Chapter 8

Origin, Development, and Evolution of Primate Muscles, with Notes on Human Anatomical Variations and Anomalies

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Introduction

Most studies of the gross morphology of the soft tissues of primates are either in-depth investigations of a single structure or organ, or investigations that focus on a single taxon (reviewed in Gibbs et al. 2002 and Diogo and Wood 2012a). Recently, we undertook a detailed comparative study of the head, neck, pectoral, and forelimb myology of each of the major primate higher taxa (Diogo and Wood 2012a) including the 18 genera listed in Table 8.1, and we have now embarked on a second comparative study that focuses on the muscles of the trunk, pelvis, and lower limb. Our studies of primates are part of a long-term project to investigate the comparative anatomy, homologies, evolution, and development of the striated muscles of all of the major groups of vertebrates (e.g., Diogo 2004a, 2004b, 2005, 2007; Diogo and Abdala 2007, 2010; Diogo et al. 2008a, 2008b, 2009a, 2009b, 2012b). We have also presented the results of these analyses in the form of anatomical atlases of the apes (e.g., Diogo et al. 2010, 2012a, 2013a, 2013b), and reported the results of comprehensive parsimony and Bayesian cladistic analyses of the myology of these taxa (e.g., Diogo and Wood 2011, 2012b; Diogo et al. 2012b, 2013d). The most parsimonious tree obtained from the analysis of the 166 head, neck, pectoral, and upper limb myological characters in the 18 primate genera and in the outgroups (Rodentia: Rattus; Scandentia: Tupaia; and Dermoptera: Cynocephalus) was congruent with the molecular trees obtained recently by Fabre et al. (2009), Arnold et al. (2010), and Perelman et al. (2011). Most of the major primate clades were supported by high parsimony bootstrap support values (BSV) and/or Bayesian credibility support values (CSV) (e.g., six of the 15 non-hominoid primate clades have CSV and/or BSV≥98). Our analysis

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Table 8.1. Summary of the total number of mandibular, hyoid (not including the small facial, extrinsic muscles of the ear), branchial, hypobranchial, pectoral, arm, forearm, and hand muscles in adults of some key primate genera. Data are from evidence provided by our own dissections and comparisons and from a review of the literature (Diogo and Wood 2011, 2012a); note that in some cases there are insufficient data to clarify whether a particular muscle is usually present, or not, in a taxon (e.g., the number of branchial muscles of *Gorilla* is given as 15 to 16 because it is not clear if the salpingopharyngeus is usually present, or not, as a distinct muscle in the members of this genus).

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was the first cladistic study based on a large morphology-based data matrix to provide compelling levels of support for the chimp-human clade (BSV 75, CSV 94). Apart from the utility of mapping myological characters on osteological or molecular phylogenies to address evolutionary questions, the results of our studies of primates, as well as of other vertebrates, suggest that myological characters can be used to generate phylogenies (see recent review of Diogo and Wood 2013).

The goal of this chapter is to draw together the broader evolutionary and developmental implications of our study of the musculature of primates. As well as increasing awareness of primate morphological evolution and evolutionary developmental biology in general, we hope that this synthesis will encourage others to analyze the myology, development, and evolution of other major mammalian and vertebrate groups.

As many of the issues discussed below concern the development of muscles and the spatial associations between them and bones/cartilages, we include a short introduction before discussing these issues. For example, with respect to limb development, fundamental ontogenetic characteristics are shared among distantly related tetrapod taxa (e.g., cartilage morphogenesis is remarkably similar across a wide range of tetrapod groups in that signaling for limb bone development usually precedes that for muscle development, cartilage in general is present prior to muscle formation (e.g., Fabrezi et al. 2007), and somatic limb muscle progenitor cells apparently do not carry intrinsic positional information (e.g., Duprez 2002)). Some studies suggest that the presence of the first tissues formed during limb development (condensations that will give rise to bones) may provide the positional signaling for the subsequent development of soft tissue (see Diogo and Abdala 2010). But muscles can also play an important role in at least some aspects of skeletal morphogenesis (e.g., muscle contraction might help regulate chondrocyte intercalation and skeletal elongation, facilitating coordination between muscular and skeletal development (e.g., Schwartz et al. 2012)) and muscle activity is required for survival of the tendon blastemas (undifferentiated cell masses) (Brand et al. 1985). However, it remains unknown whether tetrapods share a general, predictable spatial correlation between limb bones and muscles, and, if such a correlation exists, whether it reflects any link between the signaling involved in skeletal and muscle morphogenesis (e.g., Kardon 1998; DeLaurier et al. 2006; Blitz et al. 2013).

Concerning the head and neck muscles, studies using rhombomeric quail-to-chick grafts to investigate the influence of hindbrain segmentation on craniofacial patterning (e.g., Köntges and Lumsden 1996), showed that each rhombomeric neural crest cell population remains coherent throughout ontogeny, with rhombomere-specific matching of muscle connective tissue and their attachment sites for most head and neck muscles. One point not always well understood is that the specificity of muscle attachments referred to by Köntges and Lumsden (1996) relates to the connective tissue/fasciae associated with the muscles, and not with the ontogenetic and/or phylogenetic origin of the muscles. For example, the avian hyobranchialis (“branchiomandibularis” sensu Köntges and Lumsden 1996) is a branchial muscle, but it is attached anteriorly to hyoid (second arch) crest-derived skeletal domains (i.e., the retroarticular process of the mandible)(Diogo and Abdala 2010 and see next section).
This is because the anterior part of this muscle is associated with connective tissue/fasciae that is precisely derived from hyoid, and not mandibular, crest cells. The hyobranchialis was the only muscle studied by Köntges and Lumsden (1996) that derives its connective tissue from more than one branchial arch, because unlike its anterior component, the posterior portion is associated with connective tissue/fascia derived from the third and fourth arches. Accordingly, it inserts onto third and fourth arch crest-derived skeletal domains.

Other examples that illustrate the model proposed by Köntges and Lumsden (1996) concern the hypobranchial muscles hyoglossus, hypoglossus, and genioglossus. As explained by Diogo and Abdala (2010), previous mapping studies have shown that the myocytes and the innervation of these three muscles are derived from the much more posterior axial levels of the first somites (e.g., the first six somites). However, as noted by Köntges and Lumsden (1996, pp.3240–3241) their “skeletal attachment fascia are derived from the more anterior axial levels of cranial neural crests.” That is why the genioglossus and hypoglossus of birds, for instance, are attached to the paraglossals and the ventral basihyoid sensu Köntges and Lumsden (1996), which are derived from mandibular arch crest derived from the posterior midbrain. And that is why the hyoglossus (“ceratoglossus” sensu Köntges and Lumsden 1996), which is also ontogenetically and phylogenetically derived from the geniohyoideus (as are the genioglossus and hypoglossus: see Diogo and Abdala 2010), is attached to hyoid (second arch) crest-derived skeletal elements. Thus, the attachments of these three hypobranchial muscles are primarily determined by the origin of the connective tissues/fasciae with which they are associated. There are a few exceptions to the model proposed by Köntges and Lumsden (1996). For example, at least some facial muscles of mammals, which are derived from the second (hyoid) arch and are apparently associated with connective tissue/fascia also derived from this arch, move into midfacial and jaw territories populated only by frontonasal and first arch crest cells (e.g., Noden and Francis-West 2006). Also, Prunotto et al. (2004) have shown that the facial muscles behave, in terms of C-met mutations, as hypaxial migratory muscles. Thus, contrary to most other head muscles, with the exception of the hypobranchial muscles, the facial muscles are absent in organisms with C-met mutations. This suggests that these mammalian muscles migrate far away from their primary origin (see review of Diogo and Abdala 2010).

In the following sections we discuss in more detail the origin, ontogeny, and evolution of the head, neck, pectoral, and forelimb muscles.

The Developmental and Evolutionary Origins of the Head, Neck, Pectoral, and Forelimb Muscles

Head and Neck Muscles

According to the myological nomenclature used by Diogo and Abdala (2010) the main groups of head and neck muscles are: external ocular, mandibular, hyoid, branchial, epibranchial, and hypobranchial, corresponding to those proposed by Edgeworth
Edgeworth (1935) viewed the ontogeny of these muscles as discrete developmental pathways leading from presumptive premyogenic condensations to the different adult muscles in each cranial arch. The condensations of the first and second arches corresponded respectively to Edgeworth’s “mandibular and hyoid muscle plates,” and those of the more posterior, “branchial” arches corresponding to his “branchial muscle plates” (see Figure 8.1). According to Edgeworth these developmental pathways involve migration of premyogenic cells, differentiation of myofibers, directional growth of myofibers, and possibly interactions with surrounding structures. These events occur in specific locations (e.g., dorsal, medial, or ventral areas of each cranial arch, as shown in the scheme of Figure 8.1). For instance, the mandibular muscle plate gives rise dorsally to the premyogenic condensation of constrictor dorsalis, medially to the premyogenic condensation of adductor mandibulae, and ventrally to the intermandibularis (no description of a ventral mandibular premyogenic condensation was given by Edgeworth). The hyoid condensation usually gives rise to dorso-medial and ventral derivatives, and the hypobranchial condensation gives rise to the “genio-hyoideus” and to the “rectus cervicus” (as noted by Miyake et al. 1992, it is not clear if Edgeworth’s “genio-hyoideus” and “rectus cervicus” represent separate premyogenic condensations or later states of muscle development). Although some authors use different nomenclatures, most authors and recent studies support the major divisions of head and neck muscles recognized by Edgeworth (1935) (i.e., mandibular, hyoid, branchial, and hypobranchial muscles).

Although exceptions may occur, the mandibular muscles are generally innervated by the Vth nerve. Modern humans have two ventral mandibular muscles (mylohyoideus and digastricus anterior) and six “adductor mandibulae” mandibular muscles (masseter, temporalis, pterygoideus lateralis, pterygoideus medialis, tensor tympani, and tensor veli palatini). The hyoid muscles are usually innervated by the VIIth nerve. Modern humans have three “dorso-medial” hyoid muscles (stylohyoideus, digastricus posterior, and stapedius) and several facial muscles that seemingly derive from the “dorso-medial” and particularly the “ventral” hyoid muscle groups (Diogo and Abdala 2010). The branchial muscles are usually innervated by the IXth and Xth nerves.
Diogo and Abdala (2010) divided the branchial muscles *sensu lato* into three main groups. The first, which comprises the “true” branchial muscles, are subdivided into: (A) the branchial muscles *sensu stricto* that are directly associated with the movements of the branchial arches and are usually innervated by the glossopharyngeal nerve (CNIX). Modern humans have a single muscle of this subgroup, the stylopharyngeus; (B) the protractor pectoralis and its derivatives, which are instead mainly associated with the pectoral girdle and are primarily innervated by the spinal accessory nerve (CNXI). Modern humans have two muscles belonging to this subgroup, the trapezius and sternocleidomastoideus. The second group consists of the pharyngeal muscles, which are only present as independent structures in extant mammals, and which are considered to be derived from arches 4–6, and are usually innervated by the vagus nerve (CNX). Modern humans have eight muscles belonging to this group (constrictor pharyngis medius, constrictor pharyngis inferior, cricothyroidus, constrictor pharyngis superior, palatopharyngeus, musculus uvulae, levator veli palatini, and salpingopharyngeus). The third group is made up of the laryngeal muscles, which are considered to be derived from arches 4–6 and are usually innervated by the vagus nerve (CNX). Modern humans have six muscles belonging to this group (thyroarytenoideus, vocalis, cricoarytenoideus lateralis, arytenoideus transversus, arytenoideus obliquus, and cricoarytenoideus posterior).

Regarding the epibranchial and hypobranchial muscles, according to Edgeworth (1935, p.189) these are “developed from the anterior myotomes of the body” and thus “are intrusive elements of the head”; they “retain a spinal innervation” and “do not receive any branches from the Vth, VIIth, IXth and Xth nerves.” Mammals and thus primates have no epibranchial muscles. The “geniohyoideus” group of hypobranchial muscles is represented in modern humans by the geniohyoideus, genioglossus, hyoglossus, styloglossus, and palatoglossus and the intrinsic muscles of the tongue, and the “rectus cervicis” group by the sternohyoideus, omohyoideus, sternothyroideus, and thyrohyoideus. It is worth mentioning that apart from the mandibular, hyoid, branchial, hypobranchial, and epibranchial musculature, Edgeworth (1935, p.5) referred to a primitive “premandibular arch” in “which passed the IIIrd nerve”. This IIIrd nerve, together with the IVth and VIth nerves – which according to Edgeworth (1935, p.5) are “not segmental nerves; they innervate muscles of varied segmental origin and are, phylogenetically, of later development than are the other cranial nerves” – innervate the external ocular muscles of most extant vertebrates. In modern humans, the group of external ocular muscles includes the superior, inferior, medial, and lateral rectus muscles, the inferior and superior oblique muscles, and the levator palpebrae superior.

Some of the hypotheses defended by Edgeworth have been contradicted by recent studies, but many of his conclusions have been corroborated by more recent developmental and genetic studies (see Diogo and Abdala 2010). For example, Miyake *et al.* (1992, p.214) noted that “Noden (1983, 1984, 1986) elegantly demonstrated with quail-chick chimeras that cranial muscles are embryologically of somitic origin, and not as commonly thought, of lateral plate origin, and in doing so corroborated the nearly forgotten work of Edgeworth.” Miyake *et al.* (1992, p.214) also noted that developmental studies such as Hatta *et al.*
(1990, 1991) “have corroborated one of Edgeworth’s findings: the existence of one premyogenic condensation (the constrictor dorsalis) in the cranial region of teleost fish.” The existence of this and other condensations (e.g., the hyoid condensation) has received further support in developmental studies published in the last years (e.g., Knight et al. 2008; Kundrát et al. 2009). For example, in the zebrafish, immunoreactivity of the homeodomain transcription factor *engrailed* is only detected in the levator arcus palatini + dilatator operculi muscles (i.e., in the two muscles that are derived from the dorsal portion of the mandibular muscle plate – constrictor dorsalis *sensu* Edgeworth 1935). In mammals such as the mouse, *engrailed* immunoreactivity is detected in mandibular muscles that are likely derived from a more ventral (“adductor mandibulae”) portion of that plate (i.e., in the masseter, temporalis, pterygoideus medialis, and/or pterygoideus lateralis (Knight et al. 2008)). Authors such as Tzahor (2009) have shown that even within a single species, muscles from the same arch (e.g., mandibular arch) may originate from different types of cells. For example, the mandibular “adductor mandibulae complex” and its derivatives (e.g., masseter) derive from cranial paraxial mesoderm, whereas the more ventral mandibular muscle inter-mandibularis and its derivatives (e.g., mylohyoideus) originate from medial splanchnic mesoderm.

Edgeworth’s (1935) division of the head and neck muscles into external ocular, mandibular, hyoid, branchial, epibranchial, and hypobranchial muscles continues to be widely used by both comparative anatomists and developmental biologists. His scheme is similar to those used in numerous recent developmental and molecular works but, as expected, some researchers prefer to group the head and neck muscles in ways that do not always correspond to those proposed by Edgeworth. Thus Noden and Francis-West (2006) refer to three main types of head and neck muscles (Figure 8.2): (1) “extra-ocular” muscles, which correspond to Edgeworth’s extra-ocular muscles; (2) “branchial” muscles, which correspond to the mandibular, the hyoid, and most of the branchial muscles *sensu* Edgeworth; and (3) “laryngoglossal” muscles, which include the hypobranchial muscles but also part of the branchial muscles *sensu* Edgeworth (namely the laryngeal muscles *sensu* Diogo and Abdala 2010). An advantage of recognizing these three main types is to stress that in vertebrate model taxa such as salamanders, chickens, and mice, the laryngeal muscles (for example the dilatator laryngis and constrictor laryngis) receive a contribution of somitic myogenic cells (e.g., Noden 1983; Piekarski and Olsson 2007) as do the hypobranchial muscles *sensu* Edgeworth (see above). That is, the main difference between the “branchial” and “laryngoglossal” groups *sensu* Noden and Francis-West (2006) is that, unlike the “branchial” group, the “laryngoglossal” receives a contribution of somitic cells. However, recent developmental studies (e.g., Piekarski and Olsson 2007) have shown that some of the “branchial” muscles *sensu* Noden and Francis-West (2006) (i.e., some “true,” non-laryngeal, branchial muscles *sensu* the present work such as the protractor pectoralis and the levatores arcuum branchialium of salamanders and the trapezius of chickens and mice, and even some hyoid muscles such as the urodelan interhyoideus) also receive a contribution of somitic myogenic cells. Edgeworth (1935) included the protractor pectoralis and its derivatives – which
include the trapezius and sternocleidomastoideus of amniotes and thus of modern humans – in the branchial musculature, but he was aware that these muscles were at least partially originated from somites. However, it is important to note that recent studies have shown that although the trapezius might receive a somitic contribution, it is mainly derived from the branchial arches. Thus, it is essentially a branchial muscle, as originally proposed by Edgeworth (Theis et al. 2010).
Pectoral and Forelimb Muscles

Regarding the pectoral and forelimb musculature, we recognize five main groups of muscles (Diogo and Abdala 2010): the axial muscles of the pectoral girdle, the appendicular muscles of the pectoral girdle and arm, the appendicular muscles of the ventral forearm, the appendicular muscles of the hand, and the appendicular muscles of the dorsal forearm. The appendicular musculature of the pectoral girdle, arm, forearm, and hand mainly derives from the adductor and abductor muscle masses of the pectoral fin of sarcopterygian fish, and essentially corresponds to the “abaxial musculature” sensu Shearman and Burke (2009). The axial pectoral girdle musculature is derived from the postcranial axial musculature, and, together with most of the remaining epaxial and hypaxial muscles of the body (with the exception of, e.g., various muscles of the pectoral girdle and hind limb), form the “primaxial musculature” sensu Shearman and Burke (2009).

As explained by Shearman and Burke (2009), the muscles of the vertebrate body are classically described as epaxial or hypaxial according to their innervation from either the dorsal or ventral rami of the spinal nerves, respectively, whereas the terms “abaxial musculature” and “primaxial musculature” reflect embryonic criteria that are used to distinguish domains relative to embryonic patterning. The “primaxial” domain comprises somitic cells that develop within somite-derived connective tissue, and the “abaxial” domain includes muscle and bone that originates from somites but then mixes with, and develops within, lateral plate-derived connective tissue. Developmental studies carried out in recent years have shown there are important differences in the expression patterns associated with morphogenesis of the forelimb and of the hindlimb and between proximal and distal regions within each limb. For example, Hox9 paralogs are active in the arm, but not in the thigh (e.g., Young and Hallgrimsson 2005) and studies have also shown that the formation of the muscles of the pectoral girdle occurs through mechanisms that are markedly different from those leading to the formation of the muscles of the arm, forearm, and hand that arise through the classic and well-studied migration from the somites to the limb bud. The superficial pectoral girdle muscles develop by an “In-Out” mechanism whereby myogenic cells migrate from the somites into the limb bud, followed by their extension from the proximal limb bud onto the thorax (Valasek et al. 2011 (NB: these superficial muscles correspond to the appendicular pectoral girdle muscles sensu the present work, which in modern humans include the pectoralis major and minor, infraspinatus, supraspinatus, deltoideus, teres minor and major, subscapularis, and latissimus dorsi). The deep pectoral girdle muscles are induced by the forelimb field (i.e., a localized domain of gene expression) that promotes myotomal extension (the migration of cells) directly from the somites (Valasek et al. 2011) (NB: these deep muscles correspond to the axial pectoral girdle muscles sensu the present work, which in modern humans include the serratus anterior, rhomboideus major, rhomboideus minor, levator scapulae, and subclavius).

According to Valasek et al. (2011) the appearance of the forelimb is followed by pectoral girdle development that attaches the forelimb to the axial skeleton. The developmental mechanisms involved in limb development are thus able to induce and
recruit axial structures (e.g., the medial scapular border in mammals and the scapular blade in birds, as well as the deep girdle muscles and possibly even the cleithrum and sternum) for the anchorage of the limb (Valasek et al. 2011). Another important difference between the proximal portions of the limb and the distal portions of the limb (e.g., autopod) is that in the former, tendons are induced but do not segregate to form specific tendons in the absence of muscles, while in the latter, muscles are only present at later ontogenetic stages and tendon formation is initiated and segregation into individual tendons occurs in the absence of muscles. However, these distal tendons require contact with a muscle, for they have been shown to degenerate in a muscle-less limb environment (Hasson 2011).

Our myological cladistic analyses of primates (Diogo and Wood 2011, 2012a) allowed us to directly test the “In-Out” / “Myotomal Extension” morphogenetic hypothesis elaborated by Valasek et al. (2011) (Diogo and Wood 2013). According to this hypothesis, one would expect that the superficial (appendicular) pectoral girdle muscles would accumulate more anatomical changes at their proximal origin (because they extend from distal to proximal) and that the deep (axial) pectoral girdle muscles would accumulate more anatomical changes at their distal insertion (because they extend from proximal to distal). Within all of the evolutionary changes (steps) listed in that cladistic analysis there are 19 changes (of bony attachments) for a total of eight deep (axial) pectoral muscles; an average of 2.38 character state changes per muscle. Of these 19 changes in the eight muscles, two concern changes in proximal attachments (i.e., 0.25 per muscle), and five concern changes in distal attachments (i.e., 0.62 per muscle). Thus, within these deep (axial) pectoral muscles, there is a higher rate of change in the distal than in the proximal attachments, thereby supporting the hypothesis of Valasek et al. (2011). Regarding the superficial (appendicular) pectoral muscles, there are 26 changes for a total of 12 muscles (i.e., 2.17 character state changes per muscle). Within these 26 changes in the 12 muscles four concern the proximal attachments (i.e., 0.33 per muscle), and eight concern the distal attachments (i.e., 0.67 per muscle). So, within these superficial (appendicular) pectoral muscles, there is also a higher rate of change in the distal attachments than in the proximal attachments. Thus this evidence seems to contradict the hypothesis of Valasek et al. (2011), but the changes in proximal attachments relate to ribs and vertebrae. There is often intrageneric variation in the attachments of muscles in specific ribs/vertebrae so they are more difficult to polarize and code than changes in the distal attachments. Thus, the real rates of change per muscle of the proximal attachments of both the deep and the superficial pectoral muscles are therefore likely to be greater than the rate cited, therefore it would be unwise to use these data to contradict Valasek et al.’s (2011) hypothesis.

However, because coding bias concerns the proximal attachments of both the deep and the superficial muscles of all taxa, we can compare the rate of change per muscle for these two types of muscles, which, as noted above, are 2.38 and 2.17 changes per muscle, respectively. These rates are similar to the rate of 1.95 for the hand muscles (72 changes for a total of 37 muscles), but they are substantially lower than the rate of 6.4 for the arm muscles (32 changes for a total of five muscles) and higher than the rate of 1.24 for the forearm muscles (26 changes for a total of 21 muscles). Thus, our
study of primate muscles does not support Weisbecker's (2011) suggestion that the structures of the distal limb, due to their later development and their being contingent on earlier-developing more proximal elements, are more morphologically variable than more proximally located ones.

To summarize this section, it can thus be said that by combining the results of phylogenetic and evolutionary studies of primates and other animals and developmental studies of key model organisms such as mice or chickens, we can now provide a much more comprehensive – although of course still incomplete – picture of the origin, development, and evolution of the muscles of modern humans.

The Notions of Purpose and Progress in Evolution and the Parallelism Between Ontogeny and Phylogeny

Bakewell et al. (2007, p.7492) stated that their molecular (whole genome) studies show that “in sharp contrast to common belief, there were more adaptive genetic changes during chimp evolution than during human evolution” and they claim that their analysis “suggests more unidentified phenotypic adaptations in chimps than in humans.” The results of our primate parsimony and Bayesian analyses using characters from the head, neck, pectoral, and forelimb muscles indicate that since the Pan/Homo split the clade Hominina has evolved faster than the clade Panina (about 2.3 times faster according to the lengths of the branches leading to modern humans (9) and to chimpanzees (4) in the parsimony tree obtained by Diogo and Wood 2011). In turn, since the split between Gorilla and the Hominini, gorillas have only accumulated two unambiguous muscular apomorphies, whereas there are eight \( (4 + 4) \) and 13 \( (4 + 9) \) unambiguous apomorphies leading to extant chimpanzees and to modern humans, respectively (Diogo and Wood 2011). In terms of their significance for our understanding of human evolution, our results could seem paradoxical. On the one hand, the cladistic analyses suggest there are more unambiguous evolutionary steps from the base of the tree to modern humans than to any other extant primate taxon included in Table 8.1. But, on the other hand, our comparative anatomical studies show that modern humans have fewer muscles than most other primates, including chimpanzees, and have many fewer muscles than do strepsirrhines and tarsiiforms, which are often seen as “anatomically plesiomorphic” primates (Table 8.1).

Such an apparent paradox is related to the fact that, as Gould noted in The Structure of Evolutionary Theory (2002), there is a general tendency to use “progressive trends” to tell evolutionary stories, particularly in paleontological publications, in which examples of stasis are often either unreported or underreported because stasis is interpreted as “no data.” The results of our study support Gould’s contention in the sense that there is no general trend to increase the number of muscles, or muscle bundles, at the nodes leading to hominoids and to modern humans. Within the context of our study and our myological comparisons of the taxa listed in Table 8.1, because each muscle is the result of parcellation, that is, of innovation through differentiation leading to a morphogenetic semi-independence of the muscle (sensu Vermeij 1973), the simplest and most objective way to measure complexity was...
to compare the number of muscles of each taxon. This is because: (1) the number of muscles is an objective measure (e.g., the numerous researchers studying human gross anatomy basically agree on the number of muscles in the human body); (2) by using this way of measuring complexity, we combined a macroevolutionary definition of complexity similar to that of Bonner (1988; the only difference being that Bonner referred to the number of different types of cells instead of to the number of muscles) with a developmental definition of complexity that includes the notions of parcellation (e.g., Wagner and Altenberg, 1996) and morphogenetic semi-independence (e.g., Vermeij 1973). That is, with respect to the muscles in the regions we have investigated, although modern humans accumulated more evolutionary transitions than the other primates included in the cladistic study, these evolutionary transitions did not result in more muscles, or more muscle components (Table 8.1 and Diogo and Wood 2011, 2012a). For example, although some of the nine modern human apomorphies acquired since the *Pan/Homo* split involved the differentiation of new muscles (rhomboideus major and rhomboideus minor, extensor pollicis brevis and flexor pollicis longus), others involved the loss of muscles (levator claviculae and dorsoepitrochlearesis) (Diogo and Wood 2011). As a result, more muscle changes were accumulated in our evolutionary history than in that of modern chimpanzees, but there are usually more head and neck and pectoral and upper limb muscles present in modern chimpanzees than in members of our own species (Table 8.1). In fact, with respect to the number of head, neck, pectoral, and forelimb muscles and muscle bundles, one could make the case that modern humans are relatively simplified mammals (Diogo and Wood 2011, 2012a, 2013).

The notion of progress and purpose of evolution was closely related to the rise of developmental theories such as Haeckel’s theory of recapitulation (e.g., Gould 1977). This theory was based on a “scalae naturae” view of nature in which white modern human males were seen as more complex and therefore placed at the top of the scale. This scheme had profound and unfortunate social and racial implications. Unfortunately, the notion of “scalae naturae” is still deeply embedded in many current textbooks and scientific papers (e.g., Diogo et al. 2015). As noted by Gould (1977), the theory of recapitulation is no longer accepted because the ontogeny of an animal does not recapitulate the *adult* stages of its ancestors. However, as also noted by Gould (1977), this does not mean that there is no parallel between ontogeny and phylogeny; in fact, such a parallel seems to occur often in animal ontogenies and our recent developmental studies of zebrafish, salamanders, and frogs support this view (Diogo et al. 2008a, 2008b; Ziermann and Diogo 2013, 2014; Diogo and Tanaka 2014; Diogo and Ziermann 2014).

As we now have detailed data about the ontogeny of the head and neck muscles of those taxa and about the phylogeny and evolution of these muscles within the vertebrates, it is possible to compare the order in which the muscles appear in ontogeny to the order in which the muscles evolved during phylogeny. Comparisons show that in the case of the zebrafish head muscles there is in general a parallel between ontogeny and phylogeny, but there are exceptions (e.g., the early ontogenetic appearance of muscles that evolved late in phylogeny and play a particularly important role in the feeding mechanisms not only of zebrafish adults but also of embryos (Diogo et al. 2008b)).
In the salamanders and frogs there is also a general parallelism between ontogeny and phylogeny, and our preliminary comparisons in modern humans also corroborate such a parallelism (Ziermann and Diogo 2013, 2014; Diogo and Tanaka 2014; Diogo and Ziermann 2014).

However, it is important to note that this does not mean that the commonly accepted view that during ontogeny the tendency is towards the differentiation (and not the dedifferentiation) of muscles is correct. That is, the order in which muscles appear in ontogeny is usually similar to the order in which they appear in phylogeny, but muscles are often also lost/reabsorbed later in ontogeny. For instance, in neotenic salamander species such as axolotls that lack a full metamorphosis, some muscles become indistinct during ontogeny (e.g., the pseudotemporalis profundus and the levator hyoideus become completely integrated in the pseudotemporalis superficialis and in the depressor mandibulae, respectively (Ziermann and Diogo 2013)). Our recent studies in modern humans have provided similar data about the loss of muscles during ontogeny (see below). Therefore, although the differentiation of muscles is more common during ontogeny than is the dedifferentiation, by absorption or by fusion, it is necessary to emphasize that dedifferentiation is much more common than previously assumed.

The Relationship between Trisomies, “Atavisms,” Evolutionary Reversions, and Developmental Constraints

The most parsimonious tree obtained from the analysis of the complete dataset compiled by us about primate head, neck, pectoral, and upper limb muscles had a total length of 301 steps, of which 100 (33%) were non-homoplasic (i.e., they were not independently acquired or reverted elsewhere in the tree) evolutionary transitions (Diogo and Wood 2011). Of the 220 steps that were unambiguously optimized in the tree, 28 (i.e., 13%) were reversions to a plesiomorphic state (Table 8.2). Taking into account the total number of steps (301) within the tree, the number of characters (166), and the number of muscles (129) represented by the data in the cladistic analysis, there are about 1.8 evolutionary transitions per character and about 2.3 evolutionary transitions per muscle studied. These numbers stress the importance of homoplasy and of evolutionary reversions in morphological evolution. As stressed by Wiens (2011), less attention has been given historically to evolutionary reversions than to the two other types of homoplasic events, parallelism and convergence (e.g., Diogo 2005). Wiens listed several examples of violations of Dollo’s Law (which states that once a complex structure is lost it is unlikely to be reacquired), including the loss of mandibular teeth in the ancestor of modern frogs >230 million years (MY) ago and their reappearance in the anuran genus Gastrotheca during the last 5–17 MY. In Diogo and Wood (2012b) we focused on the implications of our muscle studies for understanding the role played by reversions in primate and human evolutionary history and for developmental biology. We stressed that reversions played a substantial role in primate and human evolution because one in seven of the 220 evolutionary transitions unambiguously optimized in the most parsimonious tree obtained by
Table 8.2. List of the 28 evolutionary reversions obtained in Diogo and Wood’s (2011) cladistic analysis of the primate taxa listed in Table 8.1 (Anat. region, anatomical region; Ch. state ch., character state change; Rev., reversion). For more details, see text and Diogo and Wood (2012b).

<table>
<thead>
<tr>
<th>Description of reversion</th>
<th>Ch. state ch.</th>
<th>Anat. region</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Rev. of “Biceps brachii has no bicipital aponeurosis”</td>
<td>[105:1--&gt;0]</td>
<td>Arm</td>
</tr>
<tr>
<td>b) Rev. of “Digastricus anterior is not in contact with its counterpart for most of its length”</td>
<td>[3:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>c) Rev. of “Spinotrapezius is not a distinct muscle”</td>
<td>[43:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>d) Rev. of “Chondroglossus is present as a distinct bundle of the hyoglossus”</td>
<td>[58:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>e) Rev. of “Chondroglossus is present as a distinct bundle of the hyoglossus”</td>
<td>[58:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>f) Rev. of “Pterygoideus lateralis has well differentiated inferior and superior heads”</td>
<td>[9:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>g) Rev. of “Depressor anguli oris is a distinct muscle”</td>
<td>[39:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>h) Rev. of “Trapezius inserts onto the clavicle”</td>
<td>[45:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>i) Rev. of “Rhomboideus major and rhomboideus minor are not distinct muscles”</td>
<td>[69:1--&gt;0]</td>
<td>Pectoral</td>
</tr>
<tr>
<td>j) Rev. of “Opponens pollicis is a distinct muscle”</td>
<td>[143:1--&gt;0]</td>
<td>Hand</td>
</tr>
<tr>
<td>k) Rev. of “Digastricus anterior is not in contact with its counterpart for most of its length”</td>
<td>[3:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>l) Rev. of “Frontalis is a distinct muscle”</td>
<td>[32:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>m) Rev. of “Sphincter colli profundus is not a distinct muscle” (either the muscle was lost in anthropoids and then reappeared in the Cebidae+Aotidae clade and in Cercopithecus, or was lost in Pithecia and catarrhines and then reappeared in Cercopithecus)</td>
<td>[24:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>n) Rev. of “Digastricus anterior is not in contact with its counterpart for most of its length”</td>
<td>[3:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>o) Rev. of “Cricoarytenoideus posterior does not meet its counterpart at the dorsal midline” (either the derived condition was acquired in anthropoids and then reverted in Macaca, Hylobates, and Pongo, or it was acquired in platyrrhines, in hominins, and in cercopithecids and then reverted in Macaca)</td>
<td>[56:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>p) Rev. of “Geniohyoideus is fused to its counterpart in the midline”</td>
<td>[57:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>q) Rev. of “Temporals has a pars suprazygomatica” (either the derived condition was acquired in Euarchonta and then reverted in Cynocephalus and hominoids, or it was acquired in Tupaia and Primates then reverted in hominoids)</td>
<td>[8:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>r) Rev. of “Pterygopharyngeus is not a distinct muscle” (either the derived condition was acquired in Euarchonta and then reverted in Cynocephalus and Hylobates, or it was acquired in Tupaia and Primates and then reverted in Hylobates)</td>
<td>[53:1--&gt;0]</td>
<td>Head/Neck</td>
</tr>
<tr>
<td>s) Rev. of “Levator claviculae inserts onto a more medial portion of the clavicle” (derived condition considered to have probably arisen in catarrhines and then uniquely reverted in Hylobates, but see notes in text)</td>
<td>[76:1--&gt;0]</td>
<td>Pectoral</td>
</tr>
<tr>
<td>t) Rev. of “Latissimus dorsi and teres major are fused”</td>
<td>[89:1--&gt;0]</td>
<td>Pectoral</td>
</tr>
<tr>
<td>u) Rev. of “Pectoralis minor inserts onto the coracoid process”</td>
<td>[83:1--&gt;0]</td>
<td>Pectoral</td>
</tr>
</tbody>
</table>
Diogo and Wood (2011) are reversions to a plesiomorphic state (N=28) (Table 8.2). Of those 28 reversions, six played a direct role in our own evolution in the sense that they occurred at the nodes that led to the origin of modern humans, and nine of the 28 reversions violate Dollo’s law, with the average time between a structure’s loss and reacquisition being about 50 MY (Table 8.3).

Our studies provide evidence to support the hypothesis that the reacquisition in adults of anatomical structures that were missing for long periods of time is possible because the developmental pathways responsible were maintained in the members of that clade. An example of this concerns the presence/absence of the contrahentes digitorum muscles in adult hominids. Chimpanzees display a reversion of a synapomorphy of the Hominidae (great apes and modern humans; acquired at least 15.4 MY ago: Tables 8.1 and Table 8.2) in which adult individuals have two contrahentes digitorum (in adults of other hominid taxa there are usually none) other than the muscle adductor pollicis; one going to digit 4 and the other to digit 5. Studies of the development of hand muscles (e.g., Cihak 1972) have shown that karyotypically normal modern human embryos do have contrahentes going to various fingers, but the muscles are usually lost during later embryonic development (Figure 8.3). Moreover, other studies (e.g., Dunlap et al. 1986) have shown that in karyotypically abnormal modern humans, such as individuals with trisomies 13, 18, or 21, the contrahentes muscles often persist (as “atavisms”) until well after birth (Figure 8.3).

According to some authors, cases where complex structures are formed early in ontogeny just to become lost/indistinct in later developmental stages (the so called “hidden variation”) may allow organisms to have a great ontogenetic potential early in development, so that if faced with external perturbations
Table 8.3. Time frame over which lost traits were regained within the euarchontan clade according to the cladistic analysis of Diogo and Wood (2011) and using the estimate times provided by Fabre et al. (2009). For more details, see text and Diogo and Wood (2012b).

<table>
<thead>
<tr>
<th>Structure that was regained, violating Dollo’s law (letters shown before the description of each structure correspond to letters shown in Table 8.2)</th>
<th>Number of evolutionary steps according to the hypothesis that violates Dollo’s law (in bold) versus number of evolutionary steps that one would need to assume in order to not violate Dollo’s law (in non-bold, following the description of these steps)</th>
<th>Date when feature was lost (*)</th>
<th>Date when feature was regained (**)</th>
<th>Time passed between (*) and (**)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Bicipital aponeurosis (NB: in modern humans the bicipital aponeurosis helps to reinforces the cubital fossa and to protect the branchial artery and the median nerve running under neath)</td>
<td>2 vs 4 (loss in <em>Tupaia, Cynocephalus</em>, lorisiforms, and haplorrhines)</td>
<td>94.1 MY</td>
<td>63.2 MY</td>
<td>30.9 MY</td>
</tr>
<tr>
<td>c) Spinotrapezius (NB: the spinotrapezius is a separate muscle that corresponds to the descending part of the trapezius of modern humans, which mainly depresses the scapula)</td>
<td>2 vs 4 (loss in <em>Tupaia, Cynocephalus</em>, strepsirrhines, and anthropoids)</td>
<td>94.1 MY</td>
<td>23.2 MY</td>
<td>70.9 MY</td>
</tr>
<tr>
<td>i) Rhomboideus minor (NB: in modern humans the rhomboideus minor acts together with the rhomboideus major to adduct the scapula and keep the scapula pressed against the thoracic wall)</td>
<td>3 vs 10 (loss in <em>Tupaia, Cynocephalus</em>, tarsiers, <em>Pithecia, Aotus, Saimiri</em>, hylobatids, orangs, gorillas, and chimps: see text)</td>
<td>88.8 MY</td>
<td>3.6 MY</td>
<td>85.2 MY</td>
</tr>
<tr>
<td>m) Sphincter colli profundus (NB: the sphincter colli profundus is a thin facial muscle that lies deep to the platysma cervicale)</td>
<td>3 vs 4 (loss in <em>Pithecia, Colobus</em>, Papionini and hominoidea)</td>
<td>39.8 MY or 25.0 MY</td>
<td>7.9 MY</td>
<td>31.9 MY or 17.1 MY (mean = 24.5 MY)</td>
</tr>
<tr>
<td>r) Pterygopharyngeus (NB: the pterygopharyngeus might corresponds to the pterygopharyngeal part of the superior pharyngeal constrictor of modern humans, which connects the medial pterygoid plate and its hamulus to the median raphe and mainly acts together with the other parts of the muscle to constrict the pharynx)</td>
<td>3 vs 6 (loss in <em>Tupaia</em>, strepsirrhines, tarsiers, platyrrhines, cercopithecids, and hominoids)</td>
<td>94.1 MY or 82.2 MY</td>
<td>10.7 MY</td>
<td>83.4 MY or 71.5 MY (mean = 77.4MY)</td>
</tr>
<tr>
<td>Structure</td>
<td>Number of evolutionary steps according to the hypothesis that violates Dollo’s law (in bold)</td>
<td>versus number of evolutionary steps that one would need to assume in order to not violate Dollo’s law (in non-bold, following the description of these steps)</td>
<td>Date when feature was lost (*)</td>
<td>Date when feature was regained (**</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>--------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>v) Epitrochleoanconeus (NB: the epitrochleoanconeus mainly connects the medial epicondyle of the humerus to the olecranon process of the ulna, so it potentially helps to extend the forearm and/or stabilize the elbow joint)</td>
<td>2 vs 4 (loss in hylobatids, orangs, gorillas, and Hominina)</td>
<td>19.5 MY 3.0 MY 16.5 MY</td>
<td>94.1 MY 63.2 MY 30.9 MY</td>
<td></td>
</tr>
<tr>
<td>w) Contrahentes digitorum (NB: the contrahentes adduct the digits; see text)</td>
<td>2 vs 3 (loss in orangs, gorillas, and Hominina)</td>
<td>15.4 MY 3.0 MY 12.4 MY</td>
<td>94.1 MY or 82.2 MY 10.7 MY 83.4 MY or 71.5 MY (mean = 77.4 MY)</td>
<td></td>
</tr>
<tr>
<td>x) Intermetacarpales (NB: the intermetacarpales connect the metacarpals of adjacent digits; see text)</td>
<td>5 vs 7 (loss in <em>Tupaia, Cynocephalus</em>, platyrhines, hylobatids, orangs, gorillas, and Hominina)</td>
<td>94.1 MY or 19.5 MY 3.0 MY 91.1 MY or 16.5 MY (mean = 53.8 MY)</td>
<td>94.1 MY or 19.5 MY 3.0 MY 91.1 MY or 16.5 MY (mean = 53.8 MY)</td>
<td></td>
</tr>
<tr>
<td>z) Rhomboideus minor (NB: in modern humans the rhomboideus minor acts together with the rhomboideus major to adduct the scapula and keep the scapula pressed against the thoracic wall)</td>
<td>3 vs 10 (loss in <em>Cynocephalus</em>, strepsirrhines, tarsiers, <em>Pithecia, Aotus, Saimiri</em>, hylobatids, orangs, gorillas, and chimps; see text)</td>
<td>88.8 MY 2.4 MY 86.4 MY</td>
<td>88.8 MY 2.4 MY 86.4 MY</td>
<td></td>
</tr>
</tbody>
</table>

**Total mean:** 50.9 MY
(e.g., climate change, habitat occupied by new species, etc.) evolution can use that potential (adaptive plasticity) (e.g., West-Eberhard 2003). However, authors such as Gould (1977) and Alberch (1989) have suggested that the occurrence of examples such as those cited above argue in favor of a “constrained” rather than an “adaptationist” view of evolution. This is in line with the view defended by the authors of more recent studies such as Galis and Metz (2007, pp.415–416), who stated that “without denying the evolutionary importance of phenotypic plasticity and genetic assimilation, we think that for the generation of macro-evolutionary

Figure 8.3. (A) Ontogeny of the contrahentes digitorum in the hand of karyotypically normal human embryos showing how the contrahentes to digits other than digit 1 are usually lost (reabsorbed) early in development (modified from Cihak 1972). Part of the interossei primordia (i.e., the flexores breves profundi layer) are shown between the metacarpals. r, u, p: radial, proximal, and ulnar parts of contrahentes layer; nu: ulnar nerve; ad: adductor pollicis; cpl: contrahens plate; I–V: metacarpals I–V; C-R: crown-rump length of the embryos. (B) Deep left-hand musculature of a trisomy 18 neonate (100 days old, female) showing the presence of contrahentes to digits 2 and 5 (the more superficial muscles, as well as the adductor pollicis, are not shown; modified from Dunlap et al. 1986). a: opponens pollicis; b: “interosseous palmaris of Henle”; c: interosseous dorsalis 1; d: contrahens to digit 2; e: interosseous palmaris 1; f: contrahens fascia/medial raphe; g: deep branch of ulnar nerve; h: contrahens to digit 5.
novelties the evidence for the impact of hidden variation is limited.” We are inclined to agree that hidden variation may have a limited role in the generation of evolutionary novelties. However, as explained above, hidden variation may have a more important role in the reappearance of some traits associated with these novelties, as in anatomical reversions that violate Dollo’s law.

As explained above, in Ontogeny and Phylogeny Gould (1977) argues that although Haeckel’s recapitulation hypothesis that the ontogeny of one organism recapitulates the adult stages of its ancestors (i.e., recapitulation) has been refuted, researchers often use it as a “straw man” to deny that there is often a parallel between ontogeny and phylogeny. According to Gould, such a parallel exists and it is probably driven more by phylogenetic/ontogenetic constraints than by adaptive plasticity, and studies of model organisms such as zebrafish or axolotls support this view (see above). The examples listed above about primate and modern human muscles, such as those involving the contrahentes and the intermetacarpales, also support Gould’s arguments in the sense that in both cases there is a parallel between ontogeny and phylogeny. That is, in “normal” modern human ontogeny the muscles are evident and then became lost or indistinct later in ontogeny; during the recent evolutionary history of modern humans the muscles were plesiomorphically present and then became lost. This is not recapitulation in the Haeckelian sense, for the contrahentes digitorum and the intermetacarpales of karyotypically “normal” modern human embryos do not correspond to the muscles of adult primates such as chimpanzees and of other primate/mammalian adults, but instead to the muscles of the embryos of the latter taxa. That is, the developmental pathways that result in the presence of these muscles in the adults of the latter taxa have not been completely lost in modern humans, even after several million years. This is probably because these pathways are related to those involved in the development of other structures that are present and functional in modern human adults (Diogo and Wood 2012b). Regarding the occurrence of the evolutionary reversions that resulted in the presence of the contrahentes and of distinct intermetacarpales in extant chimpanzees, this is probably related to the occurrence of heterochronic, and specifically paedomorphic, events in the lineage leading to the genus Pan (Diogo and Wood 2012b). In fact, Cihak (1972) has shown that the intermetacarpales are also present as distinct muscles in early embryos of karyotypically normal modern humans, before they fuse with some flexor breves profundi muscles to form the muscles intersossei dorsales. It is intuitively unlikely that the persistence of contrahentes in the later ontogenetic stages of karyotypically abnormal modern humans, such as individuals with trisomies 21, and particularly 13 and 18 (which usually die before or soon after birth), is the result of adaptive evolution and natural selection. What seems to be clear is that the presence of distinct contrahentes digitorum and intermetacarpales in adult chimpanzees is likely due to a prolonged or delayed development of the hand musculature of these apes, so in this respect extant chimpanzees are seemingly more neotenic than modern humans (Diogo and Wood 2012b). This is in line with recent studies that have pointed out that, although in the literature it is often stated that modern humans are in general more neotenic than other primates,
both paedomorphic and peramorphic processes have likely been involved in the 
mosaic evolution of modern humans and of other hominoids (see Bufill et al. 
2011 and references therein).

In order to investigate the developmental mechanisms related to the atypical 
development and abnormal phenotype of the striated muscles of modern human 
trisomic individuals, we are investigating the cadavers of fetal, neonatal, and adult 
modern humans with trisomies, as well as the cadavers of mouse models for Down 
Syndrome (DS) (e.g., Ts65Dn) (Diogo and Wood 2012b). The main hypothesis we 
want to test is that the disappearance of muscles such as the contrahentes and plato-
tysma cervicale during early developmental stages of karyotypically normal 
humans is related to apoptosis, and thus that the frequent persistence of these 
muscles until later ontogenetic stages in individuals with trisomies 13, 18, and 21 is 
associated with decreased muscle apoptosis. It has been suggested that modern 
human individuals with DS show an increase of apoptosis in neurons, granulo-
cytes, and lymphocytes (e.g., Elsayed and Elsayed 2009). If our studies support the 
hypothesis that these individuals have decreased apoptosis, to the point of having 
additional muscles in later ontogenetic stages, this would suggest a more nuanced 
story with respect to apoptosis (i.e., a mosaic scenario where there is more apo-
ptosis in some tissues and less in others). Moreover, by implying there is possibly a 
mismatch between the nervous (e.g., more apoptosis of cells of neurons) and 
muscular (i.e., less apoptosis and presence of extra muscles) systems, our hypo-
thesis might also shed light on the etiology of the hypotonia (low muscle tone) that 
is present in almost all babies with DS.

From a developmental genetic perspective, it is now known that members of a 
small family of proteins, termed MCIP1 and MCIP2 (myocyte-enriched calcineurin 
interacting protein), are most abundantly expressed in striated and cardiac muscles 
and that such proteins form a physical complex with calcineurin A; MCIP1 is encoded 
by DSCR1 (e.g., Gotlieb 2009). Expression of the MCIP family of proteins is upreg-
ulated during muscle differentiation, and its forced overexpression inhibits calcineu-
rin signaling leading to a decrease of muscle apoptosis. When apoptosis is abnormally 
reduced in trisomic mice embryos, excess populations of myocytes can form in the 
atroventricular region, where they may interfere with the normal migration of cells 
during cardiac development, leading to the occurrence of valvular abnormalities and 
atroventricular or ventricular septal defects similar to the congenital heart defects 
typical of modern humans with DS (Gotlieb, 2009).

**Tempo and Mode of Primate and Human Evolution, Modularity, 
and Ontogenetic Constraints**

Recent studies (e.g., Chatterjee et al. 2009; Cooper and Purvis 2009; Perelman et al. 
2011) suggest that rates of both morphological and molecular evolution vary among 
taxa. Differences in molecular rates are consistent with the concept of local molec-
ular clocks. According to Tetushkin (2003, p.729), primates “provide the most 
interesting and striking example of such heterogeneity in the tempo of molecular
evolution.” However, most recent studies dealing with evolutionary rates within mammals and primates are based on molecular evidence, and the few non-molecular studies do not focus on detailed morphology but on global features of the phenotype such as body size (Diogo et al. 2013d). Recently, we calculated the rates of muscle evolutionary change within the primate clades generated from our myology-based cladistic analyses (Diogo et al. 2013d) and compared them with the molecular rates obtained by other authors, including the rates of molecular nucleotide substitution reported by Perelman et al. (2011). We addressed the following questions: (A) Are the rates of muscle evolution the same or different across different primate taxa and across different geological time periods?; (B) Are the muscle rates more in agreement with the gradualist model, with the punctuated equilibrium model, or with other models of evolutionary rate?; and (C) Are the muscle rates in general similar to the molecular rates provided in recent papers, or is there a mismatch between morphological and molecular rates as predicted by the neutral evolution model of Kimura (1968)?

Surprisingly, we found several examples where the muscle rates of evolution in various lineages of each of the major primate clades are strikingly similar. For instance, the rate of muscle evolution at the node leading to the clade including the platyrrhine families Cebidae plus Aotidae (0.32) is the same as that at the node leading to Aotus (0.32), a single aotid genus, and is similar to that at the node leading to the whole Platyrhini clade (0.37). Moreover, the rate at the node leading to the Cercopithecidae (0.38) is the same as that at the node leading to the cercopithecid Colobus (0.38) and at the node leading to Cercopithecus (0.38). As these are the only rates that are similar across the whole primate tree obtained in our cladistic analysis (Diogo and Wood 2011), and as this happens inside two different large clades (New and Old World monkeys), it seems that for some reason the number of morphological evolutionary changes accumulated per period of time in at least some nodes within a clade is essentially constant. This would be the expectation for molecular evolutionary changes according to the neutral model of evolution, but this has not been reported previously for any type of morphological evolutionary changes, at least within the order Primates. Moreover, the muscle rates at the node leading to strepsirrhines (0.29) and then at the subsequent nodes leading to the lorisiforms (0.22) and to the lemuriforms (0.24) are also similar, particularly when one compares the differences with the range of different rates within all the primate nodes analyzed by us (0.00–2.72). The same can be said about the rates at the nodes leading to the Hominidae (1.47), Homininae (1.50), and Hominini (1.53). Thus these results lend support to the proposal by authors such as Gould (2002) that “internal” (e.g., ontogenetic) constraints play an important role in evolution. That is, in the last 25 MY, despite there having been major climate and environmental changes in Africa and Asia, the rates of muscle changes accumulated during that period at the nodes leading to the Cercopithecidae and then to Colobus, and also to Cercopithecus, are the same. Interestingly, these similarities in overall rates do not necessarily correspond to similarities in the rates for the head and neck and pectoral and forelimb regions. At the node leading to the Cercopithecidae the rate for the head
and neck changes is 0.19, at the node leading to *Colobus* it is 0.00, and at the node leading to *Cercopithecus* it is 0.38: the respective rates for the pectoral and forelimb region are 0.19, 0.38, and 0.00.

From the point of view of the authors that support the paradigm of “internal constraints,” the analysis of these partial rates would be viewed as evidence that ontogenetic constraints are so strong and interconnected that the potential for overall change accumulated in the different regions of the body is limited. This is in line with the results of recent studies showing that in early organogenesis, and particularly during the so-called “phylotypic stage,” there is substantial interactivity among different body modules and thus there is low effective modularity (e.g., Galis and Metz 2007). It has also been argued that from a developmental perspective, if extensive somatic investment is made in one structure of one body module, this could limit investment dedicated to the formation of another structure, not only from that module but also from other body modules (e.g., Galis and Metz 2007). It is also possible that constructional trade-offs constrain investment in whole phenotypes because the structural space in organisms is limiting (e.g., Hulsey and Hollingsworth 2011). However, our study also provides examples of a shift towards a faster rate of muscle evolution that is then followed by a slow-down in the rate of muscle evolution (i.e., a punctuated equilibrium mode). For instance, the overall (head, neck, pectoral, and forelimb) muscle rate leading to the Cercopithecidae is 0.75, then that leading to the Papionini is 2.56, and that leading to *Papio* is 0.26, that is, 10 times smaller than that leading to Papionini (for more details see Diogo et al. 2013d).

With respect to the third question raised above, there are several examples of substantial differences between muscle and molecular evolutionary rates at the same primate nodes, as would be predicted by the neutral model of evolution. But at other places on the tree the muscle evolutionary rates obtained in our study are similar to the published rates of molecular evolution.

In summary, our study suggests that the tempo and mode of primate and human evolution is complex, and provides examples of different modes of evolution within the primate clade. It suggests that at the level of major clades, simplistic dichotomies such as “gradual versus punctuated” and “neutral versus non-neutral” (see review of Gould 2002) do not apply. Also, contrary to the proposal that there is a “general molecular slow-down” in hominoids (e.g., Goodman et al. 1985; Steiper et al. 2004) the muscle evolutionary rates at the nodes leading to, or within, the hominoids are among the highest within the primate clade.

The relationship between Modern Human Anomalies/Variations, Digit Loss/Gain, Muscle Changes and Homeotic Transformations

Limbs with digits first appeared in aquatic taxa with more than five digits, but the transitions to terrestrial locomotion and to pentadactyly, and then to digit reduction in some clades, are particularly poorly understood (e.g., Pierce et al. 2013). Information obtained from non-pentadactyl limbs is crucial to clarify how the
functional and spatial associations between limb bones and muscles change during evolution and in the common limb birth defects found in modern humans and other species. However, anatomical and developmental studies usually focus on pentadactyl autopodia, and those dealing with non-pentadactyly tend to focus on hard tissues (e.g., Shubin and Alberch 1986; Young et al. 2009). The scarcity of information about soft tissues is paradoxical because non-pentadactyly and the specific spatial associations between limb bones and muscles are topics that have long attracted researchers’ attention (e.g., Owen 1849), and particularly because non-pentadactyly is the most common human birth defect (Castilla et al. 1996). The study of non-pentadactyly is also of interest because it allows researchers to discuss broader evolutionary themes such as the occurrence of evolutionary trends, the frequency of anatomical convergence, and the existence of evolutionary reversals that violate Dollo’s law (e.g., Diogo and Wood 2013).

Moreover, non-pentadactyly is often associated with one of the most important current topics in evolutionary developmental biology: homeotic transformations (i.e., the replacement of a body part by one that normally forms in another region of the body). For instance, in pre-axial polydactyly, one of the most common congenital anomalies of the human hand, duplication of the thumb leads to the two most radial digits having a homeotic identity of digit 1 (Castilla et al. 1996). Homeotic transformations have also played an important role in the evolution of normal phenotypes. For example, it is now commonly accepted that the digits of the adult bird wing derive from the second, third, and fourth developmental anlages (embryonic condensations), but that homeotically and morphologically these digits correspond to digits 1, 2, and 3 of other tetrapods; a similar homeotic transformation seemingly also occurred in the hand of the three-toed Italian skink Chalcides chalcides (Young et al. 2009).

In order to study the spatial associations between limb bones and muscles, we have compared the adult morphology, development, and regeneration of these structures in several wildtype and non-wildtype tetrapods (e.g., transgenic GFP – green fluorescent protein – amphibians; Diogo and Tanaka 2012, 2014; Diogo et al. 2013c; Diogo and Ziermann 2014). We also have investigated how human birth defects involving non-pentadactyl limbs influence muscle attachments and analyzed whether the anatomical patterns seen in those birth defects follow the patterns seen in wildtype non-human tetrapods with non-pentadactyl limbs, in order to infer whether the study of birth defects could reciprocally illuminate those patterns under extreme, unusual conditions. Interestingly, in both the non-pentadactyl limbs of wildtype taxa such as frogs, salamanders, crocodilians, and chickens and in the humans with birth defects, we found a surprisingly consistent pattern. This suggests that the identity and attachments of the fore and hindlimb muscles are mainly related to the physical (topological) position, and not to the number of the anlage or even to the homeotic identity of the digits to which the muscles are attached (Figure 8.4, color plate).

It is important to clarify what is meant here by “topological position,” “number of anlage,” and “homeotic identity” of the digits. Topological position refers to the adult relationship with other structures, and not to the position of the developmental anlages. For instance, the topological position of the adult avian digit derived from the second developmental anlage is digit 1, because this is the most radial digit in the
adult; in this case the topological position (digit 1) and homeotic identity (digit 1) are the same and are different from the developmental anlage from which the digit develops (the second anlage: e.g., Young et al. 2009). Accordingly, and as predicted by our hypothesis, chickens do usually have an abductor pollicis brevis that inserts onto this most radial digit; in pentadactyl taxa this muscle is always inserted onto digit 1, which derives from the first, and not the second, anlage (Diogo and Abdala 2010).
This contrasts with the case of salamanders with four hand digits (e.g., axolotls), where digit 5 is missing and digit 4 develops from the anlage of digit 4 and has a homeotic identity of digit 4, but its topological position is similar to that of digit 5 in pentadactyl tetrapods because this is the most ulnar digit. The axolotl case illustrates and supports our hypothesis because although the homeotic identity of this most ulnar digit is that of digit 4, the digit is associated with muscles that normally go to digit 5 in pentadactyl tetrapods (e.g., abductor digiti minimi; Diogo and Tanaka 2012).

As explained above, our theory is also supported by our dissections of, and a review of the literature about, modern humans with birth defects leading to non-pentadactyly. This is illustrated, for instance, by the trisomy-18 newborn illustrated in Figure 8.4, which had six digits (with two thumbs) in one hand and four digits in the other hand (with no thumb). As predicted by our theory, a hand with no thumb has all the muscles that normally go to the thumb, but these muscles go to digit 2, which is the most radial digit (Figure 8.4, color plate). As also predicted, in a hand with two thumbs (preaxial polydactyly, which is one of the most common congenital anomalies of the modern human hand (Castilla et al. 1996)), the duplication of the thumb was not accompanied by a duplication of the muscles that normally go to the thumb. Instead, the muscles that normally go to the radial side of the thumb (e.g., abductor pollicis brevis) were attached onto the radial side of the most radial thumb, while the muscles that normally go to the ulnar side of the thumb (e.g., adductor pollicis) were attached to the ulnar side of the most ulnar thumb. That is, the muscles are not simply duplicated like the thumb bones. Instead they go to each respective thumb according to the adult topological position of each of the duplicated digits; similar cases were also described by Light (1992).

There are, however, exceptions to our theory. For instance, Heiss (1957) described a case in which a modern human individual had two pentadactyl hands that had no thumbs, and in which, contrary to the cases referred to above, there were no major topological changes of the muscles (e.g., the attachment of normal thumb muscles to the most radial digit of that human subject). Instead, in both hands the normal thumb muscles were missing. In general, this configuration seems to be characteristic of the rare modern human disorder named “tri-phalangeal thumb,” which is a malformation of digit 1 including a perfect homeotic transformation of the thumb into an index finger and in which the muscles normally associated with the thumb are absent (e.g., abductor opponens/adductor pollicis; see, e.g., Young and Wagner 2011). Therefore, the analysis of these cases seems to indicate that although the identity and attachments of the limb muscles are mainly related to the physical (topological) position of the digits to which they attach, and not to the number of the anlage or even the homeotic identity of these digits, this does not represent a strict rule. That is, the evolutionary/developmental factors that lead to this common anatomical pattern can be sometimes changed in a way that allows the occurrence of other patterns and thus of more evolutionary possibilities.

Importantly, the examples provided in the above paragraph and the generally predictable muscle changes associated with changes in the number/topological position of digits in both normal and abnormal individuals of different tetrapod taxa, support Alberch's (1989) “logic of monsters.” According to this theory, which was also supported by a
detailed skeletal study of digit reduction in amphibians (Alberch and Gale 1985), there is a parallel between the variation in normal and abnormal individuals of a certain taxon (e.g., modern humans) and the diversity observed in normal individuals of different taxa (e.g., species of lizards or amphibians). This parallel is achieved through regulation of a conserved developmental program (e.g., a set of genetic and/or epigenetic interactions) such that the structure of these internal interactions constrains the realm of possible variation upon which selection can operate. In theory, such a program can break down in the evolution of some clades, but within most clades this would lead to death of the embryos (Alberch 1989).

The Similarity of the Hind and Forelimb Structures of Modern Humans, Serial Homology and Homoplasy, and Developmental Biology

The idea that the structures of the forelimb (FL) and hindlimb (HL) are “serial homologues” was first proposed by authors such as Vicq d’Azyr (1774), Oken (1843), and Owen (1849). However, a careful examination of these and other original works of these authors reveals that their FL and HL comparisons were almost exclusively based on bones, and not on soft tissues such as muscles, nerves, and blood vessels. Moreover, in most cases the use of the term “limb serial homology” clearly referred to what is currently viewed as parallelism, that is, homoplasy and not true homology. For instance, in On the Nature of Limbs (Owen 1849) the examples of striking similarity between the FL and HL refer mainly to tetrapods with highly derived limbs (e.g., bats, horses, and plesiosaurs) and Owen uses the term parallelism more often than “serial homology.” When he discusses phylogenetically plesiomorphic taxa (e.g., chondrichthyan) Owen states that those taxa “confuse” the notion of “archetype” and “serial homology,” thus he was in fact referring to homoplasy and not to the concept of serial homology as we understand it today (Diogo et al. 2013c).

However, authors continued to cite these and other similar classical studies to “show” that the structures of the FL and HL, as well as of the fish pelvic and pectoral fins (PEL and PEC), were serial homologues. Instead of questioning this idea, authors thus preferred to focus on other details about the origin of the allegedly homologous paired appendages. For example, Gegenbaur proposed that fins evolved from the gill arches of the early limbless vertebrates; more recent studies suggest that fins evolved instead from continuous stripes of competency for appendage formation located ventrally and laterally along the embryonic flank (Shubin et al. 1997; Don et al. 2013). A continuation of this theory proposed that the paired appendages evolved with a shift in the zone of competency to the lateral plate mesoderm in conjunction with the establishment of the lateral somitic frontier, thus allowing for the formation of limb/fin buds with internal supporting skeletons (Don et al. 2013). The idea that paired appendages are serial homologues is generally associated with the notion that these appendages were originally similar to each other, and that there was a subsequent functional/anatomical divergence between them (Figure 8.5A, color plate). For instance, Don et al. (2013) explain that the ancestral Tbx4/5 cluster of vertebrates probably underwent a duplication event
Anatomical difference between pelvic and pectoral appendages

After the supposed duplication leading to the presence of pectoral and pelvic appendages, there was supposedly a functional/anatomical divergence of these appendages, which would for instance be more similar in phylogenetically more plesiomorphic quadruped tetrapods such as lizards than in derived biped tetrapods such as modern humans.

Figure 8.5. (A) Simplified scheme illustrating the “serial homology followed by functional/anatomical divergence” hypothesis often shown in textbooks and followed in more technical papers, particularly within the fields of developmental biology and evo-devo. The picture of the hypothetical fish is modified from Shubin et al.’s (1997) scheme showing the origin and evolution of paired appendages. According to that scheme, establishment of serially homologous appendages was proposed to result from gene cooption during the evolution of Paleozoic vertebrates. That is, Hox genes were initially involved in specifying regional identities along the primary body axis, particularly in caudal segments, and then during the origin of jawed fish there was a cooption of similar nested patterns of expression of HoxD genes in the development of both sets of paired appendages (numbers shown within the fish body). According to this scheme the cooption may have happened in both appendages simultaneously, or Hox expression could have been initially present in a pelvic appendage and been coopted in the development of an existing pectoral outgrowth (arrow below fish body; the pictures of the other taxa are modified from Diogo and Abdala 2010 and references therein). (B) The evolutionary history of the pelvic and pectoral appendages was more complex than the “serial homology followed by functional/anatomical divergence” hypothesis suggests. This is because it was more likely the result of a complex interplay between ontogenetic, functional, topological, and phylogenetic constraints leading to cases of anatomical divergence followed by cases of anatomical convergence (“similarity bottlenecks”). This is exemplified in this simplified scheme of the evolutionary muscle transitions leading to modern humans. Figure reused with permission from Diogo and Ziermann (2015).
and that now Tb×4 is related to the HL and Tb×5 with the FL, and in their Figure 3 they state that “pectoral fins evolved first and then duplicated to form pelvic fins.” This illustrates the confusion that is often seen in evo-devo studies about (A) a duplication of the Tb×4/5 cluster and subsequent cooption for the genetic pathways associated with the ontogeny of the different paired appendages, and (B) the morphological duplication of the appendages themselves and of their individual structures.

Figure 8.5. (Continued).
(i.e., muscles and bones). As we will argue below, A is true but B is not. Because a gene operates to facilitate an outgrowth that gives rise to different limbs in the same animal it does not mean that these limbs are serial homologues, but simply that genes and gene cascades/networks have been recruited homoplastically as organizers of limb development (e.g., Willmer 2003).

In our opinion, the failure to recognize that this idea of PEC and PEL and FL and HL serial homology is unfounded is due to four factors. The first is the recurrent citation of older authors such as Vicq d’Azyr (1774), Oken (1843), and Owen (1849) without a detailed, critical analysis of their arguments. The second is the almost exclusive focus on bones. The third factor, which is related to those above and to the decline of evolutionary vertebrate morphology in the second half of the 20th century (see Diogo and Abdala 2010 and Diogo et al. 2013c), is the scarcity of evidence from detailed and unbiased comparisons of both the hard and the soft tissues of the limbs across the major vertebrate clades. The fourth is the lack of a broader integration of the data obtained in such comparisons and in the fields of contemporary developmental biology, genetics, paleontology, functional morphology, and evolutionary biology, with the information provided in the older, classical texts.

As with the re-examination of the classic texts on the “serial homology” of FL and HL structures, detailed analysis of recent developmental, genetic, paleontological, and functional studies also raises serious questions about the serial homology concept. For example, a recent paper describing phylogenetically more plesiomorphic fossil fish with both pectoral and pelvic appendages (an antiarch placoderm) shows that these appendages are markedly different anatomically (Figure 8.5B, color plate; Zhu et al. 2012). The idea that these appendages were originally different and then later became more similar in fish such as osteichthyans has been defended by a few authors (Coates and Cohn 1998). Recent functional studies have also contradicted the old idea that the tetrapod FL and HL evolved mainly in a terrestrial environment and originally had similar functions (Pierce et al. 2012). Furthermore, recent developmental and genetic studies demonstrated a surprisingly distinct lag between the developmental modes of pectoral and pelvic appendage musculature not only in fish but also in tetrapods (e.g., Cole et al. 2011; Don et al. 2013). A review of the most detailed, and unfortunately often neglected, older developmental studies of the hard and soft tissues of the FL and HL of modern humans and other tetrapods also revealed major differences between FL and HL ontogeny (Bardeen 1906; Lewis 1910; Cihak 1972). A recent publication (Diogo et al. 2013c) has reviewed these and other lines of evidence that contradict the arguments used to support the FL-HL serial homology hypothesis. The final refutation of the “paired appendages serial homology followed by functional/anatomical divergence” hypothesis (Figure 8.5A, color plate) comes from the integrative analysis of lines of evidence obtained from various biological fields together with the results of a detailed examination and comparison of the soft tissues of the paired appendages of representatives of all major extant gnathostome clades. This is because the PEC and PEL of extant plesiomorphic gnathostome fish have basically undifferentiated adductor and abductor muscles masses (Figure 8.5B, color plate). All of the numerous and in many cases strikingly similar muscles (as discussed below), as well as various bones (e.g., Don et al. 2013) of the
tetrapod FL and HL were therefore almost certainly acquired independently during the evolutionary transitions between early gnathostomes and tetrapods. That is, within a historical (phylogenetic: Wagner 1994) definition of homology these FL and HL structures cannot be considered serial homologues. One could argue that they may be homologues under the morphological or developmental definitions of homology (Wagner 1994), but this view is contradicted by the overall analysis of the evolution and homologies of the soft tissues, particularly the muscles, of the gnathostome paired appendages.

In fact, a hypothesis of morphological or developmental serial homology of these appendages implies that these appendages were originally similar and then diverged anatomically/functionally. But there is no good evidence that this is the case (Figure 8.5B, color plate). As noted above, in the more plesiomorphic fish found so far with PEC and PEL the hard tissues of these appendages are anatomically very different, and both the hard and soft tissues of the proximal region of the pectoral and pelvic appendages (particularly the girdles) remained markedly different throughout all gnathostome clades (Diogo et al. 2013c). For example, in all tetrapod clades listed in Figure 8.5B, including anatomically plesiomorphic taxa such as urodeles, there is no pelvic-thigh muscle that corresponds topologically to a pectoral-arm muscle. This may be due to phylogenetic constraints (e.g., the pelvic and pectoral girdles of fish and tetrapods were quite different anatomically). However, the more derived distal regions of the tetrapod FL and HL, particularly the autopodia (hand/foot), have a bony skeleton and a developmental plan that is quite different from those of the fish PEC and PEL (NB: even if tetrapod digits are considered to be derived from fish distal rays, as proposed for instance by Johanson et al. 2007, it is generally accepted that some tetrapod wrist/ankle bones are neomorphic structures: e.g., Don et al. 2013). That is, this case involves a major “evolutionary novelty” and thus less phylogenetic constraints, and the developmental constraints/factors resulting from further (derived) cooption of similar genes in the ontogeny of the FL and HL thus lead to a more marked similarity (a “similarity bottleneck”: Figure 8.5B, color plate) between the distal regions of these limbs in plesiomorphic tetrapods. For example, in salamanders such as axolotls 19 muscles/muscle groups of the leg-foot clearly seem to “correspond” topologically to forearm-hand structures (Figure 8.5B, color plate). It should be emphasized that the developmental changes associated with the “transition fin-limb bottleneck” refer to a phylogenetically derived cooption of a few similar genes (“genetic piracy” sensu Roth 1994). It is now accepted that the cooption of similar ancestral genes to independently form complex structures such as eyes in vertebrate and non-vertebrate animals (“deep homology”) is a case of evolutionary parallelism and thus a variety of homoplasy (Willmer 2003). It would therefore be very difficult to argue that the derived cooption of similar genes represents a true case of FL-HL serial homology under the developmental concept of homology.

Moreover, such ontogenetic factors/constraints are clearly not sufficient to explain the striking similarity between the leg-foot and forearm-hand muscles of (and thus, the other “similarity bottlenecks” leading to: Figure 8.5B, color plate) derived tetrapods such as horses or modern humans (Figure 8.6, color plate). The similarity bottlenecks shown in Figure 8.5B come from the empirical data obtained...
from our comparative studies and refer to cases in which there is a higher number of PEC muscles that are topologically similar to PEL muscles. For instance, in urodeles such as axolotls, and in modern humans, there are 19 muscles/muscle groups of the leg-foot that clearly seem to “correspond” topologically to forearm-hand structures. However, in anatomically more generalized quadrupedal mammals (e.g., rats) the number is 16 and in anatomically generalized reptiles such as lizards the number is only 14 (Figure 8.5B, color plate). As will be explained below, many of the human FL-HL muscles/muscle groups with “clear topological equivalents” were acquired independently during the evolutionary history of primates (Diogo and Wood 2012a; Diogo et al. 2013c). Such “similarity bottlenecks” have also led to various other tetrapod and even non-tetrapod derived clades (e.g., the PEL muscles of plesiomorphic teleosts were derived independently from, but are topologically very similar to, the PEC muscles of these fish: Winterbottom 1974). Apart from the influence of ontogenetic constraints, the “similarity bottlenecks” leading to derived fish and tetrapod clades (Figure 8.5B, color plate) are clearly also influenced by topological and functional constraints. For example, the only way to have a functional abductor hallucis or pollicis brevis (both muscles were homoplasically acquired during tetrapod evolution) is to have a muscle lying on the radial or tibial side and then having it insert onto the radial or tibial side of the first digit of the hand or foot (Figure 8.6, color plate).

A crucial point supporting the idea that ontogenetic constraints are not sufficient to explain the “similarity bottlenecks” leading to derived taxa such as modern humans.
(Figure 8.5B, color plate) is the fact that various leg-foot muscles that are strikingly similar topologically to forearm-hand muscles in derived taxa do not develop from similar anlagen. For example, the extensor pollicis longus and extensor hallucis longus of modern humans are remarkably similar topologically, but the former derives from the anlage of the short extensors of the hand, while the latter derives from the anlage of the long extensors of the leg (for more examples see Diogo et al. 2013c).

In summary, during the evolutionary history of the tetrapod FL and HL there are cases of evolutionary divergence leading to differences between the FL and HL musculature that are not seen in anatomically plesiomorphic tetrapods such as urodeles. There is also a substantial evolutionary parallelism/convergence leading to subsequent “similarity bottlenecks” between these limbs in derived taxa (Figure 8.5B, color plate). The strikingly similar FL and HL muscles seen for instance in groups such as modern humans are therefore the result of a complex interplay between ontogenetic, topological, functional, and even phylogenetic (Diogo et al. 2013c) constraints. A further critical point that shows the similarity of these muscles cannot be simply explained by a derived morphological/developmental integration of the FL and HL under a morphological or developmental serial homology concept (see above) is that several of these muscles, or their bundles, did not emerge at similar geological times/phylogenetic nodes. For example, the adductor hallucis and adductor pollicis of modern humans are similar because they have well-differentiated transverse and oblique heads. However, whereas the heads of the adductor hallucis are already well differentiated in phylogenetically plesiomorphic primates such as lemurs, those of the adductor pollicis only became well differentiated in the node leading to catarrhines (Old World monkeys + hominoids); for more examples see Diogo et al. (2013c).

We hope that the evidence and discussion above will at least make the readers aware of the serious problems faced by the fore-hindlimb serial homology hypothesis, and stimulate research on the puzzling and fascinating evolutionary history of the paired appendages using a new paradigm.

General Remarks and Future Directions

Muscle and other soft tissue evidence has been neglected in systematics and evolutionary and developmental biology. However, the few cladistic analyses based on soft tissues that have been published have shown that these tissues can be particularly useful for inferring phylogenetic relationships (e.g., Diogo and Wood 2012a). Moreover, the study of muscles also allows researchers to address evolutionary and developmental questions that are not tractable using other types of evidence. These include crucial questions about the evolution of the closest living relatives of modern humans and the evolution within our own clade. In the last few decades the emergence of evolutionary developmental biology has resulted in a resurgence of interest in comparative anatomy (e.g., Assis 2009). We suggest that the forthcoming decades will see a renaissance in the use of myology in evolutionary and developmental biology, including for taxa such as primates and modern humans.
Hopefully, by focusing on morphological and developmental evolution, this review will help with this renaissance by stimulating an interest in the study of muscles of vertebrates in general, and of primates and modern humans in particular. A line of future research that is particularly promising would be to marry the data obtained from comparative and developmental myological studies with paleontological and environmental data in order to better understand how, where, when, and even why changes to muscle morphology occurred during phylogeny.

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