mean age)	Prebasial angle (°)	SD (prebasial angle)
Barsoi	9	5.8	2.9	158.270	4.395
Bernese mountain dog	15	5.0	2.6	173.330	2.940
Boxer	16	6.0	3.4	180.900	3.872
Chow Chow	8	6.3	2.6	175.800	4.127
Dachshund	13	6.0	2.9	165.420	4.500
Dogue de Bordeaux	6	7.0	2.6	182.250	4.628
French bulldog	14	6.5	2.7	183.050	3.199
Great Dane	12	5.6	3.1	173.470	2.183
Greyhound	13	6.2	3.0	164.410	2.272
Newfoundland	15	5.6	3.0	172.880	3.421
St. Bernard	13	5.5	3.0	177.750	4.496
Wolf	26	5.5	2.7	170.300	3.459

wolf (*Canis lupus*), that is, the wild ancestor of all domestic dogs, the rostrum is ventrally rotated with respect to the cranial base (prebasial angle $< 180°$, klinorhynchy; Nussbaumer, 1982; Herre and Röhrs, 1990).

Skull shape is generated during prenatal development as well as during postnatal growth. Skull proportions, for example, relatively short rostrum and wide skull in brachycephalic breeds, are already expressed in neonates as Starck (1962) described on the basis of comprehensive material of German shepherd, barsoi, whippet, Pekingese, Belgian dwarfed griffon, pug, French bulldog, bullterrier, dachshund, Bedlington terrier, greyhound, and Afghan hound. Therefore, the expression of a brachycephalic skull proportions is already established during prenatal ontogeny. Airorhynchy, on the other hand, is established only during postnatal ontogeny. At birth, all domestic dogs are klinorhynch, and breeds which usually exhibit airorhynchy as adults develop their enlarged prebasial angle throughout postnatal growth (Starck, 1962; Rosenberg, 1966).

Sutures are fibrous joints between the dermal bones, or between the dermal and endochondral bones, in the vertebrate skull (Herring, 2000; Hall, 2005; Rice, 2008). They are distinct from the cartilaginous synchondroses, which connect the endochondral bones of the cranial base (Cohen, 2000; Herring, 2000; Hall, 2005; Cendekiawan et al., 2010). The function of cranial sutures and synchondroses is threefold (Cohen, 2000; Cohen, 2008; Rice, 2008): articulation and holding together the bony elements of the skull while allowing deformations (especially during birth), mechanical stress absorption, and bone growth. In sutures, growth of the adjacent bones occurs by intramembranous osteogenesis at their margins (Rice, 2008). As distinct from sutures, the bones adjacent to synchondroses grow via endochondral ossification, similar to the growth plates of long bones (Hall, 2005; Nie, 2005; Cendekiawan et al., 2010). The fusion of one suture or synchondrosis does not allow any further growth at that location (Opperman, 2000; Rice, 2008). There is a species-specific pattern in the sequence after which sutures and synchondroses close (Rager et al., 2014).

Despite the growing knowledge of genes that govern the vast phenotypic disparity of different domestic dog breeds (Fondon and Garner, 2004; Boyko et al., 2010; Schoenebeck et al., 2012; Schoenebeck and Ostrander, 2013), not much is known about the correlation between the brachycephalic skull conformation in domestic dogs and patterns of suture and synchondrosis closure. Especially the craniofacial sutures of, or adjacent to, the rostrum are worth being considered in this respect because they are directly involved in a shortening and a dorsal rotation of the bones of the rostrum in brachycephalic breeds. This study aims at investigating the patterns of cranial suture and synchondroses closure in domestic dog breeds with different skull conformations to find out if and how they are related to the brachycephalic skull conformation.

MATERIALS AND METHODS

Data Acquisition

Patterns of cranial suture closure were assessed by examining ontogenetic series of dry skulls of 26 wolves and 134 domestic dogs comprising 11 modern breeds (Table 2), which exhibit different skull conformations (Fig. 1 and Table 2). Eighteen sutures and synchondroses were coded (Fig. 2 and Table 3). The sutures have been chosen because of their position between and adjacent to the bones of the rostrum. The cranial base synchondroses have been incorporated in this study because it has been shown that the spheno-occipital synchondrosis has a higher probability to be closed at an earlier age in the brachycephalic domestic dog breeds when compared with the mesocephalic ones (Schmidt et al., 2013).

For all the analyses, only specimens ranging between 1 and 11 years were used. This age range was chosen because almost none of the coded sutures in any of the breeds examined and the wolf starts to obliterate in the first year of life while the whole skeleton is still growing. The upper age limit was chosen because all breeds examined and the wolf are represented by specimens in

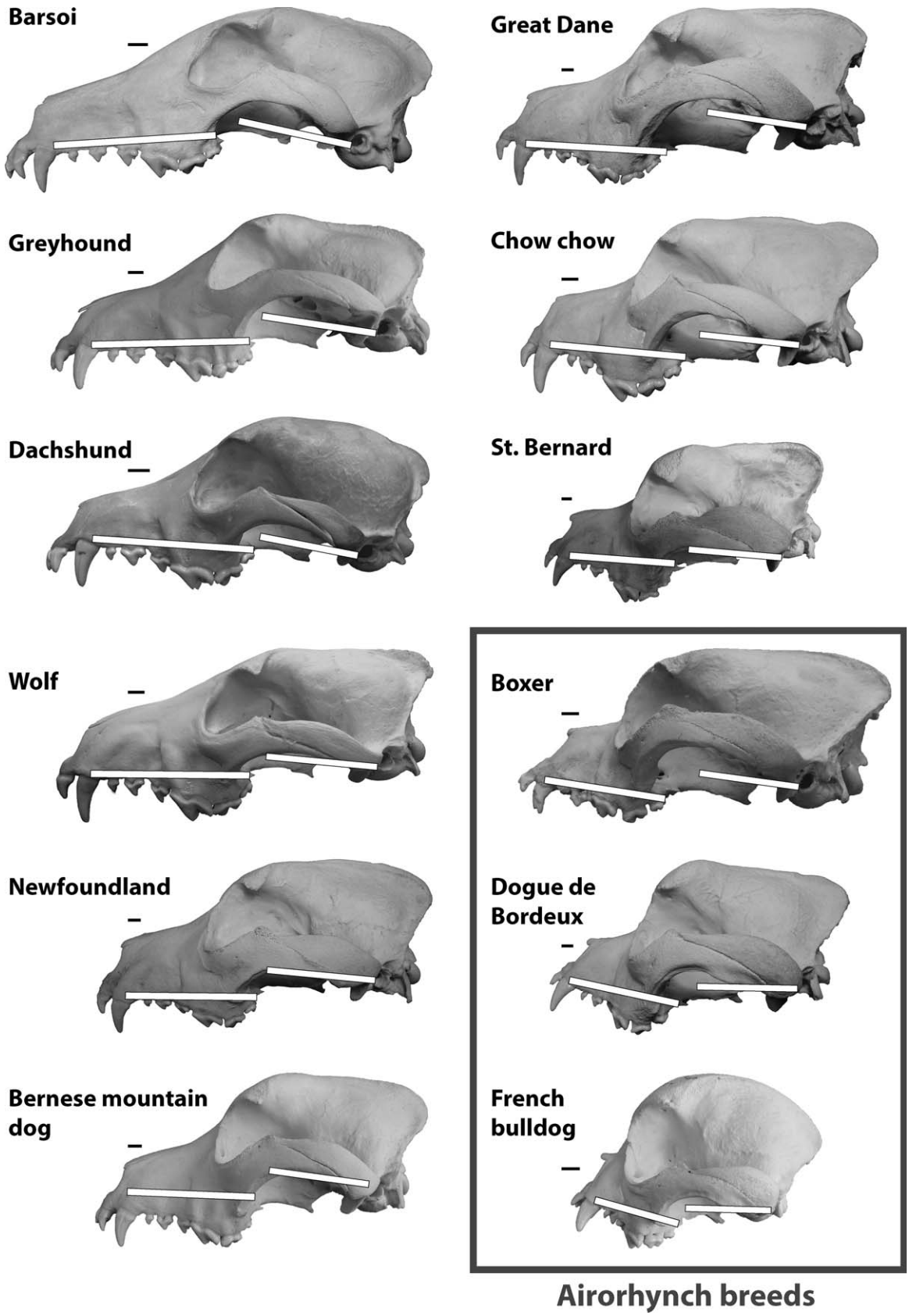

Fig. 1. Skulls of the investigated domestic dog breeds and the wolf in lateral aspect. The prebasial angles (angle between the hard palate and the cranial base of the skull) are indicated with white bars, and the breeds are sorted from top to bottom and left to right according to increasing prebasial angles, that is, increasing dorsal rotation of the rostrum (Table 2). Airorhynch breeds are indicated with a gray frame. Skulls are scaled to the same height of the skull. Scale bars are equal to 1 cm.

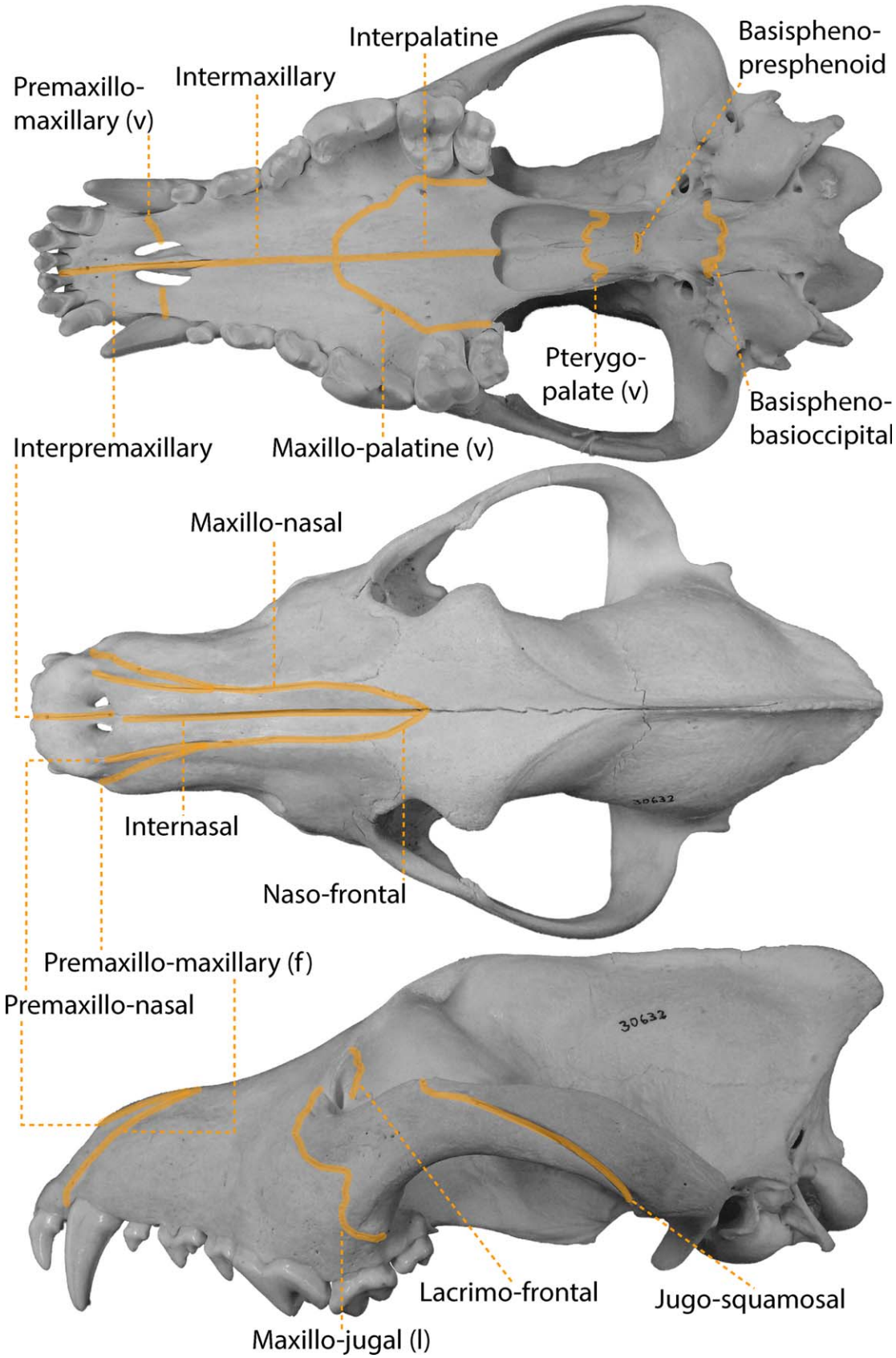

Fig. 2. Cranial sutures and synchondroses coded in this study (Table 3). Some sutures are denoted to be visible from frontal (f), lateral (l), and ventral (v) aspects. The exoccipito-supraoccipital and exoccipito-basioccipital synchondroses are not shown here.

TABLE 3. Cranial sutures and synchondroses investigated in this study

No.	Suture/Synchondrosis
1	Basispheno-presphenoid
2	Basispheno-basioccipital
3	Exoccipito-supraoccipital
4	Exoccipito-basioccipital
5	Interpremaxillary (v)
6	Intermaxillary
7	Premaxillo-maxillary (v)
8	Interpalatine
9	Maxillo-palatine (v)
10	Pterygo-palate (v)
11	Premaxillo-maxillary (f)
12	Premaxillo-nasal
13	Internasal
14	Maxillo-jugal (l)
15	Maxillo-nasal
16	Naso-frontal
17	Lacrimo-frontal
18	Jugo-squamosal (l)

F, frontal; l, lateral; v, ventral aspects. No., number of suture.

their 11th year; older individuals were increasingly scarce in some groups. This procedure moreover ensures that comparable age classes and thus degrees of suture closure were compared (Table 2). Furthermore, the sampling was deliberately biased as to obtain an evenly distributed sample concerning the absolute individual ages and to include specimens which are historically as young as possible. The second point was important because some domestic dog breeds underwent significant changes due to breeding practices throughout the last century (Nussbaumer, 1982; Drake and Klingenberg, 2008). Additionally, only specimens with closure states applicable for all investigated sutures and synchondroses were used. Both sexes were considered.

Each suture and synchondrosis was examined externally (Wilson and Sánchez-Villagra, 2009; Sánchez-Villagra, 2010; Goswami et al., 2013; Rager et al., 2014; Wilson, 2014), and the closure state was coded as depicted in Fig. 3: 0, open, the suture is completely open (Fig. 3a); 1, closing, parts of the suture are obliterated (Fig. 3b); and 2, closed, the entire suture is obliterated and not discernible from the surrounding bone (Fig. 3c). The skulls were obtained from the following institutions: Albert-Heim-Stiftung in the Naturhistorisches Museum Bern, Switzerland; Naturhistoriska Riksmuseet, Stockholm, Sweden; Paläontologisches Institut und Museum der Universität Zürich, Switzerland; and Zoologisches Museum der Universität Zürich, Switzerland.

As a proxy for bulldog-type brachycephaly in this study, we used the prebasial angle. Records of group mean prebasial angles (angle between the hard palate and the cranial base of the skull) were obtained from Nussbaumer (1982). All breeds with a reported breed mean prebasial angle $> 180°$ were defined as airorhynch and subsequently as bulldog-type brachycephalic in this study (Fig. 1).

Analyses

Two sets of analyses were performed. In the first analysis, all investigated sutures were analyzed together. The closure states (0, 1, or 2) for all investigated sutures and synchondroses were summed up per specimen and divided by the total number of investigated sutures (here 18) to obtain a relative value. The resulting closure score is higher in old specimens with many closing and closed sutures and synchondroses and lower in young specimens with many open sutures and synchondroses. The closure scores of the airorhynch groups (boxer, Dogue de Bordeaux, and French bulldog) were subsequently compared with the closure scores of the klinorhynch groups (all others). The non-airorhynch (klinorhynch) domestic dogs were further compared with the wolf. For these comparisons, nonparametric Wilcoxon tests were performed.

In the second analysis, the closure states (0, 1, or 2) were summed up per suture or synchondrosis in every group, that is, separately for the wolf and each of the different domestic dog breeds. The sums were subsequently divided by the number of specimens per group to obtain a relative value which is comparable among the groups. Again, the resulting closure score is higher in sutures which are closing or closed in many specimens of a group and lower in sutures which are open in many specimens of a group. Nonparametric Kendall's tau coefficients were used to investigate the correlation between the closure scores and the prebasial angle. The prebasial angles were used as the x-variables, and the closure scores were used as the y-variable. All analyses were computed using R version 2.15.1, RStudio version 0.98.501, and Microsoft Excel 2010.

RESULTS

When comparing the closure scores of the airorhynch [mean = 1.06, standard deviation (SD) = 0.44] with the klinorhynch (mean = 0.78, SD = 0.35) domestic dog breeds, we found a significant difference between the two ($W = 2{,}398$, $P = 0.0015$), showing that adults of bulldog-type brachycephalic breeds have more closing and closed sutures and synchondroses than klinorhynch breeds (Fig. 4). Moreover, we found that klinorhynch domestic dogs have significantly more closing and closed sutures ($W = 1{,}835$, $P = 0.0006$) than the wolf (mean = 0.53, SD = 0.24; Fig. 4).

Furthermore, we found significant positive correlations of the prebasial angle with the closure scores of the premaxillo-maxillary (v) suture ($\tau = 0.64$, $P = 0.005$), premaxillo-nasal suture ($\tau = 0.72$, $P = 0.001$), maxillo-nasal suture ($\tau = 0.74$, $P = 0.0009$), interpalatine suture ($\tau = 0.47$, $P = 0.038$), and basispheno-presphenoid synchondrosis ($\tau = 0.53$, $P = 0.005$).

DISCUSSION

The aim of this study was to investigate the breed-specific differences of cranial suture and synchondroses obliteration and its relationships to a bulldog-type brachycephalic skull conformation in domestic dogs. For this purpose, the cranial sutures and synchondroses in 11 modern domestic dog breeds and the wolf were coded (Figs. 1–3). The relative amount of closing and closed sutures in adult individuals was analyzed in the context of the variation in prebasial angle, which was used as a proxy for brachycephalic bulldog-type skull morphology if it exceeded 180° in a breed (airorhynchy; Fig. 1).

Our results show that there is a correlation between the patterns of suture and synchondrosis closure and airorhynchy in domestic dogs (Fig. 4). Especially two sutures of the nose (premaxillo-nasal and maxillo-nasal) and two

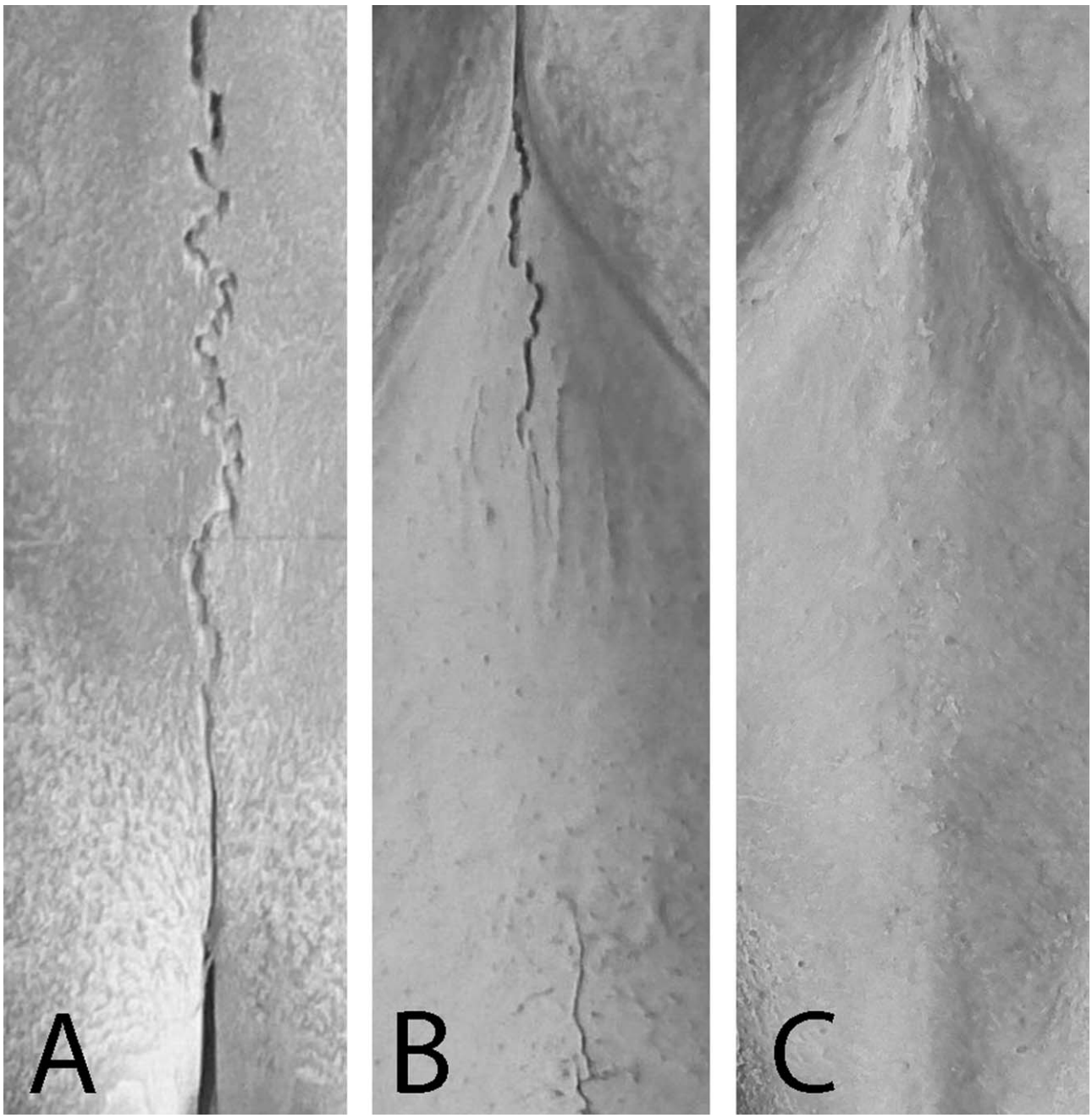

Fig. 3. Illustration of a suture displaying varying levels of closure: A, open, state 0; B, closing, state 1; and C, closed, state 2.

sutures of the palate [premaxillo-maxillary (v) and interpalatine] as well as the basispheno-presphenoid synchondrosis account for this correlation. The great amount of closing and closed basispheno-presphenoid synchondroses in airorhynch breeds complements the findings of a study on closure times of cranial base synchondroses in different domestic dog breeds up to 18 months. Schmidt et al. (2013) found that the probability of finding a closed spheno-occipital synchondrosis at a given age was significantly higher in the brachycephalic breeds when compared with the mesocephalic ones. Facial hypoplasia in combination with prematurely fused cranial base synchondroses has also been reported for other species, for example, cattle (Julian et al., 1957), mice (Chen et al., 1999), and humans (Cohen et al., 1985).

However, the causality of the bulldog-type skull conformation and patterns of suture closure in domestic dogs is not clear. It remains uncertain whether the bulldog-type skull conformation, or mechanisms related to its expression, also promotes the great amount of obliteration of nasal and palatal sutures and cranial base synchondroses (brachycephaly as a cause of a great amount of suture/

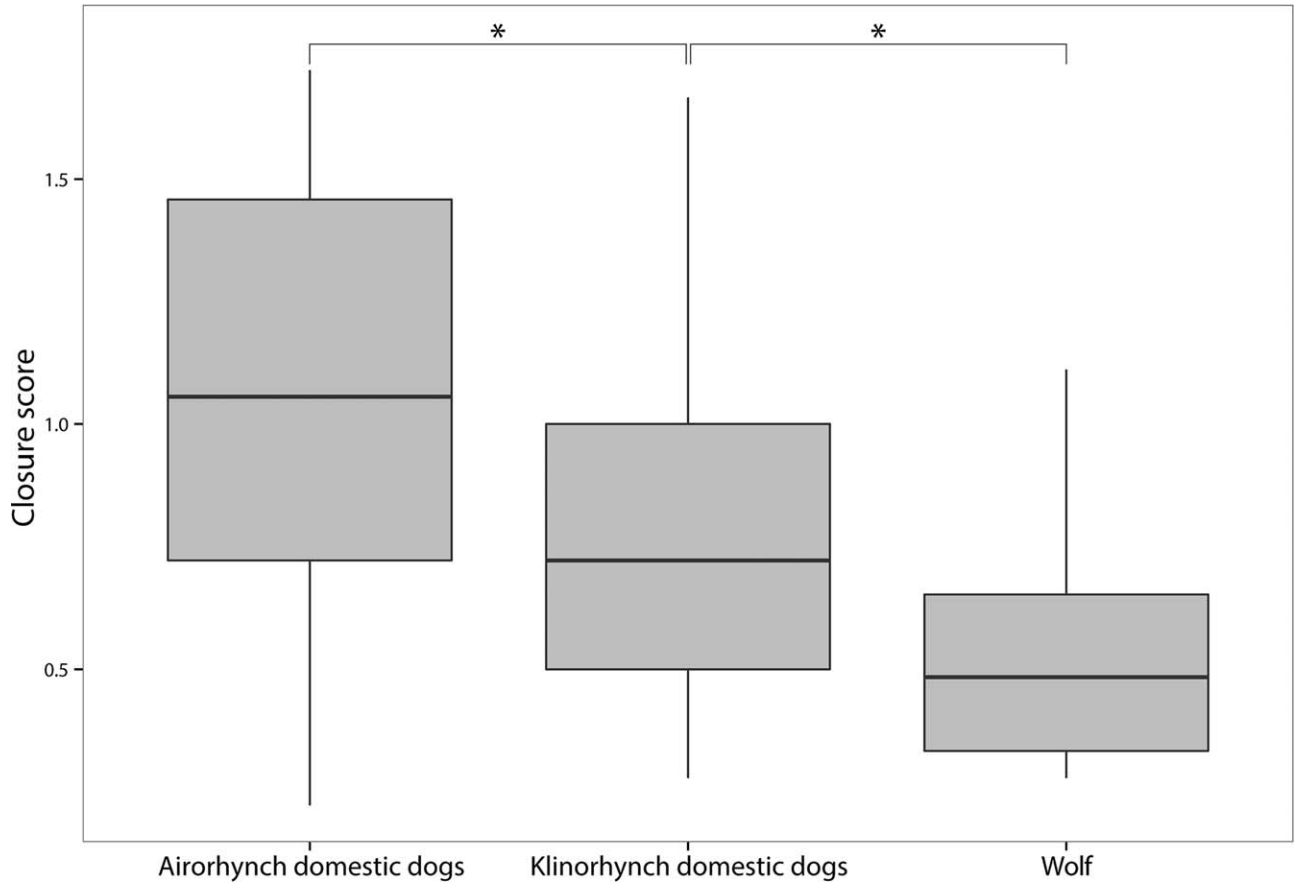

Fig. 4. Relative amount (closure score) of closing and closed sutures and synchondroses in klinorhynch and airorhynch (bulldog-type brachycephalic) domestic dogs and the wolf. Significant differences are indicated with asterisks.

synchondrosis closure) or whether the bulldog-type skull conformation is caused by the great amount of obliteration in nasal and palatal sutures and cranial base synchondroses (brachycephaly as an effect of a great amount of suture/synchondrosis closure). Evidence for the latter scenario (brachycephaly as an effect of a great amount of suture/synchondrosis closure) is presented by studies on other mammals: experimentally induced closure of cranial base synchondroses led to a decrease of facial projection, relative maxillary hypoplasia, and mandibular prognathism in rabbits (Rosenberg et al., 1997); experimentally induced closure of cranial base synchondroses and craniofacial sutures led to retrusion of the nasal region and a rethrognatic maxilla in baboons (Bütow, 1990). However, these experimentally induced changes of skull proportions in rabbits and baboons are not as distinct as in bulldog-type domestic dogs, and mechanisms underlying the generation of the bulldog-like phenotype are probably not causally related to suture and synchondrosis closure in domestic dogs at all. Evidence for such a scenario is presented by genetic studies. The glutamine-alanine tandem-repeat ratio in the domestic dog orthologue of the runt-related transcription factor 2 (*RUNX2*), an important regulator of osteoblast differentiation, was found to be positively correlated with midface length and degree of klinorhynchy in domestic dogs (Fondon and Garner, 2004). Similar results were reported for other carnivoran taxa (Sears et al., 2007), but not across other placental clades (Pointer et al., 2012). In humans, a heterozygous loss-of-function mutation in *RUNX2* causes cleidocranial dysplasia which is, among other symptoms, associated with midface hypoplasia and patent sutures and fontanelles (Mundlos, 1999; Cohen and MacLean, 2000; Schroeder et al., 2005; O'Neill, 2013a,b). These studies suggest that brachycephaly is likely at least in part the result of altered gene expression.

Biomechanical aspects might also be considered. Sutures are important sites of flexibility which transmit loads during muscle activity or traumatic impacts (Herring, 2008). It has been shown that reduced masticatory function in mice leads to early internasal suture closure (Engström et al., 1986). Thus, differences in feeding strategy and lifestyle might also have an influence on the amount of suture closure in domestic dogs and the wolf. The wolf is an active predator of mainly large mammals (Peters, 1993; Nowak, 1999). For modern domestic dogs living as house pets, as all specimens in our sample, hunting was not the primary source of food. Thus, stress regimes in the skulls of pet dogs and wolves are likely different, probably leading to a greater amount of suture obliteration in domestic dogs because of reduced biomechanical stresses acting on their skulls. Modern breeding practice in some brachycephalic

domestic dog breeds resulted in extremely short rostra and subsequently dental malocclusion and altered upper respiratory anatomy, leading to upper airway obstruction (Packer et al., 2015). Dental malocclusion and upper airway obstruction in turn can lead, among other clinical signs, to problems with mastication (Johnston, 2006; Fasanella et al., 2010). Even further reduced mechanical stresses on the skulls of these modern brachycephalic breeds might thus lead to an even greater amount of suture closure. An alternative explanation for the observed pattern of suture and synchondrosis closure could be the function for which many bulldog-type breeds have originally been bred: fighting and holding down prey on a hunt or for slaughter (Räber, 2001; Krämer, 2013). Selected traits which are beneficial for fulfilling these tasks include a strong musculature, a broad chest, great stability, the tendency to lock jaws, and a short snout with a protruding lower jaw that allows for biting without obstructed breathing (Krämer, 2013). The great amount of fusion of cranial sutures and the subsequently more rigid skull which is less prone to injuries during fighting might be a further trait which humans have unconsciously been selecting for in bulldogs.

To conclude, we detected a greater amount of suture and synchondrosis closure in brachycephalic bulldog-type than in other domestic dog breeds. An overall greater amount of suture closure of some nasal and palatal sutures and basicranial synchondroses in airorhynch breeds might either be cause or effect of the bulldog-type skull conformation. On the other hand, biomechanical influences on patterns of suture closure in domestic dogs should also be considered and further investigated.

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LITERATURE CITED

Boyko AR, Quignon P, Li L, Schoenebeck JJ, Degenhardt JD, Lohmueller KE, Zhao K, Brisbin A, Parker HG, Cargill M. 2010. A simple genetic architecture underlies morphological variation in dogs. PLoS Biol 8:e1000451.

Brehm H, Loeffler K, Komeyli H. 1985. Schädelformen beim Hund. Anat Histol Embryol 14:324–331.

Bütow K-W. 1990. Craniofacial growth disturbance after skull base and associated suture synostoses in the newborn Chacma baboon: a preliminary report. Cleft Palate Craniofac J 27:241–252.

Cendekiawan T, Wong R, Rabie ABM. 2010. Relationships between cranial base synchondroses and craniofacial development: a review. Open Anat J 2:67–75.

Chen L, Adar R, Yang X, Monsonego EO, Li C, Hauschka PV, Yayon A, Deng C-X. 1999. Gly369Cys mutation in mouse FGFR3 causes achondroplasia by affecting both chondrogenesis and osteogenesis. J Clin Invest 104:1517.

Cohen JMM, Walker GF, Phillips C. 1985. A morphometric analysis of the craniofacial configuration in achondroplasia. J Craniofac Genet Dev Biol Suppl 1:139–165.

Cohen MM. 2000. Sutural biology. In: Cohen MM, MacLean RE, editors. Craniosynostosis—diagnosis, evaluation, and management. New York: Oxford University Press. 11–23.

Cohen MM. 2008. Foreword. In: Rice D, editor. Craniofacial sutures—development, disease and treatment. Basel: Karger. p VII–VIX.

Cohen MM, MacLean RE. 2000. Anatomic, genetic, nosologic, diagnostic, and psychosocial considerations. In: Cohen MM, MacLean RE, editors. Craniosynostosis—diagnosis, evaluation, and management. New York: Oxford University Press. p 119–143.

Drake AG, Klingenberg CP. 2008. The pace of morphological change: historical transformation of skull shape in St. Bernard dogs. Proc Biol Sci 275:71–76.

Drake AG, Klingenberg CP. 2010. Large-scale diversification of skull shape in domestic dogs: disparity and modularity. Am Nat 175:289–301.

Engström C, Kiliaridis S, Thilander B. 1986. The relationship between masticatory function and craniofacial morphology. II. A histological study in the growing rat fed a soft diet. Eur J Orthod 8:271–279.

Evans HE. 1993. Miller's anatomy of the dog. 3rd ed. Philadelphia: Saunders.

Fasanella FJ, Shivley JM, Wardlaw JL, Givaruangsawat S. 2010. Brachycephalic airway obstructive syndrome in dogs: 90 cases (1991–2008). J Am Vet Med Assoc 237:1048–1051.

Fondon JW, Garner HR. 2004. Molecular origins of rapid and continuous morphological evolution. Proc Natl Acad Sci USA 101: 18058–18063.

Goswami A, Foley L, Weisbecker V. 2013. Patterns and implications of extensive heterochrony in carnivoran cranial suture closure. J Evol Biol 26:1294–1306.

Hall BK. 2005. Bones and cartilage: developmental and evolutionary skeletal biology. San Diego: Elsevier Academic Press.

Herre W, Röhrs M. 1990. Haustiere—zoologisch gesehen. Stuttgart: Gustav Fischer Verlag.

Herring SW. 2000. Sutures and craniosynostosis: a comparative, functional, and evolutionary perspective. In: Cohen MM, MacLean RE, editors. Craniosynostosis—diagnosis, evaluation, and management. New York: Oxford University Press. p 3–10.

Herring SW. 2008. Mechanical influences on suture development and patency. In: Rice D, editor. Craniofacial sutures—development, disease and treatment. Basel: Karger. p 41–56.

Johnston N. 2006. Crunch time: approaches to bite abnormalities and malocclusions. Vet Times. p 10–13.

Julian LM, Tyler WS, Hage TJ, Gregory PW. 1957. Premature closure of the spheno-occipital synchondrosis in the horned Hereford dwarf of the "short-headed" variety. Am J Anat 100: 269–287.

Klatt B. 1913. Über den Einfluss der Gesamtgrösse auf das Schädelbild nebst Bemerkungen über die Voergeschichte der Haustiere. Wilhelm Roux Arch Entwickl Mech Org 36:387–471.

Krämer E-M. 2013. Faszination Rassehunde—Herkunft & Aufgaben, Temperament & Wesen. Stuttgart: Franckh-Kosmos Verlag.

Lüps P. 1974. Biometrische Untersuchungen an der Schädelbasis des Haushundes. Zool Anz 192:383–413.

Martin CL. 2009. Ophthalmic disease in veterinary medicine. Boca Raton: CRC Press.

Mundlos S. 1999. Cleidocranial dysplasia: clinical and molecular genetics. J Med Genet 36:177–182.

Nie X. 2005. Cranial base in craniofacial development: developmental features, influence on facial growth, anomaly, and molecular basis. Acta Odontol Scand 63:127–135.

Nowak RM. 1999. Walker's mammals of the world. 6th ed. Baltimore: John Hopkins University Press.

Nussbaumer M. 1982. Über die Variabilität der dorso-basalen Schädelknickungen bei Haushunden (On the variability of dorso-basal curvatures in skulls of domestic dogs). Zool Anz 209:1–32.

O'Neill MJF. 2013a. #119600: Cleidocranial dysplasia. Online Mendelian Inheritance in Man, OMIM®, Johns Hopkins University, Baltimore, MD.

O'Neill MJF. 2013b. #600211: Runt-related transcription factor 2. Online Mendelian Inheritance in Man, OMIM®, Johns Hopkins University, Baltimore, MD.

Opperman LA. 2000. Cranial sutures as intramembranous bone growth sites. Dev Dyn 219:472–485.

Packer RMA, Hendricks A, Tivers MS, Burn CC. 2015. Impact of facial conformation on canine health: brachycephalic obstructive airway syndrome. PLoS ONE 10:1–21.

Peters G. 1993. *Canis lupus* Linnaeus, 1758—wolf. In: Stubbe M, Krapp F, editors. Handbuch der Säugetiere Europas. Band 5: Raubsäuger—Carnivora (Fissipedia). Teil 1: Canidae, Ursidae, Procyonidae, Mustelidae 1. Wiesbaden: Aula-Verlag. p 47–106.

Pointer MA, Kamilar JM, Warmuth V, Chester SGB, Delsuc F, Mundy NI, Asher RJ, Bradley BJ. 2012. RUNX2 tandem repeats and the evolution of facial length in placental mammals. BMC Evol Biol 12:1–11.

Räber H. 2001. Enzyklopädie der Rassehunde. Stuttgart: Franckh-Kosmos Verlag GmbH & Co.

Rager L, Hautier L, Forasiepi A, Goswami A, Sánchez-Villagra M. 2014. Timing of cranial suture closure in placental mammals: phylogenetic patterns, intraspecific variation, and comparison with marsupials. J Morphol 275:125–140.

Rice DP. 2008. Developmental anatomy of craniofacial sutures. In: Rice D, editor. Craniofacial sutures—development, disease and treatment. Basel: Karger. p 1–21.

Rosenberg K. 1966. Die postnatale Proportionsänderung der Schädel zweier extremer Wuchsformen des Haushundes. J Anim Breed Genet 82:1–36.

Rosenberg P, Arlis HR, Haworth RD, Heier L, Hoffman L, LaTrenta G. 1997. The role of the cranial base in facial growth: experimental craniofacial synostosis in the rabbit. Plast Reconstr Surg 99: 1396–1407.

Sánchez-Villagra MR. 2010. Suture closure as a paradigm to study late growth in recent and fossils mammals: a case study with giant deer and dwarf deer skulls. J Vertebr Paleontol 30: 1895–1898.

Schmidt MJ, Volk H, Klingler M, Failing K, Kramer M, Ondreka N. 2013. Comparison of closure times for cranial base synchondroses in mesaticephalic, brachycephalic, and Cavalier King Charles spaniel dogs. Vet Radiol Ultrasound 54:497–503.

Schoenebeck JJ, Hutchinson SA, Byers A, Beale HC, Carrington B, Faden DL, Rimbault M, Decker B, Kidd JM, Sood R, et al. 2012. Variation of BMP3 contributes to dog breed skull diversity. PLoS Genet 8:1–11.

Schoenebeck JJ, Ostrander EA. 2013. The genetics of canine skull shape variation. Genetics 193:317–325.

Schroeder TM, Jensen ED, Westendorf JJ. 2005. Runx2: a master organizer of gene transcription in developing and maturing osteoblasts. Birth Defects Res C Embryo Today 75:213–225.

Sears KE, Goswami A, Flynn JJ, Niswader LA. 2007. The correlated evolution of Runx2 tandem repeats, transcriptional activity, and facial length in Carnivora. Evol Dev 9:555–565.

Starck D. 1962. Der heutige Stand des Fetalisationsproblems. J Anim Breed Genet 77:129–155.

Stockard CR. 1941. The genetic and endocrine basis for differences in form and behaviour as elucidated by studies of contrasted pure-line dog breeds and their hybrids. With special contributions on behaviour by O. D. Anderson and W. T. James. *American Anatomical Memoirs*. Philadelphia: Wistar Institute of Anatomy and Biology.

Turner SM. 2008. Small animal ophthalmology. Elsevier Health Sciences.

Wilson LA. 2014. Cranial suture closure patterns in Sciuridae: heterochrony and modularity. J Mamm E 21:257–268.

Wilson LAB, Sánchez-Villagra MR. 2009. Heterochrony and patterns of cranial suture closure in hystricognath rodents. J Anat 214:339–354.