Available online at www.sciencedirect.com
SCIENCE DIRECT
ELSEVIER
Journal of Human Evolution 50 (2006) 232–236
JHE

News and Views

# Of muscle-bound crania and human brain evolution: The story behind the *MYH16* headlines

Melanie A. McCollum [a,d,*], Chet C. Sherwood [b,d], Christopher J. Vinyard [c,d], C. Owen Lovejoy [b,d], Fred Schachat [e]

[a] *Division of Basic Medical Sciences, Mercer University School of Medicine, Macon, GA 31207, USA*
[b] *Department of Anthropology, Kent State University, Kent, OH 44242, USA*
[c] *Department of Anatomy, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272, USA*
[d] *Division of Biomedical Sciences, Kent State University, Kent, OH 44242, USA*
[e] *Department of Cell Biology, Division of Physiology, Duke University Medical School, Durham, NC 27710, USA*

Received 1 July 2005; accepted 10 October 2005

*Keywords:* Masticatory myosin; Muscle fiber plasticity; Calvarial growth; Human encephalization

## Introduction

In a recent letter to *Nature*, Stedman et al. (2004) reported that the sarcomeric myosin heavy chain (MyHC) gene *MYH16*, the orthologue of the "superfast" (a.k.a., Type IIM or "masticatory") myosin-encoding genes expressed in the masticatory muscles of other mammals (Desjardins et al., 2002), has an incorporated stop codon in humans, but not in other anthropoids. This finding, in and of itself, is not novel, as both Berg et al. (2001) and Schachat and Briggs (1999, 2002) had previously reported that *MYH16* was converted to a pseudogene by a two nucleotide deletion. It had also been previously reported that the jaw adductors of humans fail to express the "masticatory" myosin isoform characteristic of other mammals (Rowlerson et al., 1981, 1983; Hoh, 2002). What *is* novel is the priority given *MYH16* mutation in human evolution. According to Stedman et al., mutation of the *MYH16* gene and loss of its functional protein product, by significantly reducing the force production capability of the muscles of mastication, not only led to the dramatic gracilization of the skull evident in post 2.5 million-year old *Homo*, but may have also permitted its subsequent marked increase in cranial capacity.

As we discuss here, it is unlikely that *MYH16* mutation would have led to the dramatic changes in early hominid masticatory mechanics suggested by Stedman et al. It is also unlikely, therefore, that *MYH16* gene inactivation played a significant role in the craniofacial evolution of *Homo*. We further demonstrate that the scenario of human brain evolution proposed by Stedman et al. is inconsistent with current knowledge of neurocranial growth and development.

## *MYH16* gene function and muscle plasticity

The human *MYH16* pseudogene, if active, would encode a special form of myosin heavy chain expressed, in vertebrates at least, exclusively in the muscles of mastication and other first arch muscles (Schachat and Briggs, 1999, 2002; Berg et al., 2001). Fibers that express masticatory myosin are moderately fast fibers capable of developing high force at the expense of high ATPase activity and tension cost (reviewed in Hoh, 2002). According to Stedman et al., the conversion of *MYH16* to a pseudogene led directly and immediately to a significant (as much as 80%) reduction in the size of type II fibers within the jaw musculature, and an immediate change in masticatory mechanics. While such an overall, profound effect is conceivable, it is difficult to envision how it would not have

* Corresponding author. Division of Basic Medical Sciences, Mercer University School of Medicine, 1550 College Street, Macon, GA 31207, USA.
*E-mail address:* mccollum_m@mercer.edu (M.A. McCollum).

0047-2484/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jhevol.2005.10.003

been a detrimental myopathy with severe consequences. Could there be an alternative scenario for the loss of the *MYH16* protein in humans?

Overlooked in the Stedman et al. analysis of *MYH16* evolution is the fact that muscle fibers can upregulate, downregulate, or switch their expression of specific contractile protein isoforms in response to a variety of changing physiological conditions. These transitions in fiber types, examples of which include the transition from type II to type I fibers under circumstances of prolonged muscle activity and the opposite transition – from type I to type II – during extended periods of muscle inactivity, are a means of optimizing the efficiency and economy of energy usage (reviewed in Pette and Staron, 1997; Smerdu and Erzen, 2001). The muscles of mastication, which differ significantly from limb muscles in their expression of a large number of hybrid fiber types, are no exception to the physiologically-regulated plasticity of mammalian striated muscle fiber expression. As reviewed by Korfage et al. (2005a, b), the fiber-type composition of masticatory muscles is known to change in response to such factors as age (number of type II and hybrid fibers increases with age), levels of circulating thyroid hormone (number of MyHC-fetal-positive fibers increases with decreasing hormone levels), and circulating levels of testosterone (number of type II fibers increases with increasing hormone levels). That diet also influences the fiber-type composition of masticatory muscles is indicated by studies of experimental animals sustained on either hard or soft diets. For example, in comparison to rats fed a hard diet, the masseter muscles of rats fed a soft diet express a greater number of type IIB fibers (Miehe et al., 1999 reviewed in Korfage et al., 2005b). In addition, although type I fibers in the deep masseter of rats fed on normal and soft diets were found not to differ, more type IIB and type IIA fibers were noted in the deep masseters of the soft-diet group (Kiliaridis et al., 1988 reviewed in Korfage et al., 2005b). These factors, along with variation in both the activation of muscles during chewing and the influence of differing facial configurations on bite force magnitudes (i.e., long-face *vs*. short-face), all contribute, in humans at least, to the large intraspecific variation in fiber-type composition observed in the masticatory musculature (Korfage et al., 2005b).

In light of the inherent plasticity of muscle fibers, it is not surprising to find significant interspecific variation in muscle fiber-type composition as well. For example, in the limbs, the locomotory muscles of small mammals are typically composed of a greater percentage of fast fiber types IIX and IIB (Lucas et al., 2000; Smerdu et al., 1994). In contrast, the percentage of fast type IIB fibers in the locomotory muscles of larger mammals are typically reduced and are undetectable in several species including cats, baboons, and humans (Lucas et al., 2000). In humans, fibers that might normally express type IIB myosin instead express IID/X myosin (Smerdu et al., 1994). As another example, expression of the highly specialized extraocular/laryngeal myosin in large primates is exceptionally low when compared to its expression in smaller mammals (Asmussen et al., 1993; Pedrosa-Domellof et al., 2000; Briggs and Schachat, 2000, 2002). Extraocular/laryngeal myosin is generally credited for the novel contractile properties of extraocular muscle. It composes 20-30% of the total extraocular muscle myosin and as much as 50% of the myosin in some laryngeal muscles. In humans, extraocular myosin comprises only 5% of the myosin in extraocular muscles and is essentially undetectable in adult laryngeal muscle (Perie et al., 2000). Analyses of the genes that encode the IIB (*MYH4*) and extraocular/laryngeal (*MYH13*) myosin heavy chains have revealed that their reduced expression in large mammals has occurred without any obvious disruption in gene structure, as both are still transcribed to produce a translatable mRNA (Winters et al., 1998; Weiss et al., 1999; Pedrosa-Domellof et al., 2000; Schachat and Briggs, 2002).

With respect to interspecific variation in the expression of "masticatory" myosin, it is important to note that humans are not unique in their failure to express this particular isoform. "Masticatory" myosin is lacking in the jaw-closing muscles of a number of mammals, most notably ungulates, rodents, rabbits, and kangaroos (Kang et al., 1994; Sfondrini et al., 1996; Hoh, 2002; Qin et al., 2002). Comparative genetic studies suggest that the masticatory MyHC gene originated through duplication of an ancestral striated MyHC gene expressed in the mandibular arch musculature of early gnathostomes, and that it has since been retained as the primitive phenotype in vertebrates (Qin et al., 2002). Functional loss of masticatory myosin in a number of non-carnivorous mammalian species is believed to have followed shifts in dietary strategies that ultimately freed these taxa from the need for powerful jaw closure. As a consequence, these taxa are believed to have replaced their masticatory myosin with functionally more appropriate myosin isoforms (e.g., slow/β-cardiac fibers in ungulates, Kang et al., 1994; fast MyHCs in rodents, Sfondrini et al., 1996).

At present, data regarding the mechanisms underlying the interspecific variation of masticatory myosin expression are not available; it is not known whether the functional loss of masticatory myosin in rodents and other non-carnivores is a function of physiological downregulation or pseudogenization. However, the very fact that muscle fibers readily change their myosin heavy chain expression suggests that masticatory myosin in hominids could very well have been significantly, if not totally downregulated *prior* to its conversion to a pseudogene. If this were the case, inactivation of the *MYH16* gene would have had little impact on the muscles of mastication of early hominids and far less severe consequences for its carriers. In fact, the introduction of a nonsense mutation in the *MYH16* gene may have been below the threshold of selection. If this alternative is correct, then the real question of interest is whether the change in masticatory function that occurred during hominid evolution and that led to *MYH16* downregulation and inactivation was diet-related, as has been recently suggested (Hoh, 2002), or instead reflected changes in social behaviors that would have eliminated the need for an aggressive bite, as was suggested over 20 years ago (Rowlerson et al., 1983).

## *MYH16* downregulation/inactivation and the hominid fossil record

An important element of Stedman et al.'s scenario of hominid cranial evolution concerns the age of the *MYH16* mutation. They estimated this event at approximately 2.4 mya, which roughly coincides with the first appearance of the genus *Homo* (Suwa et al., 1996), and precedes the appearance of the more gracile skull form of *H. ergaster/erectus*. As they emphasized, "…an abrupt evolutionary alteration in the size and contractile force generated by these [masticatory] muscles would have had pleiotropic effects on craniofacial morphology in the first homozygous *MYH16*-null human ancestor" (Stedman et al., 2004, p. 417). Of course, if *MYH16* gene expression was significantly downregulated prior to its later inactivation by pseudogenization, as discussed above, the date of such an event is largely immaterial to early hominid cranial evolution.

At most, the age of the *MYH16* inactivating mutation limits the recency of the gene's downregulation in hominid evolution. If we accept Stedman et al.'s date for the inactivation of *MYH16*, which was based on an analysis of only a small, 1,065 bp segment of the gene, then functional loss of masticatory myosin could have occurred anywhere between the time of the chimpanzee-human divergence through 2.4 mya. However, as reported by Perry et al. (2005), analysis of a much larger sequence of the *MYH16* gene (ca. 30,000 bp) yields a date of inactivation of approximately 5.3 mya – over twice the age reported by Stedman et al. If this more ancient date is more accurate, downregulation of the *MYH16* gene and functional loss of masticatory fibers occurred significantly earlier in hominid evolution, long before the gracilization of the *Homo* cranium.

## *MYH16* downregulation/inactivation and neurocranial growth

Stedman et al. proposed that the marked increase in cranial capacity observed in Pleistocene *Homo* may owe its origin to a reduction in masticatory muscle mass and the corresponding loss in contractile force caused by *MYH16* inactivation. Such a scenario assumes that forces generated by powerful muscles of mastication can inhibit growth of the brain and neurocranium. However, most of brain growth – 80-90% in humans (see Courchesne et al., 2000 for a comprehensive summary of these data), and 85-95% in chimpanzees (Herndon et al., 1999) – occurs prior to eruption of the first permanent molar, while the mature chewing cycle is still being coordinated, and while the force-producing capabilities of the masticatory musculature are absolutely smaller (Storey, 1988; Dechow and Carlson, 1990; Moyers and Carlson, 1996). Data regarding the size and contractile properties of the masticatory musculature at this early stage of ontogeny are currently unavailable, but measured bite forces (a proxy for muscle size and contractile force) in children between the ages of six and eight years – roughly the ages of eruption of the first permanent molar and permanent incisors – are less than half (44%) those of adults (Braun et al., 1996). In light of their small size and corresponding force-generating potential, it is unlikely that the muscles of mastication typical of such young individuals could significantly restrict neurocranial growth induced by a rapidly expanding brain.

As demonstrated in growing macaques, bite force increases with positive allometry relative to body mass (but not jaw length; Dechow and Carlson, 1990). Even at comparatively larger sizes it is unlikely that forces generated by the muscles of mastication could constrain neurocranial growth. As reported by Sun et al. (2004), the rate of calvarial suture growth observed in growing miniature swine failed to correlate in any way with the magnitude of the sutural strains generated during chewing. Also of significance, Sun et al. found that the compressive sutural strains generated by the masticatory musculature do not retard suture growth. Instead, in these animals calvarial suture growth rate declined between three and seven months of age. As Sun et al. note, these findings are fully consistent with the long-standing model that cranial suture growth is regulated primarily by the tension arising from growth of the brain and its associated intracranial structures (e.g., Moss, 1954; Young, 1959; Moss and Young, 1960).

Considerable indirect evidence also attests to the inability of masticatory muscles and the strain they generate to constrain an otherwise expanding brain. For example, the massive sagittal extracranial crests of extant male gorilla crania make them the most "muscle-bound" of all extant hominoids. Yet, when brain volume is scaled against spinal cord size, the gorilla brain is no smaller than is that of other great apes (Rilling and Insel, 1999). As another example, the Inuit, who have long been recognized as generating unusually high masticatory forces (Hylander, 1977), possess cranial capacities that are among the largest of all modern populations (Hrdlička, 1942). Among fossil hominid taxa, the well-developed extracranial crests and expansive temporal fossae of East African hyper-robust *Australopithecus* species reflect the large size of their masticatory muscles. Despite encapsulation by this massive musculature, the brain in this lineage still enlarged from a chimpanzee-like 410 ml at 2.5 mya in *A. aethiopicus* (Walker et al., 1986) to a more substantial 545 ml at 1.4 mya in *A. boisei* (Walker et al., 1986; Suwa et al., 1997; Elton et al., 2001).

## Human encephalization

Modern humans are able to achieve a high degree of encephalization because their pattern of brain growth deviates from the pattern typical of most primates. Because of obstetric constraints associated with modifications of pelvic dimensions for bipedality (Lovejoy, 2005), modern human neonatal brain size is relatively small compared to its final adult size – comprising only 25% of adult volume. This contrasts with the relatively larger brains of newborn macaques (70% of adult size) and chimpanzees (40% of adult size) (Martin, 1983). Nevertheless, the human neonatal brain is approximately two times larger in absolute size than the neonatal brains of any of the great apes (Martin, 1983), indicating that a large portion of human brain enlargement is subsidized by maternal

investment toward rapid brain growth *in utero*. Subsequently, postnatal brain growth in humans continues at its fetal rate through the first year, after which the pace declines. In other primates, brain growth rates decrease immediately after birth. Thus, greater encephalization in humans is attained mostly by acceleration of brain growth rates in fetal and early postnatal stages (Leigh, 2004). Although the fossil record does not yet give us a clear indication as to when the characteristic pattern of human brain growth first emerged (see Coqueugniot et al., 2004, and Leigh, in press regarding the ontogeny of brain growth in *H. erectus*), it is clear that human brain enlargement has involved significant increases in the rate of brain growth during early ontogeny, long before the masticatory muscles have reached peak force-generating potential.

In this regard, experimental and clinical studies have identified a host of genes that control the development of brain size in mammals *via* regulation of the differentiation, proliferation, and apoptosis of cortical progenitor cells (Krubitzer and Kahn, 2003). Several of these genes, including *ASPM, MCPH1*, and *CASP3*, appear to have undergone accelerated rates of protein evolution at several points along the lineage leading to humans, with evidence of upsurges in nonsynonymous amino acid substitutions in the last common ancestor of great apes and humans, and again in the descent of humans (Dorus et al., 2004; Kouprina et al., 2004; Wang and Su, 2004; Evans et al., 2005; Mekel-Bobrov et al., 2005). These findings suggest that the increased encephalization of apes and humans resulted from strong positive selection at several loci, without any relationship to the natural history of the *MYH16* gene. Examination of the *cis*- and *trans*-regulators of these genes, as well as their phenotypic correlates, is much more likely to yield meaningful information regarding human neuroanatomical specializations than does any examination of masticatory muscle gene expression.

## References


Asmussen, G., Traub, I., Pette, D., 1993. Electrophoretic analysis of myosin heavy chain isoform patterns in extraocular muscles of the rat. FEBS Lett. 335, 243–245.

Berg, J.S., Bradford, C.P., Cheney, R.E., 2001. A millennial myosin census. Mol. Biol. Cell 12, 780–794.

Braun, S., Hnat, W.P., Freudenthaler, J.W., Marcotte, M.R., Honigle, K., Johnson, B.E., 1996. A study of maximum bite force during growth and development. Angle Orthod. 66, 261–264.

Briggs, M.M., Schachat, F., 2000. Early specialization of the superfast myosin in extraocular and laryngeal muscles. J. Exp. Biol. 203, 2485–2894.

Briggs, M.M., Schachat, F., 2002. The superfast extraocular myosin (MYH13) is localized to the innervation zone in both the global and orbital layers of rabbit extraocular muscle. J. Exp. Biol. 205, 3133–3142.

Coqueugniot, H., Hublin, J.J., Veillon, F., Houet, F., Jacob, T., 2004. Early brain growth in *Homo erectus* and implications for cognitive ability. Nature 431, 299–302.

Courchesne, E., Chisum, H.J., Townsend, J., Cowles, A., Covington, J., Egaas, B., Harwood, M., Hinds, S., Press, G.A., 2000. Normal brain development and aging: quantitative analysis at in vivo MR imaging in healthy volunteers. Radiology 216, 672–682.

Dechow, P.C., Carlson, D.S., 1990. Occlusal force and craniofacial biomechanics during growth in rhesus monkeys. Am. J. Phys. Anthropol. 83, 219–237.

Desjardins, P.R., Burkman, J.M., Shrager, J.B., Allmond, L.A., Stedman, H.H., 2002. Evolutionary implications of three novel members of the human sarcomeric myosin heavy chain gene family. Mol. Biol. Evol. 19, 375–393.

Dorus, S., Vallender, E.J., Evans, P.D., Anderson, J.R., Gilbert, S.L., Mahowald, M., Wyckoff, G.J., Malcom, C.M., Lahn, B.T., 2004. Accelerated evolution of nervous system genes in the origin of *Homo sapiens*. Cell 119, 1027–1040.

Elton, S., Bishop, L.C., Wood, B., 2001. Comparative context of Plio-Pleistocene hominin brain evolution. J. Hum. Evol. 41, 1–27.

Evans, P.D., Gilbert, S.L., Mekel-Bobrov, N., Vallender, E.J., Anderson, J.R., Vaez-Azizi, L.M., Tishkoff, S.A., Hudson, R.R., Lahn, B.T., 2005. *Microcephalin*, a gene regulating brain size, continues to evolve adaptively in humans. Science 309, 1717–1720.

Herndon, J.G., Tigges, J., Anderson, D.C., Klumpp, S.A., McClure, H.M., 1999. Brain weight through the life span of the chimpanzee. J. Comp. Neurol. 409, 567–572.

Hoh, J.F.Y., 2002. ‘Superfast’ or masticatory myosin and the evolution of jaw-closing muscles of vertebrates. J. Exp. Biol. 205, 2203–2210.

Hylander, W.L., 1977. The adaptive significance of Eskimo craniofacial morphology. In: Dahlberg, A.A., Graber, T.M. (Eds.), Orofacial Growth and Development. Mouton Publishers, Paris, pp. 129–169.

Hrdlička, A., 1942. Catalogue of human crania in the United States National Museum collections: Eskimo in general. Proc. U.S. Nat. Mus. 91, 169–429.

Kang, L.H.D., Hughes, S., Pettigrew, J.D., Hoh, J.F.Y., 1994. Jaw-specific myosin heavy chain gene expression in sheep, dog, monkey, flying fox and microbat jaw-closing muscles. Basic Appl. Myol. 4, 381–392.

Kiliaridis, S., Engstrom, C., Thilander, B., 1988. Histochemical analysis of masticatory muscle in the growing rat after prolonged alteration in the consistency of the diet. Arch. Oral Biol. 33, 187–193.

Korfage, J.A., Koolstra, J.H., Langenbach, G.E., van Eijden, T.M., 2005a. Fiber-type composition of the human jaw muscles – (part 1) origin and functional significance of fiber-type diversity. J. Dent. Res. 84, 774–783.

Korfage, J.A., Koolstra, J.H., Langenbach, G.E., van Eijden, T.M., 2005b. Fiber-type composition of the human jaw muscles – (part 2) role of hybrid fibers and factors responsible for inter-individual variation. J. Dent. Res. 84, 784–793.

Kouprina, N., Pavlicek, A., Mochida, G.H., Solomon, G., Gersch, W., Yoon, Y.H., Collura, R., Ruvolo, M., Barrett, J.C., Woods, C.G., Walsh, C.A., Jurka, J., Larionov, V., 2004. Accelerated evolution of the ASPM gene controlling brain size begins prior to human brain expansion. PLoS Biol. 2, E126.

Krubitzer, L., Kahn, D.M., 2003. Nature versus nurture revisited: an old idea with a new twist. Prog. Neurobiol. 70, 33–52.

Leigh, S.R. Brain ontogeny and life history of *Homo erectus*. J. Hum. Evol., in press. doi:10.1016/j.jhevol.2005.02.008

Leigh, S.R., 2004. Brain growth, life history, and cognition in primate and human evolution. Am. J. Primatol. 62, 139–164.

Lovejoy, C.O., 2005. The natural history of human gait and posture. Part 1. Spine and pelvis. Gait Posture 21, 95–112.

Lucas, C.A., Kang, L.H.D., Hoh, J.F.Y., 2000. Monospecific antibodies against the three mammalian fast limb myosin heavy chains. Biochem. Biophys. Res. Commun. 272, 303–308.

Martin, R.D., 1983. Human Brain Evolution in an Ecological Context. American Museum of Natural History, New York.

Mekel-Bobrov, N., Gilbert, S.L., Evans, P.D., Vallender, E.J., Anderson, J.R., Hudson, R.R., Tishkoff, S.A., Lahn, B.T., 2005. Ongoing adaptive evolution of ASPM, a brain size determinant in *Homo sapiens*. Science 309, 1720–1721.

Miehe, B., Fanghanel, J., Kubein-Meesenburg, D., Nagerl, H., Schwestka-Polly, R., 1999. Masticatory musculature under altered occlusal relationships – a model study with experimental animals. Ann. Anat. 181, 37–40.

Moss, M.L., 1954. Growth of the calvaria in the rat: the determination of osseous morphology. Am. J. Anat. 94, 333–361.

Moss, M.L., Young, R.W., 1960. A functional approach to craniology. Am. J. Phys. Anthropol. 18, 281–292.

Moyers, R.E., Carlson, D.S., 1996. Maturation of the orofacial musculature. In: Enlow, D.H., Hans, M.G. (Eds.), Essentials of Facial Growth. W.B. Saunders, Philadelphia, pp. 233–240.

Pedrosa-Domellof, F., Holmgren, Y., Lucas, C.A., Hoh, J.F.Y., Thornell, L.E., 2000. Human extraocular muscles: unique pattern of myosin heavy chain expression during myotube formation. Invest. Ophthalmol. Vis. Sci. 41, 1608–1616.

Perie, S., Agbulut, O., St Guily, J.L., Butler-Browne, G.S., 2000. Myosin heavy chain expression in human laryngeal muscle fibers. A biochemical study. Ann. Otol. Rhinol. Laryngol. 109, 216–220.

Perry, G.H., Verrelli, B.C., Stone, A.C., 2005. Comparative analyses reveal a complex history of molecular evolution for human MYH16. Mol. Biol. Evol. 22, 379–382.

Pette, D., Staron, R.S., 1997. Mammalian skeletal muscle fiber type transitions. Int. Rev. Cytol. 170, 143–223.

Qin, H., Hsu, M.K.H., Morris, B.J., Hoh, J.F.Y., 2002. A distinct subclass of Mammalian striated myosins: structure and molecular evolution of "superfast" or masticatory myosin heavy chain. J. Mol. Evol. 55, 544–552.

Rilling, J.K., Insel, T.R., 1999. The primate neocortex in comparative perspective using magnetic resonance imaging. J. Hum. Evol. 37, 191–223.

Rowlerson, A., Pope, B., Murray, J., Whalen, R.G., Weeds, A.G., 1981. A novel myosin present in cat jaw-closing muscles. J. Muscle Res. Cell Motil. 2, 415–438.

Rowlerson, A., Mascarello, F., Veggetti, A., Carpene, E., 1983. The fibre-type composition of the first branchial arch muscles in Carnivora and Primates. J. Muscle Res. Cell Motil. 4, 443–472.

Schachat, F., Briggs, M.M., 1999. Identification of two patterns of exon organization in the human striated muscle myosin heavy chains. Mol. Biol. Cell 10, 34a.

Schachat, F., Briggs, M.M., 2002. Phylogenetic implications of the superfast myosin of extraocular muscles. J. Exp. Biol. 205, 2189–2201.

Sfondrini, G., Reggiani, C., Gandini, P., Bovenzi, R., Pellegrino, M.A., 1996. Adaptations of masticatory muscles to a hyperpropulsive appliance in the rat. Am. J. Orthod. Dentofacial Orthop. 110, 612–617.

Smerdu, V., Erzen, I., 2001. Dynamic nature of fibre-type specific expression of myosin heavy chain transcripts in 14 different human skeletal muscles. J. Muscle Res. Cell Motil. 22, 647–655.

Smerdu, V., Karsch-Mizrachi, I., Campione, M., Leinwand, L., Schiaffino, S., 1994. Type IIx myosin heavy chain transcripts are expressed in type IIb fibers of human skeletal muscle. Am. J. Physiol. 267, C1723–C1728.

Stedman, H.H., Kozyak, B.W., Nelson, A., Thesier, D.M., Su, L.T., Low, D.W., Bridges, C.R., Shrager, J.B., Minugh-Purvis, N., Mitchell, M.A., 2004. Myosin gene mutation correlates with anatomical changes in the human lineage. Nature 428, 415–418.

Storey, A.T., 1988. Maturation of the oral musculature. In: Moyers, R.E. (Ed.), Handbook of Orthodontics, fourth ed. Year Book Medical Publishers, Inc., Chicago, pp. 73–97.

Sun, Z., Lee, E., Herring, S.W., 2004. Cranial sutures and bones: growth and fusion in relation to masticatory strain. Anat. Rec. Part A 276A, 150–161.

Suwa, G., White, T.D., Howell, F.C., 1996. Mandibular postcanine dentition from the Shungura Formation, Ethiopia: crown morphology, taxonomic allocations, and Plio-Pleistocene hominid evolution. Am. J. Phys. Anthropol. 101, 247–282.

Suwa, G., Asfaw, B., Beyene, Y., White, T.D., Katoh, S., Nagaoka, S., Nakaya, H., Uzawa, K., Renne, P., WoldeGabriel, G., 1997. The first skull of *Australopithecus boisei*. Nature 389, 489–492.

Walker, A.C., Leakey, R.E., Harris, J.M., Brown, F.H., 1986. 2.5 myr *Australopithecus boisei* from west of Lake Turkana, Kenya. Nature 322, 517–522.

Wang, Y.Q., Su, B., 2004. Molecular evolution of microcephalin, a gene determining human brain size. Hum. Mol. Genet. 13, 1131–1137.

Weiss, A., Schiaffino, S., Leinwand, L.A., 1999. Comparative sequence analysis of the complete human sarcomeric myosin heavy chain family: implications for functional diversity. J. Mol. Biol. 290, 61–75.

Winters, L.M., Briggs, M.M., Schachat, F., 1998. The human extraocular muscle myosin heavy chain gene (*MYH13*) maps to the cluster of fast and developmental myosin genes on chromosome 17. Genomics 54, 188–189.

Young, R.W., 1959. The influence of cranial contents on postnatal growth of the skull in the rat. Am. J. Anat. 105, 383–415.