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ORIGINAL ARTICLE

Sagittal Plane Kinematics of the Jaw and Hyolingual Apparatus During Swallowing in *Macaca mulatta*

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Abstract Studies of mechanisms of feeding behavior are important in a society where aging- and disease-related feeding disorders are increasingly prevalent. It is important to evaluate the clinical relevance of animal models of the disease and the control. Our present study quantifies macaque hyolingual and jaw kinematics around swallowing cycles to determine the extent to which macaque swallowing resembles that of humans. One female and one male adult *Macaca mulatta* were trained to feed in a primate chair. Videofluoroscopy was used to record kinematics in a sagittal view during natural feeding on solid food, and the kinematics of the hyoid bone, thyroid cartilage, mandibular jaw, and anterior-, middle-, and posterior-tongue. Jaw gape cycles were defined by consecutive maximum gapes, and the kinematics of the swallow cycles were compared with those of the two consecutive non-swallow cycles preceding and succeeding the swallow cycles. Although there are size differences between macaques and humans, and macaques have shorter durations of jaw gape cycles and hyoid and thyroid upward movements, there are several important similarities between our macaque data and human data reported in the literature: (1) The durations of jaw gape cycles during swallow cycles are longer than those of non-swallow cycles as a result of an increased duration of the jaw-opening phase; (2) Hyoid and thyroid upward movement is linked with a posterior tongue movement and is faster during swallow than non-swallow cycles; (3) Tongue elevation propagates from anterior to posterior during swallow and non-swallow cycles. These findings suggest that macaques can be a useful experimental model for human swallowing studies.

Keywords Deglutition · Deglutition disorders · Feeding · Animal models · Macaque monkeys · Swallowing kinematics

Introduction

Feeding-related disorders and symptoms, particularly impaired mastication and swallowing (i.e., dysphagia) as a result of aging [1] and major neurological disorders [2, 3] such as cerebral vascular accident [4], Parkinson's disease [5], and amyotrophic lateral sclerosis (ALS) [6] have

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become significant societal burdens; indeed, one in 17 people will develop some form of dysphagia in their life time [7]. Human experimentation has greatly advanced our knowledge of human feeding physiology and pathophysiology but human research is constrained by limits on human exposure to the ionizing radiation associated with videofluoroscopic studies of hyolingual kinematics. Therefore, in order to elucidate the neurophysiological and musculoskeletal mechanisms underlying disorders of mastication and swallowing in humans various non-human mammals have been studied.

Choices of specific animal models of dysphagia are made based on the aims of specific studies as well as historic use of particular species for particular behaviors. For example, rodents have been used for models of swallowing control and neurological diseases [8, 9]; pigs for electromyographic (EMG) studies of activity of hyoid muscles during suckling and swallowing [10]; rabbits for EMG studies of masticatory muscles and their cortical control [11]; and cats for the laryngeal closure reflex and its neural control by the brainstem [12, 13]. However, these mammals have significantly different craniofacial, dental, and hyolingual anatomy from humans, have different jaw and hyolingual kinematics, and have different swallowing mechanisms than humans [14–17], all of which impair the generalizability of the results to humans.

An ideal model organism for understanding human feeding function and dysfunction would be one that closely resembles humans in as many aspects as possible. Macaques are more closely related to humans than any animal model commonly used for the study of feeding. Although chimpanzees and bonobos are more closely related to humans, in vivo research on great apes as a model for human disease has been greatly restricted in the United States due to the Great Ape Protection and Cost Savings Act of 2011 [18–21]. Macaque monkeys have long served as model organisms for studies of the neural control of human movements, particularly for reach and grasp movements [22–24], but also for feeding motor behaviors [15, 16, 25, 26], including studies of the neural control mechanisms of feeding behavior at the cortical [27–29] and subcortical levels [30–34]. Macaques have similar, though not identical, musculoskeletal and neural morphology and feeding behavior compared to humans, and therefore are a promising and practical alternative to chimpanzees for the study of human chewing and swallowing biomechanics and motor control.

Although macaques and humans have broad similarities in musculoskeletal and neurological morphology, some of the differences between the two species are related to the vertical cervical spine, facial shortening, lower hyolaryngeal apparatus, and direct cortical input to laryngeal motoneurons in humans [35–40]. With regard to musculoskeletal structures, macaques have more prognathism than humans but less than other mammals; a less acute basicranial and craniocervical angle than humans but more acute than most other mammals; human-like reduced palatal rugae; smaller valleculae than most other mammals; a “floating” hyoid bone connected to the basicranium by ligaments and muscles, while the hyoid of many other mammals is connected to the basicranium through a series of bones; similar dentition except for sexually dimorphic canines; a short styloid process; and similar attachment sites for most of the feeding musculature [16, 41, 42]. The most salient differences between macaques and humans are the morphology and position of the hyoid and laryngeal cartilages. The macaque basihyoid is more vertically elongate and shield-shaped, featuring a concavity that accommodates an air sac between the thyroid cartilage and basihyoid [41, 43]. Macaques and infant humans exhibit the general mammalian condition of having a high hyoid relative to the mandible and consequently a flatter tongue, while in adult humans the hyoid is positioned below the mandible and the dorsal surface of the tongue is more round [35, 44]. Moreover, the human thyroid cartilage is further descended from the hyoid itself, while in macaques the thyroid cartilage is more closely linked with the hyoid [43].

The morphological differences that have accumulated over the thirty million years [45] since the last common ancestor of humans and macaques do not seem to have significantly altered their feeding behavior. Macaques, like humans, also store food in the valleculae for a few chewing cycles prior to the swallow [15], and both species intercalate swallows between chews within feeding sequences [46, 47]. Given that both humans and macaques swallow within a few cycles of transporting food to the valleculae, both animals may have similar sensorimotor integration that initiates the transition from chewing to swallowing during natural feeding [15, 17, 48]. The squeeze-back mechanism of swallowing, in which the tongue contacts the palate from anterior to posterior to ‘squeeze’ the bolus into the oropharynx, is the only mechanism employed in human and macaque swallowing of solid foods, whereas other mammals utilize undulation of the tongue for transport for the bolus to the oropharynx when swallowing solid foods [14–17]. Although there are some arguments as to how many phases are defined within each gape cycle [49], the four-phase gape cycle of mandibular movement, fast close (FC), slow close (SC), slow open (SO), and fast open (FO), has been successfully applied to characterize videofluoroscopic (VF) data of human feeding sequences [47] and a recent study explained variation in phase durations of gum chewing behavior in human [50] in a similar way to a comparative study looking at various animal species including non-human primates [51]. Additionally, tongue and hyoid movements are coordinated with the above-mentioned four-phase gape cycle of mandibular movement similarly in humans and macaques [16, 47]. Although the tongue is coordinated with the mandible, this coordination is less rigid in macaques and humans than in other mammals, indicating that tongue movements in both species are more independent from those of the mandible [16, 52]. Greater independence of tongue movements relative to the mandible implies that humans and macaques may have more sophisticated motor control for the tongue than in other mammals, perhaps due to the fact that they both have direct corticobulbar tracts to the hypoglossal nucleus [53].

However, published studies during feeding in macaques are limited to qualitative descriptions of kinematic data, and no studies have statistically compared hyolingual and jaw kinematics during chews and swallows. Previous work has quantified hyolingual kinematics in crab-eating macaques (*Macaca fascicularis*); however, this work has not been replicated in rhesus macaques (*Macaca mulatta*) [15, 16, 26]. Furthermore, the previous research using macaques did not capture laryngeal kinematics. Given the differences in hyolaryngeal anatomy between humans and macaques discussed above, a comparison of laryngeal kinematics and its relationship with hyolingual kinematics between the two species is needed to further evaluate the utility of the rhesus macaque as a model for human swallowing.

Few human studies have analyzed hyolingual and jaw kinematics in natural feeding rather than voluntary, or cued swallows, and few studies of either humans or non-human primates compare hyolingual and jaw kinematics during swallows with their preceding and succeeding non-swallow cycles. Hence, we sought to precisely quantify macaque hyolingual and jaw kinematics during swallowing and neighboring masticatory cycles in order to determine the nature and extent to which macaque feeding behavior resembles, or differs from, that of humans. This information will also be utilized in future studies to allow us to more precisely define the key timings of swallowing-related kinematics in relation to cortical neural activity as it has been shown that cortical activity changes a few to several hundred millisecond prior to swallowing [54]. Specifically, this study aims to determine kinematic similarities and differences between: (1) swallow cycles and non-swallow jaw gape cycles preceding and succeeding the swallow cycles; and (2) our macaque data and human data reported in the literature.

Materials and Methods

All of the surgical and behavioral procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Chicago (AAALAC accredited) and conformed to the principles outlined in the Guide for the Care and Use of Laboratory Animals (NIH publication no. 86-23, revised 1985) as well as to the requirements of the Animal Welfare Act. Activities related to animal care including housing, feeding, and environmental enrichment were performed in accordance with IACUC-approved standard operating procedures (SOPs) at the University of Chicago. Our enrichment program exceeded the recommended guidelines. Two adult monkeys *Macaca mulatta* (monkey O, 7 years old, female, 6.6 kg; monkey Y, 6 years old, male, 12 kg) were housed in cages whose dimensions were at least 6 ft^2 for the base area and 70 inches in height. Animals were single housed because pair housing attempts (same-gender) resulted in aggressive and dominance behaviors that raised safety concerns in veterinary and research staff.

Subjects

The two adult monkeys were fitted with head posts for attachment of a halo and operantly conditioned to eat while restrained and sitting upright in a primate chair. Pole and collar were used for chairing but the neck collar was removed during training and data recording. Both animals had all adult teeth erupted and in occlusion and neither evidenced any dental or muscle abnormalities of the feeding system. CT scanning and 3-D reconstruction revealed slight asymmetry in the mandible of monkey O. In this individual, the right hemi-mandible was longer than the left one (81.9 vs. 85.1 mm, respectively) and the angle between the condylar axis (i.e., the axis connecting the medial and lateral condylar poles) and main axis of the mandible (in the transverse plane) was more acute in the left condyle than in the right condyle (78° vs. 88°, respectively).

Both monkeys were euthanized humanely. Euthanasia was consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. Both monkeys were perfused transcardially through the left ventricle. Heads, including orofacial skeleton, muscles, and brains, were collected for other studies. The end point of the study was evaluated as a humane one by IACUC.

Jaw and Tongue Kinematics

At least one month prior to data recording, under isoflurane anesthesia, three 2-mm-diameter tantalum balls (RSA Biomedical, Umeå, Sweden) were implanted into the anterior, middle, and posterior regions of the tongue midline through hypodermic needles and at least three Vitallium^{TM} cortical bone screws (OFSQ13, 3I Implant Company, West Palm Beach, FL, USA) were affixed to the mandible. The heads of the bone screws protruded percutaneously and served as attachment sites for optical kinematic markers and as markers for fluoroscopic recording [55, 56]. Both the tantalum balls and the bone screws remained in place until the animals were sacrificed. Figure 1 illustrates the positions of the markers in the two animals. There were slight differences in marker positions between the two animals that could account for some of the inter-individual variation in the results reported here. However, overall the kinematic patterns of the two animals were very similar.

The data reported here come from 223 feeding sequences (130 from monkey O and 93 from monkey Y) recorded during two sessions (5 days and 1 day apart for each monkey respectively) with each animal. The animals were fed a range of solid food items. The data presented here are the means of values recorded during feeding on grapes, nuts, and apples. Analyses of the effects of foods of different hardness and consistency on macaque swallowing kinematics will be presented elsewhere. The food items were large enough to be placed comfortably in the animals' mouths by the investigators without requiring the animals to bite pieces off for ingestion prior to mastication. While the animals fed, two-dimensional lateral view fluoroscopic recordings of jaw and tongue movements were made at 50 or 100 Hz using an OEC 9600 C-arm fluoroscope retrofitted with a Redlake Motion Pro 500 video camera (Redlake MASD LLC, San Diego, CA, USA).

In each frame of videofluoroscopy data, ProAnalyst image processing software (Xcitex, Woburn, MA, USA) was used to extract two-dimensional coordinates for the three tantalum markers in the tongue, one point on a screw coupled to the jaw, and the most anterior-superior point of the hyoid bone, the most anterior point of the superior notch of thyroid cartilage, the posterior nasal spine, the incisive canal point, and the anterior-inferior corner of the C4 vertebra. The movements of these structures were expressed in two-dimensional coordinates relative to: an x-axis, defined as a horizontal line parallel to the palatal plane (a line passing through the posterior nasal spine and the incisive canal points) and passing through the C4 vertebra point (the origin); and a y-axis perpendicular to the x-axis, crossing it at the origin (Fig. 1).

In each jaw gape cycle, which was defined by consecutive maximum gapes, four jaw movement phases, fast close (FC), slow close (SC), slow open (SO), and fast open (FO), used here were based on the definitions in [57] (Fig. 2). Operational definitions for those four phases are shown in Table 1. Custom written code in IgorPro (WaveMetrics, Inc., Portland, OR, USA) was used to find the maximum value (peak) and minimum value (negative peak) of all marker movements in vertical and horizontal dimensions during each gape cycle (Fig. 2).

Swallows were identified by the passage of the bolus through the oropharynx. The food was not mixed with contrast material, so bolus passage was identified by merging of the radiographic shadows of bolus, tongue, soft palate, and pharynx, accompanied by marked elevation of hyoid and thyroid. In this study, we compared kinematics of the two consecutive gape cycles preceding the swallow (cycles 2pre and 1pre), during the swallow cycle, and the

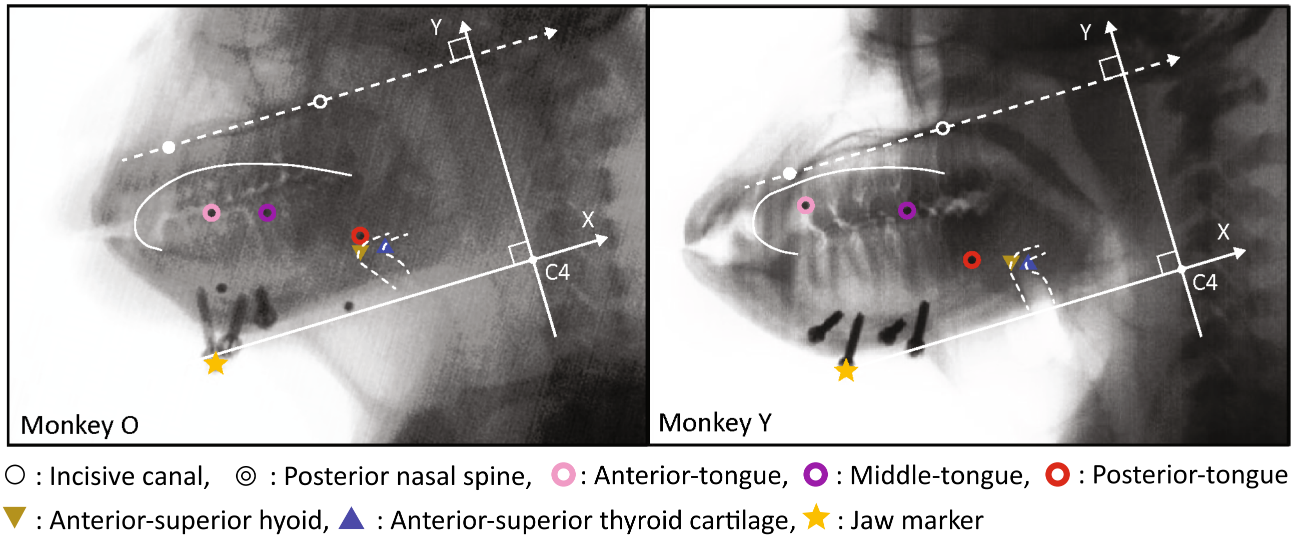


Fig. 1 Marker positions and coordinate systems in the two animals. The positions of the markers in the anterior-, middle-, posterior-tongue, jaw, hyoid and thyroid cartilage were expressed as two-dimensional coordinates in sagittal planes. The horizontal axis of the coordinate system is parallel to the palatal plane (defined by a line passing through the posterior nasal spine and the posterior edge of the incisive canal) and passing through the anteroinferior corner of the C4 vertebral body (the origin). The orthogonal to this line is the vertical axis

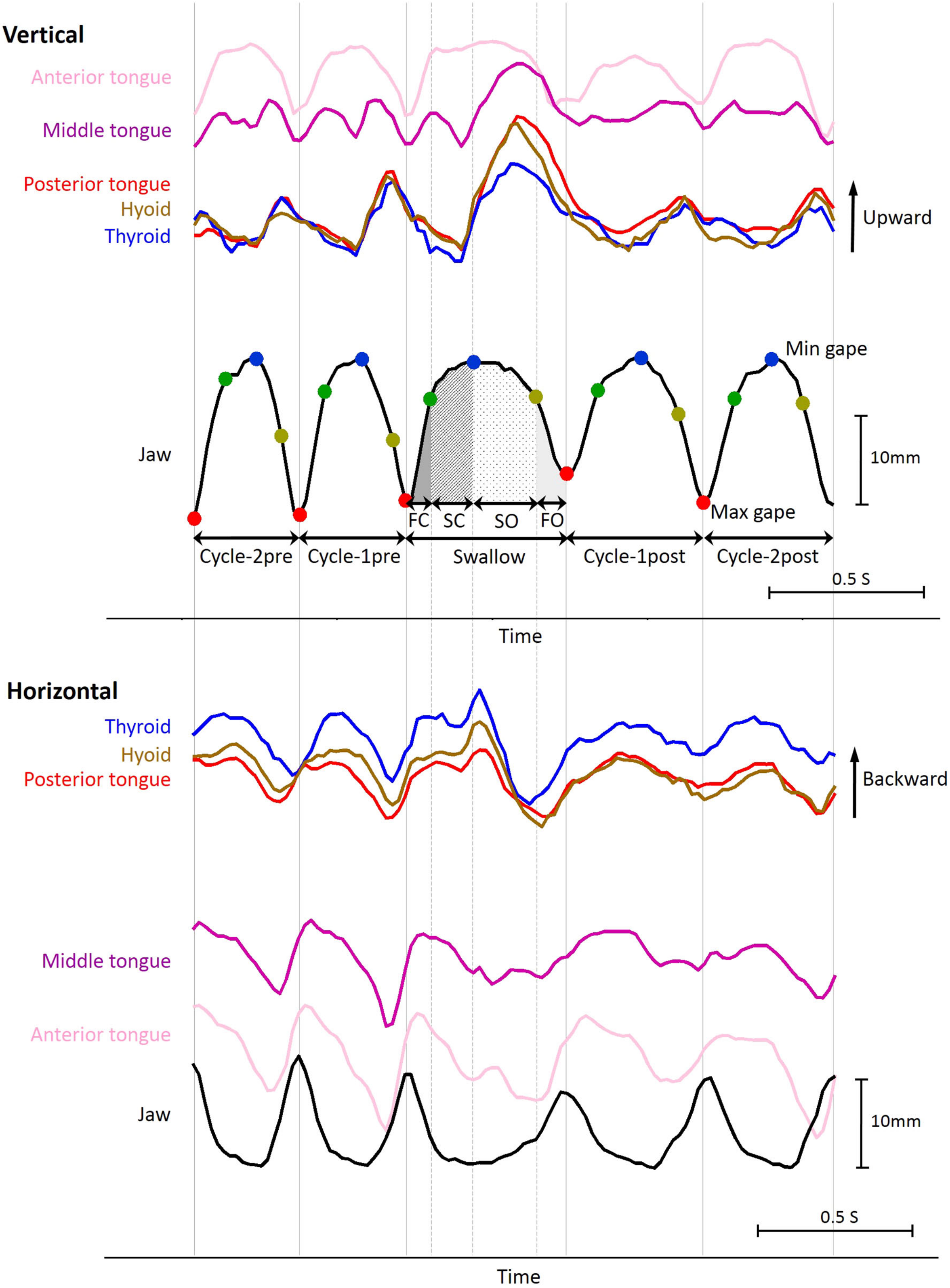


Fig. 2 Representative marker movements in the vertical and horizontal dimensions over time in one subsequence of monkey O, eating nuts. A subsequence consists of five consecutive jaw gape cycles: the swallow and its two preceding and two following non-swallow cycles. For each gape cycle, four jaw movement phases were defined—*FC* fast close, *SC* slow close, *SO* slow open, *FO* fast open

Table 1 Operational definitions of the four phases in the gape cycle

Phase	Descriptions
Fast close (FC)	Rapid closing phase: starting at maximum gape the mandible is rapidly elevated onto the food item and the hyoid apparatus nears its extreme posteroventral position, equivalent to closing stroke when there is no slow close phase
Slow close (SC)	The phase when bite force is applied to the food item and mandible movement is slower than during FC; equivalent to the power stroke of some authors
Slow open (SO)	During this phase, the rate of jaw movement may vary widely over short time intervals, but the overall rate is slow; the tongue is protracted to collect sensory information on the external properties, mass and mobility of the food item and to fit to the food item in preparation for transport
Fast open (FO)	Phase in which the rate of jaw movement is high; begins as mandible opening velocity increases and the tongue and hyoid are pulled down and back, transporting the food towards the pharynx

two consecutive cycles following the swallow (cycles 1post and 2post). These consecutive five gape cycles constituted a subsequence. A total of 481 subsequences, including 481 swallows, was analyzed, including 158 subsequences from monkey O and 323 subsequences from monkey Y.

Statistics

Mean values of the location and timing of marker extrema (highest, lowest, most anterior, most posterior) were calculated and used to describe average movement profiles. Average values of cycle duration, and vertical and horizontal displacements were compared across gape cycles using Friedman's repeated measures analysis because data from each group, 2pre, 1pre, swallow, 1post, and 2post, failed normality tests (Shapiro-Wilk with $P < 0.05$ and Lilliefors test with $P = 0.05$). Tukey's test was used for multiple comparisons. Individual differences between the two monkeys in each of five cycles were tested using Mann–Whitney rank sum test. All statistical analyses were performed with SigmaPlot 12.5 (Systat Software, Inc., Chicago, IL, USA).

Results

Jaw Gape Cycle Durations

Gape cycle durations in swallow cycles were significantly longer than those during non-swallow cycles preceding (cycle 2pre and 1pre) and following swallows (cycle 1post and 2post), primarily due to lengthening of the SO and FO phases of the swallow gape cycle (Fig. 3; Supp. Table 1). The durations of the two gape cycles immediately following swallows were significantly longer than those preceding the swallows.

Hyolingual Kinematics

The average coordinates of the positions of the tongue markers and the hyoid and thyroid at the movement extrema most-forward, most-backward, lowest and highest in each animal are shown in Fig. 4 and Supp. Fig. 1. The timings of these extrema relative to the four phases (FC, SC, SO, FO) in a gape cycle are shown in Fig. 5 for averaged values and Supp. Fig. 2 for individual animals. Hyoid and thyroid movement durations are shown in Supp. Fig. 3. The amplitudes of horizontal and vertical movements of tongue, hyoid, and thyroid are shown in Supp. Fig. 4.

Tongue Kinematics

In all cycles, maximum tongue protrusion (most-forward) occurred during FO, prior to maximum gape, and maximum tongue retrusion (most-backward) occurred during SC, prior to minimum gape. During swallows, all tongue markers reached their most-backward extrema relatively earlier in the gape cycle than in non-swallow cycles. In both non-swallow and swallow cycles, the timing of the highest positions of the tongue markers revealed a wave of tongue elevation moving from anterior to posterior. Maximum elevation of the anterior tongue marker occurred earliest, around minimum gape, followed by the middle tongue marker in SO, then the posterior tongue marker during FO (Fig. 5). The anterior tongue marker exhibited different patterns from those by the middle and posterior tongue markers as follows:

Anterior tongue—In left lateral view, the anterior tongue marker exhibited counter-clockwise rotations during both non-swallow and swallow cycles (Fig. 4). On average, the anterior tongue marker reached its lowest position almost synchronously with maximum gape, moved upwards and backwards to its most posterior position near the start of SC, reached its highest position almost synchronously with minimum gape, then moved to its most anterior position during FO (Fig. 5; Table 1). The anterior tongue exhibited only small differences in relative timing and amplitude between non-swallow and swallow cycles. In both monkeys, the anterior tongue marker showed significantly more horizontal displacement during swallows

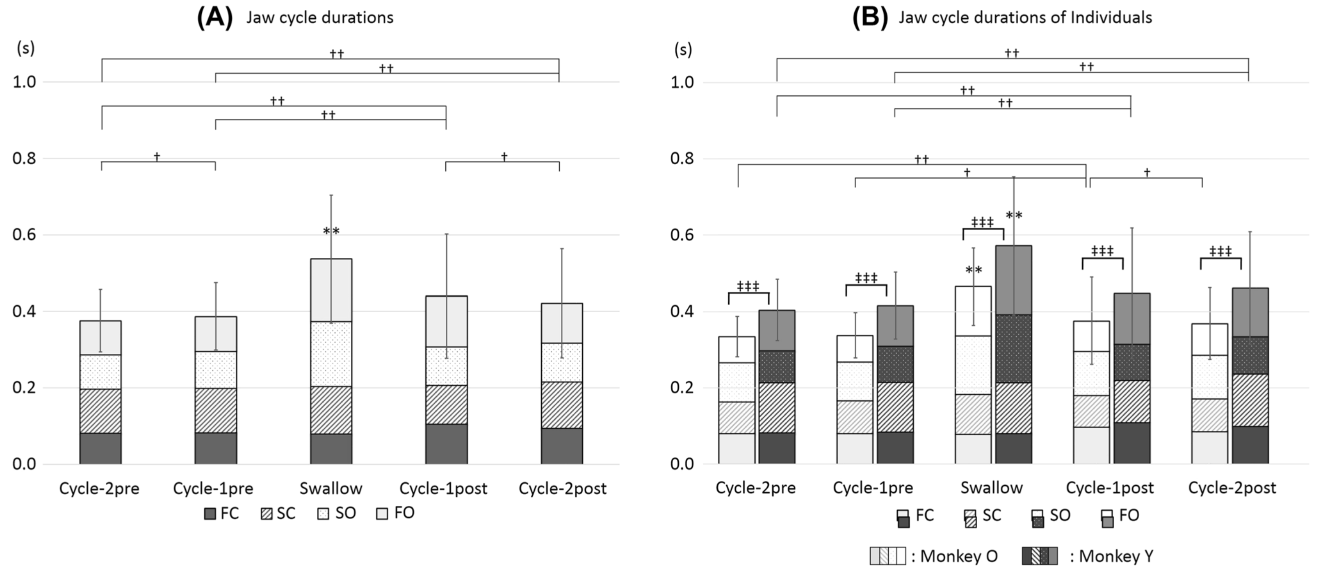


Fig. 3 Variation in jaw cycle durations divided across the four phases (FC, SC, SO, FO) of the gape cycle. **a** Values are mean ± S.D. of two animals (pooled). **b** Values are mean ± SD in each animal, *light color bar* is monkey O and dark color bar is monkey Y. Symbols **, ††, and † show differences between cycles which were tested using Friedman Repeated Measures Analysis. **, †, and †† in (**b**) show these test results within each individual. Tukey's test was used for post-hoc multiple comparisons. **$P < 0.01$ vs. others, $^{\dagger\dagger}P < 0.01$, $^{\dagger}P < 0.05$. Symbol ‡‡‡ shows differences between the two individuals that were tested by Mann–Whitney Rank Sum Test. ‡‡‡ $P < 0.001$

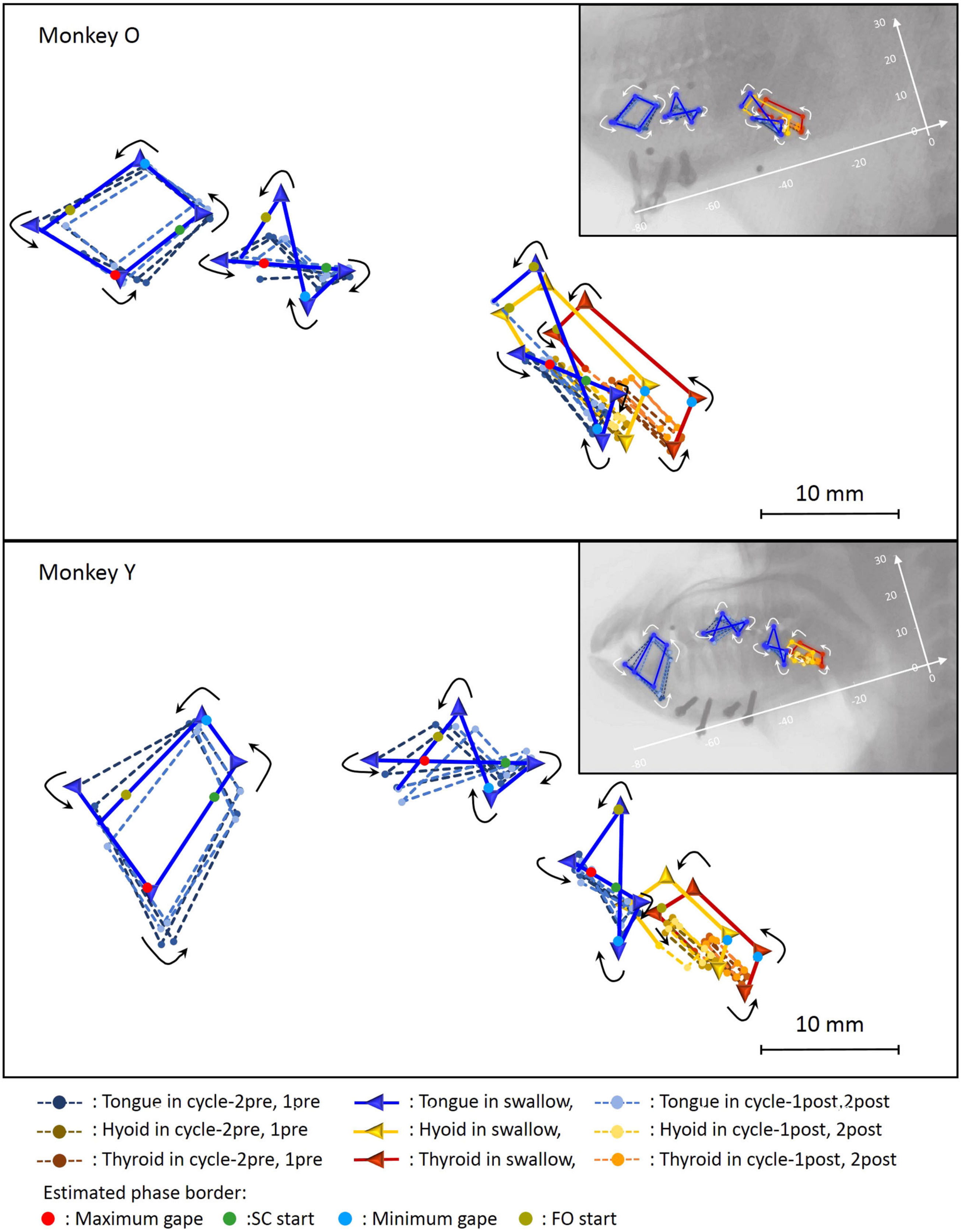
than non-swallow cycles. However, the two monkeys differed in the vertical displacement of the anterior tongue marker during swallows. In monkey Y, the anterior tongue marker showed *less* vertical displacement during swallows than non-swallows, whereas in monkey O it showed *more* vertical displacement during swallows than non-swallow cycles. In monkey Y, anterior tongue vertical displacements in swallows differed from all other cycles, whereas in monkey O, they only differed from cycle 1post (Supp. Fig. 4).

Middle and posterior tongue—In left lateral view, the middle and posterior tongue markers exhibited figure-eight movement profiles during both non-swallow and swallow cycles, starting at their most-posterior extreme during SC, moving down and forward to their lowest position prior to minimum gape, up to their highest position early in opening, then down and forwards to their most anterior position later in opening (Figs. 4, 5; Table 1). In contrast with the anterior tongue marker, the middle and posterior tongue markers reached their lowest positions immediately prior to or around minimum gape and their highest positions during SO (middle marker) or FO (posterior marker).

In both monkeys, the vertical and horizontal movement amplitudes of both middle and posterior tongue markers were larger during swallows than non-swallows (Supp. Fig. 4). In addition, in both monkeys, the vertical movement amplitude of both middle and posterior tongue markers, and in monkey Y the horizontal movement amplitude of middle and posterior markers, were larger during cycle 1pre than in other non-swallow cycles. In monkey Y, the vertical movement amplitudes of both middle and posterior tongue markers were smallest during cycle 1post and the same tendency could be seen in monkey O.

Hyoid and Thyroid Kinematics

In non-swallow cycles, the hyoid and thyroid movements were small, alternating between upward and forward movement starting in SC and proceeding through minimum gape, and downward and backward movement starting in opening and proceeding through maximum gape (Figs. 4, 5; Table 1). The sequences of the extrema were the same for both hyoid and thyroid in all non-swallow cycles: in cycles 1pre, 2pre, and 2post, the sequence was clockwise in left lateral view, starting from most-backward in SC, moving to lowest before minimum gape, to most-forward in SO, followed by highest in FO. The hyoid sequence slightly preceded the thyroid sequence. In cycle 1post, the sequence was again clockwise in left lateral view, but started with the most-forward position in FC followed by lowest, most-backward, and highest. This difference in cycle 1post was probably attributable to the hyoid and thyroid moving so far forward during the swallow cycle that, although they were moving posteriorly during jaw closing of cycle 1post, the hyoid and thyroid were still further forward during closing than they were during opening in cycle 1post (Table 2).


Monkey O
30
20
10
0
0
-20
-40
-60
-80
10 mm
Monkey Y
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10
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-20
-40
-60
-80
10 mm
: Tongue in cycle-2pre, 1pre
: Hyoid in cycle-2pre, 1pre
: Thyroid in cycle-2pre, 1pre
: Tongue in swallow,
: Hyoid in swallow,
: Thyroid in swallow,
: Tongue in cycle-1post,2post
: Hyoid in cycle-1post, 2post
: Thyroid in cycle-1post, 2post
Estimated phase border:
● : Maximum gape
● :SC start
● : Minimum gape
● : FO start

◀**Fig. 4** Average coordinates of the positions of anterior tongue, middle tongue, posterior tongue, hyoid, and thyroid markers at most-forward, most-backward, lowest and highest positions in each animal. **a** The positions of anterior tongue, middle tongue, posterior tongue markers. **b** The positions of hyoid, and thyroid markers. In both (**a**) and (**b**), the black arrows indicate the directions of movement at the extrema. The estimated timing of the phase boundaries relative to the extrema timing is also shown (see Fig. 5)

In contrast with non-swallow cycles, the sequence of movement extrema for hyoid and thyroid during swallow cycles was *counter-clockwise* in left lateral view, starting with lowest in SC, most-backward just after minimum gape, highest late in SO, and most-forward in at the start of FO (Fig. 5; Table 1). The amplitudes of these movements were larger during swallow cycles than non-swallow cycles (Supp. Fig. 3).

In both swallow and non-swallow cycles, hyoid and thyroid upward movement started during SC, slightly earlier than middle and posterior tongue. In non-swallow cycles, hyoid and thyroid reached their highest positions in early FO, almost simultaneously with the timing of the highest extrema of the posterior tongue, but trailing the middle tongue. In contrast, during swallow cycles, hyoid and thyroid reached their highest positions earlier in the gape cycle, during SO, and almost coincident with the timing of the highest position of the middle tongue.

In addition, overall hyoid and thyroid upward movements not only occurred earlier in swallow than non-swallow cycles, but also the duration of this upward movement (interval from lowest to highest hyoid and thyroid position) differed between individuals (Fig. 5). In monkey O, hyoid and thyroid upward movement during swallowing was longer than in all non-swallow cycles. In contrast, in monkey Y, hyoid upward duration was shorter than in cycle 1post, but did not differ from other non-swallow cycles. Thyroid upward movement in monkey Y during swallowing did not differ from that in non-swallow

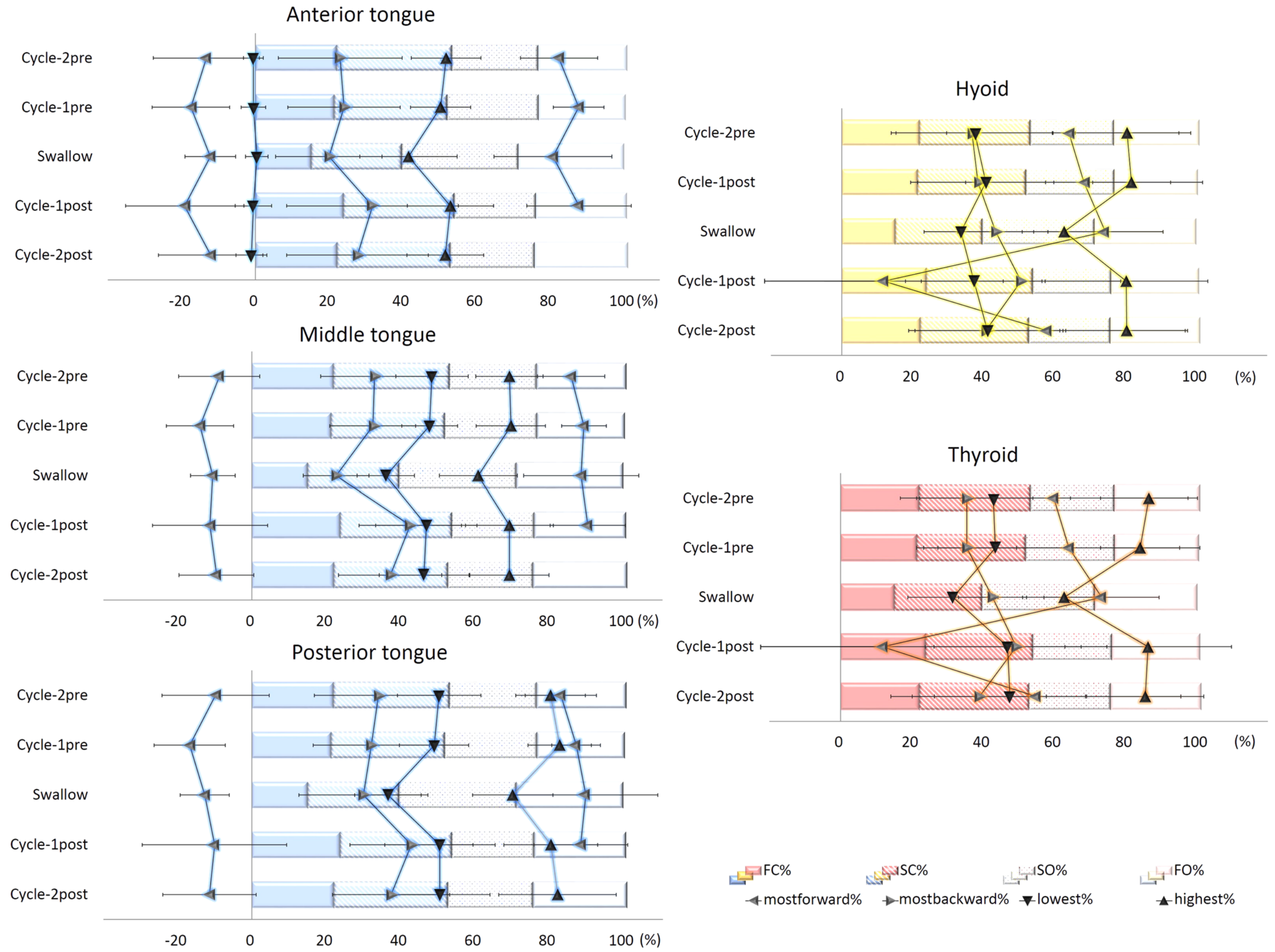

Fig. 5 Timing of tongue, hyoid, and thyroid kinematics relative to the average durations of the four phases of the gape cycle. Values shown as arrow heads are mean ± SD of the ratio of each timing (most-forward, most-backward, lowest, and highest) in each cycle. Values are average of the two animals

cycles. The larger amplitude and relatively smaller or unchanging duration of hyoid and thyroid upward movements during swallows requires that average hyoid and thyroid upward movement velocities are higher during swallowing than non-swallowing.

It is also noteworthy that the variations of the durations of these upward movements were smaller in swallows than non-swallows in both animals. In contrast, jaw cycle durations showed increased variance in swallows compared to preceding swallow cycles (Supp. Fig. 3).

Hyoid, thyroid cartilage, and middle and posterior tongue markers exhibited similar vertical movement profiles, which showed large vertical displacements from cycle 2pre through 1pre to swallow, but anterior-tongue did not (Supp. Fig. 4). In contrast, horizontal displacements of most markers and points were significantly larger in swallow than non-swallow cycles.

Discussion

Temporal Variables

In *Macaca mulatta*, mandible gape cycle durations in swallow cycles are significantly longer than those in the chewing cycles preceding and succeeding the swallow, mostly due to increased duration of jaw opening phases during swallows. This is consistent with previous reports in humans [58] and rabbits [59]. Hiiemae et al. [47] and Palmer et al. [58] reported that in humans, swallow cycle durations during eating solid food are 1.123–1.346 s. The mean swallow cycle duration in our study (0.537 ± 0.167 s; mean ± SD) is significantly shorter than that of humans, although we cannot say whether this is due to differences in size or shape between macaques and humans or the foods used in the experiments. In their study of rabbits, Naganuma et al. [59] did not distinguish chewing cycles preceding swallows from those succeeding the swallows; however, the duration of the swallowing cycles was significantly longer than that of the chewing cycles, also due to an elongated opening phase. Natural feeding sequences on fruit (grapes) from mastication to swallowing were studied in *Macaca fascicularis* [28, 29]. Although these authors did not compare the durations between chewing and swallowing cycles, they reported that cycle durations in rhythmic chewing of two monkeys were 0.290–0.442 s and pre-swallow cycles were 0.332–0.555 s. These values of pre-swallow cycles are similar to the cycle durations in cycles 2pre and 1pre reported here (monkey O: cycle 2pre; 0.334 ± 0.053 s, cycle 1pre; 0.338 ± 0.059 s, monkey Y: cycle 2pre; 0.404 ± 0.080 s, cycle 1pre; 0.416 ± 0.087 s).

Table 2 Phases of jaw gape cycle when hyolingual markers reach their most-forward, most-backward, lowest and highest positions in *Macaca mulatta* in comparison with human

		Phase of jaw gape cycle			
		Most-forward	Most-backward	Lowest	Highest
Anterior tongue	Macaca	FO	SC	FO-FC (maximum gape)	SC-FO (minimum gape)
	Human	Middle and late jaw opening	Closing	Slightly after maximum gape	Immediately after minimum gape
Middle tongue	Macaca	FO	SC	SC	SO
Posterior tongue	Macaca	FO	SC	SC	FO (non-swallow)
					SO-FO (swallow)
Hyoid	Macaca	SO	SC (non-swallow)	SC	FO (non-swallow)
		FO(swallow)	SO (swallow)		SO (swallow)
		FC(1post)			
	Human	Opening	Minimum gape	Minimum gape	Opening
Thyroid	Macaca	SO	SC (non-swallow)	SC	FO (non-swallow)
		FO (swallow)	SO (swallow)		SO (swallow)
		FC (1post)			

In the present study, we analyzed the two cycles before and the two cycles after the swallow as both macaques and humans exhibit intercalation of swallowing into mastication cycles during solid food eating [31, 32]. Previous studies have not reported cycle durations of post-swallow cycles, making comparisons difficult, but our data suggest that gape cycle durations succeeding swallows are longer than those preceding swallows. One of the few studies analyzing post-swallow cycles demonstrated modifications to EMG activity in post-swallow cycles compared to pre-swallow cycles [10]. Although they used a suckling pig as a model, their results are consistent with our own in demonstrating cycle modification immediately following the swallow. Better data are needed from humans in order to compare with the data presented here.

Prior studies of macaque hyolingual and jaw kinematics excluded the hyoid bone since its movements were too variable [16]. High variability was not the case in our study, perhaps because hyoid kinematics are less variable immediately prior to, during, and following swallows, which were not the focus of Hiiemae et al.'s study [16]. In both non-swallow and swallow cycles, the hyoid starts moving upward during SC and reaches its highest position during jaw opening (Fig. 3). In swallow cycles, the hyoid reaches its highest position during SO, which is earlier than in non-swallow cycles. In swallow cycles, the duration of hyoid upward movement (interval from lowest to highest hyoid position) is significantly shorter than the preceding cycle and shorter than the following cycle. On the other hand, the vertical displacement magnitude of the hyoid during swallows is nearly twice as large as that in non-swallow cycles. These results suggest that the velocity of hyoid upward movement in swallows is faster than in non-swallow cycles. The mean duration of hyoid upward movement in our study (0.153 ± 0.055 s) is shorter than human hyoid elevation time estimated by a laryngeal signal waveform (0.39 s) [39], but this may be due to the shorter overall gape cycle time in macaques. The proportion of hyoid upward duration to cycle duration in our macaques is 29.38 ± 8.59% (monkey O: 32.82 ± 6.09%, monkey Y: 27.70 ± 9.12%) whereas in humans this proportion is 28.97–34.73%, suggesting that the relative timing of kinematics of macaque mandible and hyoid/thyroid during swallows is similar to that of humans.

The sequence of thyroid, hyoid, and tongue movements has implications for the external forces producing hyolingual movements during feeding. Hyoid movement is accompanied by jaw opening and closing, and the suprahyoid muscles that are important sources of hyoid movement (mylohyoid, geniohyoid, digastric) are also jaw openers [60]. On average, in non-swallow cycles, the hyoid reaches its vertical extrema slightly before the thyroid but reaches its horizontal extrema slightly after the thyroid. In contrast, on average, during swallows, hyoid and thyroid movements occur almost simultaneously. This tighter coupling in swallow cycles in contrast with the slight difference in their timing in non-swallow cycles could have many causes: the simplest explanation is that during swallow cycles hyoid and thyroid movements are coupled by the thyrohyoid membrane and by action of the thyrohyoid muscle. Evaluation of this hypothesis must await collection of EMG data from the macaque swallowing-related muscles.

The stylohyoid, posterior digastric, and mylohyoid muscles began to shorten simultaneously during the initial stage of swallowing. The shortening of these muscles occurs during the upward movement of the hyoid bone. Subsequently, the geniohyoid, thyrohyoid, and anterior digastric muscles begin to shorten, synchronizing with the forward movement of the hyoid bone. A significant correlation was observed between the shortened muscle lengths of the stylohyoid, posterior digastric, and mylohyoid muscles and the upward movement of the hyoid bone [61].

Tongue movements in the oral stage of swallowing are related to bolus transport from the oral cavity to the pharynx, whereas hyoid movements may be related to both oral and pharyngeal stages of swallowing. Ishida et al [62] suggested that in humans "upward displacement of the hyoid bone in swallowing was related primarily to events in the oral cavity, while its forward displacement was related to pharyngeal processes, especially the opening of the upper esophageal sphincter." Matsuo and Palmer [52] documented in humans high correlations between vertical displacement of anterior and posterior tongue markers and vertical displacement of the jaw and hyoid, but lower correlations in horizontal displacement. Moreover, they showed that for vertical movement the correlation of the anterior marker was higher with the jaw than the hyoid and vice versa for the posterior marker, and for horizontal movement, the correlations of both the anterior and posterior were higher with the hyoid than the jaw. Our results in macaques show that the timing of the vertical movement of the hyoid is similar to that of the middle tongue marker (the lowest and highest) and the posterior tongue marker (the lowest), while the horizontal movement timing of the hyoid is not similar to that of the tongue. It is possible that the horizontal (forward) movement of the hyoid is related to pharyngeal movements and opening of the upper esophageal sphincter, as suggested by Ishida et al. for humans. This hypothesis will be evaluated in the future.

Coupling

The vertical movements of the anterior tongue marker are closely coupled to the vertical movements of the mandible, reaching their vertical extrema in phase with maximum and minimum jaw elevation. Hiiemae et al. [16] found a similar result for non-swallow cycles in macaques and our results suggest that the vertical coupling of the anterior tongue with the mandible is common across all cycle types. In contrast, the movements of the middle and posterior tongue markers reach their lowest positions just prior to minimum gape and their highest positions during jaw opening. The middle tongue markers are in the part of the tongue closest to the molar teeth, where most food breakdown occurs during SC, suggesting that the lowering of the middle tongue during SC may serve to move the tongue out of the way as the teeth approach each other and the bolus. The elevation of the middle and posterior tongue during jaw opening reflects the fact that the tongue moves up and forward during opening to reposition the bolus for the next cycle [26, 63]. However, it is clear that much tongue movement during feeding occurs in transverse and coronal planes not captured by the analysis presented here [64, 65], and analysis of these movements will be required to fully explain the patterns of marker movement reported here.

In contrast with the apparent uncoupling of anterior and posterior tongue movements in the vertical dimension, the tongue markers show more synchronous movement in the horizontal dimension. All tongue markers are most anteriorly positioned during FO and most posteriorly positioned during SC. Moreover, all tongue markers reach their most-backward extrema earlier in the gape cycle during swallows than in non-swallow cycles. This may reflect the fact that the tongue markers always reach their most posterior positions during SC, but during swallows both SC and FC phases are short relative to SO and FO.

In both non-swallow and swallow cycles, the timing of the highest positions of the tongue markers reveals a wave of tongue elevation moving from anterior to posterior, with the anterior tongue reaching its highest position at minimum gape, the middle tongue reaching its highest position during SO, and the posterior tongue reaching its highest position at the SO-FO transition (swallows) or shortly after (non-swallows). This wave of tongue elevation functions to sweep the bolus posteriorly in the oral cavity through the squeeze-back mechanism identified by Franks et al. [15]. The conservation of this wave of activity in cycles prior to and after the swallow, as well as during the swallow itself, is suggestive of a conserved intra-oral transport mechanism in macaques. A similar pattern may also occur in humans. Hori et al. [66] reported that in humans tongue pressure production proceeds from anterior to posterior during mastication. Tongue pressure reaches its peak near the start of opening phase and then ceases during the opening phase. They did not investigate tongue pressure profiles during swallows, but a previous study reported that oral pressure waves propagate toward the pharynx to propel bolus transportation during swallows [67].

Moreover, while our study was of natural feeding on solid food, many standard swallow study protocols objectively assess difficulty of swallowing using liquid swallows of various volumes [68, 69] or of solid food [49, 50]. However, detailed kinematic analysis of such clinical data has not been performed to characterize preceding, during, and following swallows in human during natural feeding. Some studies characterize durations of gape cycles during human solid food feeding in a manner similar to that used here. However, they only classify three types of cycles, chewing, transport, and swallow [17]: no attempt was made to capture dynamic changes in mastication cycles around swallow cycles. As a result, we are not able to comprehensively compare the changes in hyolingual and jaw movement preceding, during, and following swallows in humans to that in macaques. Further comparisons with human data, [64, 65, 70–74] are necessary to fully understand the relevance of studies of macaque feeding for studies of mastication and swallowing disturbances in human.

Limitations in Our Study

Although we used many subsequences, our data were limited to two individuals, one for each gender, recorded from only two days each. Behaviorally, the animals were head-fixed such that the feeding was not completely natural. Furthermore, in order to ensure that the food was palatable for animals to eat consistently, we did not mix image contrast agents such as BaSO4 with the food: more detailed studies of bolus and hyolingual kinematics will require to use of image contrast agents.

Conclusions

We found similarities and differences between macaque and human jaw and hyolingual kinematics during swallowing and neighboring cycles by comparing our macaque data with human data in the literature. Macaques and humans are similar in the following ways:

- Jaw gape cycle durations in swallow cycles are longer than those in non-swallow cycles due to increased duration of jaw opening.
- Hyoid upward movement is linked with posterior tongue movement and is faster during swallows.
- Tongue elevation exhibits a wave of activity from anterior to posterior during swallows as well as during mastication.

In contrast, jaw gape cycle duration in macaques is shorter than humans as is the duration of hyoid and thyroid upward movement. The differences are probably due to the difference in jaw and hyolingual apparatus size between macaques and humans.

Previous studies have described the association between hyolingual kinematics and swallowing impairment in humans [75–77]. In patients with dysphagia, both the oral stage and pharyngeal stages of swallowing are often adversely affected by reduced coordination between tongue and jaw movement [78]. The fact that the coupling of macaque jaw and tongue kinematics is similar to that of human makes the macaque a powerful model for human feeding behavior, especially for swallowing.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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