Aging-related changes in the skulls of Japanese macaques (*Macaca fuscata*)

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Abstract We investigated aging-related changes in the skulls of Japanese macaques (*Macaca fuscata*). A total of 145 (70 males, 75 females) skulls from macaques aged 7.0–26.9 years (males) and 7.0–30.7 years (females) were measured for 22 craniometric items. Some skull dimensions increased from young adulthood (7.0 years) to the peak at 13.3–19.0 years in males and at 19.7–22.6 years in females. Some dimensions remained at their peak value right through into very old age whereas others continued increasing during this stage of life. Continued increase of cranial size in adulthood has been also observed in humans, but the magnitude of change was greater in macaques. Facial and mandibular dimensions showed larger and more significant increases than neurocranial dimensions in macaques, as in humans, including facial height, bizygomatic breadth, mandibular body height, and ramus breadth in both sexes. Intertemporal distance and biorbital breadths after 16.0 years of age decreased significantly in males, and cranial and posterior basicranial lengths increased only in males. We suggest that these craniometric changes are associated with the development of the insertion area onto which muscles attach (by accumulation of physical stress). The face and mandible are greatly influenced by tooth loss and/or dental disorders, both of which are evident in humans. In the present study large changes were also found in skulls that had lost several teeth.

Key words: aging, skull, face, cranium, *Macaca fuscata*

Introduction

Aging involves a decline in the ability to adapt to environmental stress (Bogin, 2001). Senescence is defined by changes that occur primarily in the postreproductive period in humans (around 50 years of age or more; Fedigan and Pavelka, 2001), which overall reduce the functional capacities of the organism and tissues in the decades after menopause (Borkan et al., 1982; Bogin, 2001). Although nonhuman primates maintain their reproductive activity almost until their death (Pavelka and Fedigan, 1999), physical aging advances from young adulthood throughout adult life (Hamada and Yamamoto, 2010).

Elderly adults can be characterized by the extent of aging in the musculoskeletal system, such as by a decrease in stature or kyphosis in the vertebral column (Hamada and Yamamoto, 2010). Bone is an organ that shows deterioration with age in both humans and nonhuman primates (Mazess, 1982; Black et al., 2001). Aging-related changes in human skulls are receiving increased attention and have been stud-

ied, for example in forensic research (Albert et al., 2007) and esthetic surgery (Bartlett et al., 1992). Postcranial skeletal changes in aging are obvious in both humans and nonhuman primates. Continuous expansion in the human postcranial skeleton (transverse diameters) has been documented for various bones (Smith and Walker, 1964; Garn et al., 1967; Pfeiffer, 1980; Ruff and Hayes, 1982). It is also seen in nonhuman primates, as shown by macaques (Bowden et al., 1979; Kimura, 1994) and chimpanzees (Morbeck et al., 2002).

There is controversy with respect to changes of the skull with age in adult humans. With sexual maturation, cranial growth in humans has been considered to cease or be insignificant (Tallgren, 1974). However, it has been recognized that cranial growth does not end at the adolescent stage in humans, but continues at a slow rate throughout adulthood (Hrdlička, 1936; Israel, 1977; Ruff, 1980; Forsberg et al., 1991), and it has been suggested that the cranium decreases in size in very old people (Hrdlička, 1936; Israel, 1973b). A small increase in the thickness of the skull during adult life has been suggested (Adeloye et al., 1975), but no statistically significant increase was found (Lynnerup, 2001). However, these conclusions are subject to sampling bias (small sample sizes, samples limited to certain historic anatomical collections or homogeneous populations), different age ranges, the confounding effects of pathology, methodologies in data collection, and the statistical methods adopted

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(Lynnerup, 2001; Albert et al., 2007).

The phylogenetic closeness and marked biological similarities to humans make macaques and baboons a good model of human skeletal aging (Walker, 1995; Colman and Binkley, 2002). The similarities include posture (Black et al., 2001), reproductive endocrinology (Pavelka and Fedigan, 1999), bone loss following estrogen depletion (Colman and Binkley, 2002), and histomorphometry (Jerome et al., 1994). In contrast, mice lack the osteonal bone remodeling (Jilka, 2013) and the murine cortex is composed mostly of the circumferential lamellae (Enlow and Brown, 1958). The life cycle of macaques is the same as that of humans (Hamada and Yamamoto, 2010), including the elderly stage. In general, macaques age at a rate of 2.5–3.5 times that of humans (Colman and Anderson, 2011; Duncan et al., 2011). Although a good model of human aging, macaques have not been well studied in terms of the effect of aging on the skull.

Little is known about aging-related changes in the skulls of nonhuman primates. Exceptionally, some studies noticed a decrease in the intertemporal distance in male Japanese macaques in wild populations (Mouri et al., 2004), an enlargement of the medullary cavity of bones that border the facial suture in pig-tailed macaques (Kokich et al., 1979), and endocranial suture closure in rhesus macaques (Wang et al., 2006).

In the present study we investigated aging-related changes in skulls of Japanese macaques (*Macaca fuscata*), and compared them with those in human skulls. The objectives of this study were to determine whether skulls of nonhuman primates increase or decrease in size and/or change shape with age, whether changes in skull with age differ between sexes, whether magnitude of size or shape change in macaques is comparable to those in humans, and whether facial dimensions are influenced by tooth loss in macaques.

Materials and Methods

Subjects

A total of 145 skulls from adult Japanese macaques (*M. fuscata*) of known age, comprising 70 males and 75 females (Table 1), were used. In general, the adult stage is considered to start at the age when body growth stops, represented by such whole-body dimensions as stature (or its proxy, trunk length in nonhuman primates) (Hamada and Yamamoto, 2010). However, the age at which body growth stops has not been determined for Japanese macaques because body weight fluctuates within a given individual and shows great variation among individuals after adolescence (Hamada and Yamamoto, 2010); and the growth in linear dimension is too slow to identify the exact age at which growth ceases (Hamada and Yamamoto, 2010). Thus 7 years of age, when the permanent teeth have fully erupted (Iwamoto et al., 1987), has been regarded as the age demarcating the adult stage.

All the subject macaques were being fed, at least in the period before their death, at the Primate Research Institute of Kyoto University. All skulls were stored at the institute. No macaques suffered from serious disease or received serious experimental treatment. The ages of the macaques are expressed in centesimal age. Although the dates of birth of 11

Table 1. Sample sizes of the skull by sex and age

Age (years)	Male		Female	
	Total	Tooth loss subject	Total	Tooth loss subject
7.0–9.9	17	0	15	0
10.0–3.9	19	0	20	0
14.0–17.9	14	0	17	0
18.0–21.9	9	0	8	0
>22	11	4	15	5
Total	70	4	75	5

individuals were not known, their years of birth and dates of death were recorded. For the ages of these macaques we used the date June 15 for their birth, as Japanese macaques have a definite birth season, from March to August (Nozaki and Oshima, 1987). The years of birth of the individuals ranged from 1966 to 2001, and the years of death ranged from 1976 to 2009. Ages of male and female subjects ranged from 7.0 to 26.9 years and from 7.0 to 30.7 years, respectively (Table 1).

Twenty linear dimensions and two angles of skull and mandible were measured on each specimen (Table 2, Figure 1) (Mouri, 1994; Mouri et al., 2004): 7 neurocranial dimensions (cranial length, cranial base length, cranial height, cranial breadth at the nuchal line, posterior basicranial length, postorbital breadth, and intertemporal distance), 10 facial dimensions (facial length, facial height, bizygomatic breadth, zygomatic height at temporozygomatic suture, orbital breadth, orbital height, biorbital breadth, nasal length, maxilloalveolar breadth, and maxillary angle), and 5 mandibular dimensions (ramus breadth, mandibular body height, mandibular body thickness, bicondylar breadth, and mandibular angle). Measurements were made in triplicate, and a median value was used for analysis. All measurements of the skull were made to the nearest 0.01 mm using a digital sliding caliper (Mitutoyo Corp., Japan). Maxillary angle was calculated using the cosine rule of a triangle with three linear sizes of sides. Since the three linear sizes (ZO–ZR, ZR–EAM, and EAM–ZO; Table 2) of the triangle are not on the sagittal plane, the maxillary angle is also oblique to the sagittal plane. The mandibular angle was obtained photogrammetrically (Figure 1e). The photographic setup consisted of a tripod (Dolly pod DP-3D, Velbon Tripod Co., Ltd.) holding a digital camera (FinePix HS20EXR, Fujifilm Co., Ltd.). The tripod was adjusted to maintain the optical axis of the lens horizontal and at the height of the subject. The lateral view of the left side of the mandible was positioned approximately 3 m from the objective lens of the camera and was adjusted so that the sagittal plane of the mandible was perpendicular to the optical axis of the lens. After raising the optical axis of the lens to the alveolar process at the middle of the second mandibular molar, photographs were taken. The mandibular angle was measured from images with Image J 1.46 (Ferreira and Rasband, 2013). The items measured are showed in Table 2 and Figure 1. The status of dentition and of the alveolar bone were recorded for each specimen.

Table 2. Measurements taken on the skull

Abbreviation	Variable and definition
CL	Cranial length: maximum length of neurocranium in the midsagittal plane measured from nasion
CBL	Cranial base length: from basion to nasion
CH	Cranial height: from basion to bregma
CBN	Cranial breadth at nuchal line: maximum breadth at lateral nuchal line
PBL	Posterior basicranial length: from basion to inion
POB	Postorbital breadth: horizontally minimum and vertically maximum breadth of postorbital region
ITD	Intertemporal distance: distance between the right and left inferior temporal lines at the coronal suture
FL	Facial length: from basion to prosthion
FH	Facial height: from nasion to prosthion
BZB	Bizygomatic breadth: from zygion to zygion
ZH	Zygomatic height at temporozygomatic suture: minimum distance measured from superior zygomatic process to inferior temporal process across middle temporozygomatic suture
OB	Orbital breadth: from right maxillofrontare to right frontomale orbitale.
OH	Orbital height: height of right orbit in the parasagittal plane measured from zygomaticomaxillary suture at inferior orbital margin.
BOB	Biorbital breadth: from frontomale temporale to frontomale temporale
NL	Nasal length: from nasion to rhinion
MAB	Maxilloalveolar breadth: maximum breadth across the alveolar borders of the maxilla measured on the lateral surfaces at the middle of the second maxillary molars
MXA	Maxillary angle: the angle taken between the length from zygomaticomaxillary suture at inferior orbital margin (ZO) to zygomaticomaxillary suture at root of zygomatic arch (ZR) and the length from zygomaticomaxillary suture at inferior orbital margin (ZO) to the middle of the external auditory meatus at the upper margin of the meatus (EAM)
RB	Ramus breadth: minimum breadth of the mandibular ramus
MBH	Mandibular body height: direct distance from alveolar process at middle of second mandibular molar to the inferior border of the mandible measured perpendicular to the mandibular occlusal plane following the buccal cusps of the molars
MBT	Mandibular body thickness: maximum breadth in lateral mandibular body at the height of mandibular body measured perpendicular to mid-sagittal plane of mandible
BCB	Bicondylar breadth: direct distance between the most lateral points on the two condyles
MA	Mandibular angle: angle formed by the mandibular occlusal plane following the buccal cusps of molars and the posterior border of the ramus

Statistical analyses

Teeth in subjects were almost all retained until death, but 9 subjects had lost several teeth (Table 1): 4 males (ages from 23.7 to 26.0 years) and 5 females (ages from 25.2 to 30.0 years) had lost 8–11 teeth and 6–18 teeth, respectively. Tooth loss is an important factor of change in facial dimensions (Goldstein, 1936; Bartlett et al., 1992). Therefore, subjects that had lost many teeth were analyzed separately (4 males and 5 females) and then were compared with those subjects of comparable ages with all teeth retained, which comprised of 6 males (ages from 23.3–26.9 years) and 6 females (ages from 25.3–30.7 years). The effect of tooth loss on facial dimensions could thus be evaluated.

Statistical analyses were performed using functions of Excel (Microsoft Co. Ltd.). To describe age change patterns, Loess smoothing, locally weighted scatterplot smoothing (Past version 2.17 software; Hammer et al., 2001), was used. We compared craniometric dimensions and angles at start, peak size, and end of the adult stage. The age at peak size was derived from the Loess smoothing function. For measurements that did not show an increase–peak–decrease age-change pattern (continuous increase or decrease), sizes at the

start and end were compared. The sizes at start (young adult, 7.0 years) and peak in each measurement were represented by medians of data of 7.0–9.0 years in both sexes, and those of peak age ± 1 year in both sexes, respectively. Because of the small sample size of data from very old subjects, end size was represented by the median of the data of the five oldest subjects, i.e. 24.0–26.9 years for males and 25.5–30.7 years for females. Percent differences (median) between sizes at start, peak, and end were obtained and differences of angle measurements were calculated by subtracting the two values to create an absolute value. Differences between start, peak, and end sizes (medians) and between sexes were tested by Mann–Whitney *U*-test using Past version 2.17 software (Hammer et al., 2001). Differences between lost-teeth and retained-teeth subjects and between sexes were also tested by Mann–Whitney *U*-test.

As cranial variables are not independent of one another, principal component analysis (PCA) was applied to both males and females using Past (Hammer et al., 2001). The relationship between scores of principal components (PCs) and ages was determined by the Loess smoothing function.

Figure 1. Schematic illustration of most of the measurements taken on the skull (see Table 2 for abbreviations): (a) skull in ventral view; (b) skull in anterior view; (c) skull in lateral view; (d) skull in dorsal view; (e) mandible in lateral view; (f) mandible in transverse view.

Results

Some dimensions and angles showed aging-related patterns. Skull measurements at start (young adulthood), peak, and end (very old age) are presented in Table 3, Table 4, and Table 5, and Figure 2. Changes with age were significant ($P < 0.05$) in 14 and 7 cranial dimensions in males (Table 3, Table 5) and females (Table 4, Table 5), respectively.

Neurocranial dimensions

The four neurocranial dimensions, i.e. CL, PBL, CBL, and ITD, changed significantly with age in males but not in females (Table 4). CL, PBL, and CBL in males peaked at 16.1 years with an increase of 4.55% ($P < 0.01$), at 16.0 years with 5.19% ($P < 0.05$), and at 14.5 years with 6.25% ($P < 0.05$), respectively. After the peaks these dimensions did not decrease at all. PBL also showed a significant increase between the start age and the end age in males by 4.66% ($P < 0.05$). ITD decreased greatly with age in males by 68.89% from the start to the end ($P < 0.001$, Figure 2). Other dimensions, such as CBN and POB in males, remained stable or changed slightly, but not statistically significantly (Table 3).

Facial dimensions

Facial cranial dimensions tended to show statistically significant changes with age, but several facial dimensions showed no or slight age changes, including OB, OH, NL, and MXA in both sexes. FH continuously increased through very old age in both sexes with increases of 13.83% ($P < 0.001$) in males and 12.10% ($P < 0.01$) in females. FL increased significantly with age in males and peaked at approximately 16.0 years of age with an increase of 13.44% ($P < 0.001$). After the peak, FL in males decreased slightly. On the other hand, this dimension increased only slightly in females. BZB and BOB also increased significantly with age in both sexes. After the peaks, these dimensions decreased slightly or not at all in both sexes; however, exceptionally BOB in males decreased significantly ($P < 0.01$). MAB increased significantly with age in both sexes, peaked at 13.3 years of age in males with an increase of 4.24% ($P < 0.05$), and increased 3.96% from the start (7.0 years) to the end (30.7 years) in females ($P < 0.01$). ZH increased significantly with age only in males, and reached a peak at 19.0 years of age with an increase of 16.06% ($P < 0.05$), whereas this dimension changed slightly in females, but not statistically significantly.

Table 3. Medians in start, peak, and end and age change (%) in males

Dimension	Start size (7.0–9.0 years)	Peak size (peak age ±1.0 years)	Age at peak	End size (24.0–26.9 years)	Age change of Start–Peak (%)	Age change of Peak–End (%)	Age change of Start–End (%)
CL (mm)	94.79	99.10	16.1	96.37	4.55**	–2.75	1.67
CBL (mm)	73.79	78.40	14.5	75.55	6.25*	–3.64	2.39
CH (mm)	57.99	59.90	13.9	58.13	3.29	–2.95	–0.24
CBN (mm)	72.81	74.50	13.5	72.95	2.32	–2.08	0.19
PBL (mm)	41.01	43.14	16.0	42.92	5.19*	–0.51	4.66*
POB (mm)	46.80	47.01	18.1	45.42	0.45	–3.38	–2.95
ITD (mm)	23.05	—	—	7.17	—	—	–68.89***
FL (mm)	96.99	110.03	16.0	105.16	13.44***	–4.43	8.42*
FH (mm)	68.54	—	—	78.02	—	—	13.83***
BZB (mm)	93.59	101.00	14.6	100.62	7.92**	–0.38	7.51*
ZH (mm)	7.97	9.25	19.0	8.50	16.06*	–8.11	6.65
OB (mm)	29.49	—	—	28.06	—	—	–4.85
OH (mm)	25.87	—	—	24.80	—	—	–4.14
BOB (mm)	67.93	74.66	16.0	66.37	9.91**	–11.10**	–2.30
NL (mm)	36.15	—	—	40.00	—	—	10.65
MAB (mm)	42.49	44.29	13.3	44.14	4.24*	–0.34	3.88
RB (mm)	28.57	31.26	17.0	31.20	9.42*	–0.19	9.21
MBH (mm)	24.50	26.95	18.1	27.13	10.00*	0.67	10.73*
MBT (mm)	10.23	—	—	11.22	—	—	9.68**
BCB (mm)	77.76	—	—	80.88	—	—	4.01

* $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ statistically significant difference using Mann–Whitney U -test between start size vs. peak size, peak size vs. end size, and start size vs. end size.

Table 4. Medians in start, peak, and end and age change (%) in females

Dimension	Start size (7.0–9.0 years)	Peak size (peak age ±1.0 years)	Age at peak	End size (25.5–30.7 years)	Age change of Start–Peak (%)	Age change of Peak–End (%)	Age change of Start–End (%)
CL (mm)	91.68	94.90	20.2	90.75	3.51	–4.37	–1.01
CBL (mm)	71.17	73.23	19.7	70.35	2.89	–3.93	–1.15
CH (mm)	56.91	58.10	19.7	54.95	2.09	–5.42	–3.44
CBN (mm)	66.16	69.18	23.3	68.79	4.56	–0.56	3.98
PBL (mm)	38.98	39.20	22.6	39.00	0.56	–0.51	0.05
POB (mm)	45.26	46.13	11.6	45.54	1.92	–1.27	0.62
ITD (mm)	25.00	26.25	10.0	23.00	5.00	–12.38	–8.00
FL (mm)	87.61	90.80	23.5	90.00	3.64	–0.88	2.73
FH (mm)	63.00	—	—	70.62	—	—	12.10**
BZB (mm)	86.02	92.25	22.6	89.01	7.24**	–3.51	3.48
ZH (mm)	7.62	8.00	19.7	7.50	4.99	–6.25	–1.57
OB (mm)	27.15	27.90	20.2	26.93	2.76	–3.48	–0.81
OH (mm)	24.31	24.17	20.1	23.07	–0.58	–4.55	–5.10
BOB (mm)	62.84	66.45	20.2	63.89	5.74**	–3.85	1.67
NL (mm)	33.71	—	—	34.78	—	—	3.17
MAB (mm)	40.36	—	—	41.95	—	—	3.96**
RB (mm)	26.13	28.11	20.2	27.03	7.58*	–3.84	3.44
MBH (mm)	22.26	25.05	19.7	23.65	12.67***	–5.70	6.24*
MBT (mm)	9.70	10.77	19.7	10.12	11.03	–6.04	4.33
BCB (mm)	72.21	75.53	20.2	71.98	4.60	–4.70	–0.32

* $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ statistically significant difference using Mann–Whitney U -test between start size vs. peak size, peak size vs. end size, and start size vs. end size.

Table 5. Angle measures and age change (°) in males and females

Measure	Start	Peak (peak age ±1.0 years)	Age at peak	End	Age change of Start–Peak (°)	Age change of Peak–End (°)	Age change of Start–End (°)
Male (7.0–26.9 years)							
MXA (°)	59.08	61.42	11.0	57.99	3.96	–5.58	–1.84
MA (°)	102.10	—	—	110.17	—	—	8.07*
Female (7.0–30.7 years)							
MXA (°)	59.29	60.99	—	59.27	2.87	–2.82	–0.03
MA (°)	100.78	—	—	106.28	—	—	5.50**

* $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ statistically significant difference using Mann–Whitney U -test between start size vs. end size.

Figure 2. Scatter plots showing age change in all skulls (without teeth loss) with Loess smoothing. Male, ○ and dashed line; female, ● and solid line.

Mandibular dimensions

Mandibular dimensions in general showed significant changes with age (Table 3, Table 4, Table 5). Exceptionally,

however, BCB changed slightly but not significantly. MBH and RB increased significantly with age in both sexes, and then tended to remain stable or decrease not at all.

Figure 2. (continued)

MBT in males increased continuously with age by 9.67% from the start to the end ($P < 0.01$), whereas this dimension changed in females, but not statistically significantly. MA

showed a significant increase with age in both sexes by 8.07° in males ($P < 0.05$) and 5.50° in females ($P < 0.01$).

Table 6. Factor loadings of PC1, PC2, and PC3 of craniometric variables obtained from the principal component analysis using both sexes

Variable	PC1	PC2	PC3
CL	0.236	0.195	0.013
CBL	0.260	0.130	0.079
CH	0.200	0.145	0.395
CBN	0.257	0.092	0.122
PBL	0.213	-0.237	0.048
POB	0.156	0.360	0.304
ITD	-0.193	0.429	0.202
FL	0.269	-0.119	-0.020
FH	0.248	-0.013	-0.366
BZB	0.278	-0.087	0.033
ZH	0.188	-0.171	0.096
OB	0.227	0.298	0.086
OH	0.138	0.476	-0.372
BOB	0.261	0.099	0.205
NL	0.203	0.170	-0.511
MAB	0.205	-0.208	0.089
RB	0.250	-0.120	0.026
MBH	0.216	-0.107	-0.242
MBT	0.154	-0.250	0.162
BCB	0.250	-0.094	0.001
Eigenvalue	11.80	1.64	1.01
Proportion	58.98	8.18	5.05

Size and shape change of skull with age

In a PCA using 20 linear cranial measurements and based on a correlation matrix, the first three principal components accounted for 58.98%, 8.18%, and 5.05% of total variation, respectively (Table 6). The first principal component (PC1), representing size change, showed that all dimensions apart from ITD had positive loadings. The PC1 scores showed age-change patterns similar to many dimensions (Figure 3a). Males had higher PC1 scores than females. Age at the peak PC1 score was 16.0 and 20.2 years in males and females, respectively.

The second principal component (PC2), describing shape change with age, showed that females had higher scores than males (Figure 3b). OH (0.476), ITD (0.429), POB (0.360), and OB (0.298) were positively loaded, whereas PBL (-0.237), MAB (-0.208), and MBT (-0.250) were negatively loaded (Table 6). The PC2 scores showed a rather rapid decrease from 7.0 to 11.0 years, remained stable from 11.0 to 17.0 years, and then decreased again in males, although remained almost unchanged from 7.0 to 30.7 years in females (Figure 3b).

The third principal component (PC3) represented shape change, with NL (-0.511), OH (-0.372), and FH (-0.366) negatively loaded and CH (0.395) positively loaded (Figure 3c, Table 6). PC3 showed gradual decreases in both males and females (Figure 3c).

The effect of tooth loss on facial and mandibular dimensions

Thirteen facial and mandibular dimensions of subjects that had lost several teeth were compared with those subjects

Figure 3. Plots of (a) first principal component scores, (b) second principal component scores, and (c) third principal component scores against age with Loess smoothing. Male, ○ and dashed regression line; female, ● and solid regression line.

of comparable ages with all teeth retained (Table 7). The results of the comparison in this study showed that two dimensions of lost-teeth subjects differed significantly from retained-teeth subjects in both sexes. FH and MBH in males were 16.75% ($P < 0.01$) and 17.29% ($P < 0.01$) smaller than the medians for male macaques with all teeth retained, respectively, whereas these measurements in females were 11.16% ($P < 0.05$) and 15.45% ($P < 0.01$) smaller than female subjects with all teeth retained, respectively.

Table 7. Comparison of facial and mandibular dimensions between retained-teeth and lost-teeth subjects

Dimension	Retained-teeth subjects		Lost-teeth subjects		Percentage change between retained- and lost-teeth subjects
	Median	Range	Median	Range	
FL (mm)					
Male	106.50	101.39–112.68	98.36	94.28–107.37	–7.74
Female	92.13	86.50–98.51	87.96	79.33–94.52	–4.53
FH (mm)					
Male	78.88	77.77–87.32	65.67	63.22–71.64	–16.75**
Female	71.40	64.42–80.05	63.12	56.01–70.66	–11.60*
BZB (mm)					
Male	101.30	96.41–107.85	99.03	96.34–105.49	–2.24
Female	89.24	81.70–89.84	89.70	87.60–91.70	0.51
ZH (mm)					
Male	8.94	7.50–10.38	9.30	7.11–11.34	4.03
Female	7.18	6.09–9.10	6.91	6.28–10.80	–3.20
OB (mm)					
Male	28.83	27.04–31.69	27.94	27.05–30.19	–3.09
Female	26.90	26.19–30.06	26.69	25.42–27.32	–0.78
OH (mm)					
Male	24.91	23.27–26.80	24.85	23.39–26.51	–0.24
Female	23.33	22.00–27.50	24.50	24.12–27.39	5.02
BOB (mm)					
Male	66.86	64.81–72.09	69.51	66.08–71.75	3.96
Female	63.68	59.65–66.18	63.22	62.85–65.96	–0.72
NL (mm)					
Male	38.70	34.75–42.92	37.08	34.75–40.51	–4.19
Female	35.28	31.97–38.63	34.79	31.19–36.86	–1.39
MAB (mm)					
Male	43.57	41.76–46.37	43.47	40.00–44.72	0.00
Female	41.74	41.25–43.78	41.41	37.30–43.69	–0.79
RB (mm)					
Male	30.15	27.48–33.17	31.04	27.95–32.68	2.95
Female	26.29	23.11–27.59	26.23	25.64–27.30	–0.23
MBH (mm)					
Male	27.01	25.89–28.62	22.34	20.10–25.88	–17.29**
Female	24.33	23.24–26.00	20.57	18.78–21.41	–15.45**
MBT (mm)					
Male	11.14	9.99–11.98	11.08	9.99–11.18	–0.54
Female	10.49	9.80–12.06	10.60	10.16–10.95	1.05
BCB (mm)					
Male	79.52	76.29–83.84	78.14	76.20–81.27	–1.74
Female	72.96	70.71–74.65	76.02	70.77–76.39	4.19

* $P < 0.05$ and ** $P < 0.01$ statistically significant difference using Mann–Whitney U -test for retained-teeth males ($n = 6$, ages from 23.3–26.9 years) vs. lost tooth males ($n = 4$, ages from 23.7–26.0 years) and retained-teeth females ($n = 6$, ages from 25.3–30.7 years) vs. lost-teeth females ($n = 5$, ages from 25.2–30.0 years).

Discussion

Cross-sectional aging studies suffer from secular trends or environmental variability that masks ontogeny (Baer, 1956). Although we studied macaque skulls cross-sectionally, all of them originated from captive monkeys fed under the same conditions during their lifespans. Thus, secular trends or environmental factors may not have had any effect on cranial dimensions in this study.

The results of the present study indicate that some of the cranial dimensions showed aging-related changes, with a pattern increasing from young adulthood (7.0 years) to mid-adulthood (13.3–19.0 years in males and 19.7–22.6 years in females) and unchanged from mid-adulthood to very old age (26.9 years or more) or increasing from young adulthood to very old age. It is probable that the increase from 7.0 years to mid-adulthood or very old age comprises both total physical growth, which ends at 10.0 or 15.0 years

of age (Hamada, 1994; Hamada and Yamamoto, 2010) and specific increases in the head and face. Maximal stages of skull size in some measurements, including bizygomatic, biorbital, and ramus breadths and mandibular body height, tended to be attained later in females than in males. This corresponds with the data that trunk length and epiphyseal unions in postcranial skeletons tended to occur later in females than in males in Japanese macaques (Kimura, 1994; Hamada, 2008). Intertemporal distance and biorbital breadth (after 16.0 years) decreased significantly in males. Facial and mandibular dimensions tended to show greater and more significant change with age than neurocranial dimensions, including facial height, bizygomatic breadth, mandibular body height, and ramus breadth in both sexes. Furthermore, as for proportional changes in the face, facial height increased more than bizygomatic breadth in both sexes, making the face relatively longer with age in macaques. In addition, proportions changed, i.e. orbital height to orbital or biorbital breadth.

Continued increase of cranial size in adulthood has been observed in humans (Goldstein, 1936; Garn et al., 1967; Nasjeleti and Kowalski, 1975; Israel, 1973a, 1977; Susanne, 1977; Ruff, 1980; Bartlett et al., 1992). Human skulls attain maximal size at about 70 years of age (Israel, 1973b). In macaques, ages at maximal skull size are estimated (by PCA) to be 16.0 ± 3 and 20.2 ± 3 years in males and females, respectively, i.e. 48.0 and 60.6 year equivalents in human age.

The magnitude of extensive development after completion of tooth eruption in skull dimensions is much greater in macaques than in humans. For example, facial height increases by 3.66% in men from 20.0 to ≥ 60.0 years (Nasjeleti and Kowalski, 1975), or 1.49% in men and 1.28% in women aged from 18.0 to 42.0 years of age (Formby et al., 1994). In contrast, facial height in male macaques increased by 13.83% from young adulthood to 26.9 years and by 12.10% in females from 7.0 to 30.7 years. Similarly, facial length in male macaques is larger than that of men (Ruff, 1980) and bizygomatic breadth is also larger in both male and female macaques than that of men and women (Susanne, 1977;

Bartlett et al., 1992). Neurocranial dimensions, such as cranial length, show smaller contrasts between humans (Israel, 1977) and macaques than facial dimensions.

The magnitude of age change in skull dimensions, which differs between humans and macaques, may be associated with mechanical stress from mastication, which is likely to stimulate an increase in facial dimensions and a change in neurocranial dimensions. Previous studies have demonstrated that hard, tough, and unprocessed diets play an important role in increasing the general sizes of the skull and face (Carlson and Van Gerven, 1977; Sardi et al., 2006), and thus the softer and more processed foods in human diets are considered to reduce masticatory stress in the craniofacial skeleton (Carlson and Van Gerven, 1977; Lieberman et al., 2004; Sardi et al., 2006; Paschetta et al., 2010), resulting in a smaller increase in facial size than in macaques.

Sex differences in aging-related changes in cranial dimensions are not large in humans (Ruff, 1980). However, sex differences in these changes in macaques are rather large. Various degrees of sex difference were found in macaques, large in facial and small in neurocranial dimensions. Human-macaque differences in sex difference and sex differences in macaques may be associated with the stress of mastication (Wang et al., 2006). Larger masticatory forces are applied to the face in male macaques than in females (Dechow and Carlson, 1990).

Expansion of the cranium may be associated with the development of bones as a response to physical stress from masticatory and/or postural muscles. The increase in cranial and posterior basicranial lengths in male macaques may be associated with the development of the nuchal crest or insertion processes (tubercles) on which the nuchal muscles attach. The large decrease in intertemporal distance and post-orbital breadth may be the result of development or stress from temporalis (Figure 4).

Facial crania and mandibles are greatly influenced by tooth loss and/or dental disorders in humans (Israel, 1973c; Bartlett et al., 1992; Merrot et al., 2005). In the present study subject macaques that had lost many teeth exhibited a reduction of the alveolar bone and also large changes in the face

Figure 4. The differences in temporal line and bone around inion between old males (a) and females (b) in Japanese macaques.

and mandible. These changes were especially true for mandibular body height and facial height compared with those of subjects of comparable ages with all teeth retained (Figure 5, Figure 6). Similar findings have been reported for humans

(Israel, 1973c; Bartlett et al., 1992) and for other nonhuman primates; alveolar resorption occurred in captive rhesus macaques (Lapin et al., 1979) and wild chimpanzees (Kilgore, 1989; Morbeck et al., 2002).

Figure 5. Atrophy of alveolar process of maxilla (a) and mandible (b) in some Japanese macaques that have lost teeth; lateral view.

Figure 6. Scatter plots showing how tooth loss causes large decreases in facial and mandibular body height in Japanese macaques. ○ male, ◆ male with tooth loss, ● female, △ female with tooth loss.

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References

- Adeloye A., Kattan K.R., and Silverman F.N. (1975) Thickness of normal skull in the American blacks and whites. *American Journal of Physical Anthropology*, 43: 23–30.
- Albert A.M., Ricanek K., Jr., and Patterson E. (2007) A review of the literature on the aging adult skull and face: implication for forensic science research and applications. *Forensic Science International*, 172: 1–9.
- Baer M.J. (1956) Dimensional changes in the human head and face in the third decade in life. *American Journal of Physical Anthropology*, 14: 557–575.
- Bartlett S.P., Grossman R., and Whitaker L. (1992) Age-related changes of the craniofacial skeleton: an anthropometric and histological analysis. *Plastic and Reconstructive Surgery*, 90: 592–600.
- Black A., Tilmont E.M., Handy A.M., Scott W.W., Shapses S.A., Ingram D.K., Roth G.S., and Lane M.A. (2001) A nonhuman primate model of age-related bone loss: a longitudinal study in male and premenopausal female rhesus monkeys. *Bone*, 28: 295–302.
- Bogin B. (2001) *The Growth of Humanity*. Wiley-Liss, New York.
- Borkan G.A., Hults D.E., and Mayer P.J. (1982) Physical anthropological approaches to aging. *Yearbook of Physical Anthropology*, 25: 181–202.
- Bowden D.M., Teets C., Witkin J., and Young D.M. (1979) Long bone calcification and morphology. In: Bowden D.M. (ed.), *Aging in Nonhuman Primates*. Van Nostrand Reinhold, New York, pp. 335–347.
- Carlson D.S. and Van Gerven D.P. (1977) Masticatory function and post-Pleistocene evolution in Nubia. *American Journal of Physical Anthropology*, 46: 495–506.
- Colman R.J. and Anderson R.M. (2011) Nonhuman primate calorie restriction. *Antioxidants and Redox Signaling*, 14: 229–239.
- Colman R.J. and Binkley N. (2002) Skeletal aging in macaque monkeys. In: Erwin J.M. and Hof P.R. (eds.), *Aging in Nonhuman Primates. Interdisciplinary Topics in Gerontology*, Vol. 31, Karger, Basel, pp. 32–47.
- Dechow P.C. and Carlson D.S. (1990) Occlusal force and craniofacial biomechanics during growth in the rhesus monkey. *American Journal of Physical Anthropology*, 83: 219–237.
- Duncan A.E., Colman R.J., and Kramer P.A. (2011) A longitudinal study of radiographic spinal osteoarthritis in a macaque model. *Journal of Orthopaedic Research*, 29: 1152–1160.
- Enlow D.H. and Brown S.O. (1958) A comparative histological study of fossil and recent bone tissues. Part III. *Texas Journal of Science*, 10: 187–230.
- Fedigan L.M. and Pavelka M.S.M. (2001) Is there adaptive value to reproductive termination in Japanese macaques? A test of maternal investment hypotheses. *International Journal of Primatology*, 22: 109–125.
- Ferreira T. and Rasband W. (2013) ImageJ 2012 revised user guide, <https://www.e-biogenouest.org/resources/583>
- Formby W.A., Nanda R.S., and Currier G.F. (1994) Longitudinal changes in the adult facial profile. *American Journal of Orthodontics and Dentofacial Orthopedics*, 105: 464–476.
- Forsberg C.M., Eliasson S., and Westergren H. (1991) Face height and tooth eruption in adults—a 20-year follow-up investigation. *European Journal of Orthodontics*, 13: 249–254.
- Garn S.M., Rohmann C.G., Wagner B., and Ascoli W. (1967) Continuing bone growth throughout life: a general phenomenon. *American Journal of Physical Anthropology*, 26: 313–318.
- Goldstein M.S. (1936) Changes in dimensions and form of the face and head with age. *American Journal of Physical Anthropology*, 22: 37–89.
- Hamada Y. (1994) Standard growth patterns and variations in growth patterns of the Japanese Monkeys (*Macaca fuscata*) based on an analysis by the spline function method. *Anthropological Science*, 102 (Supplement): 57–76.
- Hamada Y. (2008) Body growth and aging in Japanese macaques. In: Takatsuki S. and Yamagiwa J. (eds.), *Japanese Mammalogy 2: Medium and Large Mammals*. University of Tokyo Press, Tokyo, pp. 53–75 (in Japanese).
- Hamada Y. and Yamamoto A. (2010) Morphological characteristics, growth and aging in Japanese macaques. In: Nawagata N., Nakamichi M., and Sugiura H. (eds.), *The Japanese Macaques*. Springer Verlag, Berlin, pp. 27–52.
- Hammer Ø., Harper D.A.T., and Ryan P.D. (2001) PAST: Paleontological statistics software package for education and data analysis. *Palaeontologia Electronica* 4: 9pp., http://palaeo-electronica.org/2001_1/past/issue1_01.htm
- Hrdlicka A. (1936) Growth during adult life. *Proceedings of the American Philosophical Society*, 76: 847–897.
- Israel H. (1973a) Age factor and the pattern of change in craniofacial structures. *American Journal of Physical Anthropology*, 39: 111–128.
- Israel H. (1973b) Recent knowledge concerning craniofacial aging. *Angle Orthodontist*, 43: 176–184.
- Israel H. (1973c) The failure of aging or loss of teeth to drastically alter mandibular angle morphology. *Journal of Dental Research*, 52: 83–90.
- Israel H. (1977) The dichotomous pattern of craniofacial expansion during aging. *American Journal of Physical Anthropology*, 47: 47–52.
- Iwamoto M., Watanabe T., and Hamada Y. (1987) Eruption age of permanent teeth in Japanese macaques. *Primate Research*, 3: 18–28 (in Japanese with English summary).
- Jerome C.P., Carlson C.S., Register T.C., Bain F.T., Jayo M.J., Weaver D.S., and Adams M.R. (1994) Bone functional changes in intact, ovariectomized, and ovariectomized, hormone-supplemented adult cynomolgus monkeys (*Macaca fascicularis*) evaluated by serum markers and dynamic histomorphometry. *Journal of Bone and Mineral Research*, 9: 527–540.
- Jilka R.L. (2013) The relevance of mouse models for investigating age-related bone loss in humans. *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 68: 1209–1217.
- Kilgore L. (1989) Dental pathologies in ten free-ranging chimpanzees from Gombe National Park, Tanzania. *American Journal of Physical Anthropology*, 80: 219–227.
- Kimura T. (1994) Age changes of postcranial skeletons in adult Japanese macaques. *Anthropological Science*, 102 (Supplement): 27–41.
- Kokich V.G., Shapiro P.A., and Moffett B.C. (1979) Craniofacial sutures. In: Bowden D.M. (ed.), *Aging in Nonhuman Primates*. Van Nostrand Reinhold, New York, pp. 356–368.
- Lapin B.A., Krilova R.I., Cherkovich G.M., and Asanov N.S. (1979) Observations from Sukhumi. In: Bowden D.M. (ed.), *Aging in Nonhuman Primates*. Van Nostrand Reinhold, New York, pp. 335–347.
- Lieberman D.E., Krovitz G.E., Yates F.W., Devlin M., and St Claire M. (2004) Effects of food processing on masticatory strain and craniofacial growth in a retrognathic face. *Journal of Human Evolution*, 46: 655–677.
- Lynnerup N. (2001) Cranial thickness in relation to age, sex and general body build in a Danish forensic sample. *Forensic Science International*, 117: 45–51.
- Mazess R.B. (1982) On aging bone loss. *Clinical Orthopaedics and*

- Related Research, 165: 239–252.
- Merrot O., Vacher C., Merrot C., Godlewski G., Frigard B., and Goudot P. (2005) Changes in the edentate mandible in the elderly. *Surgical and Radiologic Anatomy*, 27: 265–270.
- Morbeck M.E., Galloway A., and Sumner D.R. (2002) Getting old at Gombe: skeletal aging in wild-ranging chimpanzees. In: Erwin J.M. and Hof P.R. (eds.), *Aging in Nonhuman Primates. Interdisciplinary Topics in Gerontology*, Vol. 31. Karger, Basel, pp. 48–62.
- Mouri T. (1994) Postnatal growth and sexual dimorphism in the skull of the Japanese macaque (*Macaca fuscata*). *Anthropological Science*, 102 (Supplement): 43–56.
- Mouri T., Endo H., and Watanabe T. (2004) Why do female Japanese macaques lack sagittal crest? *Morphological Sciences*, 8: 25–34 (in Japanese).
- Nasjeletti C.E. and Kowalski C.J. (1975) Stability of upper face height–total face height ratio with increasing age. *Journal of Dental Research*, 54: 1241.
- Nozaki M. and Oshima K. (1987) Seasonal changes of the gonadotropic function in the female Japanese monkey. In: Miura T. (ed.), *Seasonal Effects on Reproduction, Infection and Psychoses. Progress in Biometeorology*, Vol. 5. SPB Academic, The Hague, pp. 41–49.
- Paschetta C., de Azevedo S., Castillo L., Martínez-Abadías N., Hernández M., Lieberman D.E., and González-José R. (2010) The influence of masticatory loading on craniofacial morphology: a test case across technological transitions in the Ohio valley. *American Journal of Physical Anthropology*, 141: 297–314.
- Pavelka M.S.M. and Fedigan L.M. (1999) Reproductive termination in female Japanese monkeys: a comparative life history perspective. *American Journal of Physical Anthropology*, 109: 455–464.
- Pfeiffer S. (1980) Age changes in the external dimensions of adult bone. *American Journal of Physical Anthropology*, 52: 529–532.
- Ruff C.B. (1980) Age difference in cranial dimensions among adults from Indian Knoll, Kentucky. *American Journal of Physical Anthropology*, 53: 101–108.
- Ruff C.B. and Hayes W.C. (1982) Subperiosteal expansion and cortical remodeling of the human femur and tibia with aging. *Science*, 217: 945–948.
- Sardi M.L., Novellino P.S., and Pucciarelli H.M. (2006) Craniofacial morphology in the Argentine Center-West: consequences of the transition to food production. *American Journal of Physical Anthropology*, 130: 333–343.
- Smith R.W. and Walker R.R. (1964) Femoral expansion in aging women: implications for osteoporosis and fractures. *Science*, 145: 156–157.
- Susanne C. (1977) Individual age changes of the morphological characteristics. *Journal of Human Evolution*, 6: 181–189.
- Tallgren A. (1974) Neurocranial morphology and ageing: a longitudinal Roentgen cephalometric study of adult Finnish women. *American Journal of Physical Anthropology*, 41: 285–294.
- Walker M.L. (1995) Menopause in female rhesus monkeys. *American Journal of Primatology*, 35: 59–71.
- Wang Q., Strait D.S., Paul C., and Dechow P.C. (2006) Fusion patterns of craniofacial sutures in rhesus monkey skulls of known age and sex from Cayo Santiago. *American Journal of Physical Anthropology*, 131: 469–485.