INTERMUSCULAR RELATIONSHIP OF HUMAN MUSCLE FIBER TYPE PROPORTIONS: SLOW LEG MUSCLES PREDICT SLOW NECK MUSCLES

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ABSTRACT: *Introduction:* Our aim in this study was to examine whether the muscle fiber type proportions in different muscles from the same individual are interrelated. *Methods:* Samples were excised from five skeletal muscles in each of 12 human autopsy cases, and the fiber type proportions were determined by immunohistochemistry. We further examined the intermuscular relationship in fiber type proportion by reanalyzing three previously published data sets involving other muscles. *Results:* Subjects demonstrated a predominantly high or low proportion of type 1 fibers in all examined muscles, and the overall difference between individuals was statistically significant ($P < 0.001$). Accordingly, the type 1 fiber proportions in most muscles were positively correlated (median $r = 0.42$, range −0.03–0.80). Similar results were also obtained from the three reanalyzed data sets. *Conclusions:* We suggest the existence of an across-muscle phenotype with respect to fiber type proportions; some individuals display generally faster muscles and some individuals slower muscles when compared with others.

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In humans, about 40% of the total body weight is skeletal muscle. Individual variation in the use of skeletal muscles is the dominant cause of variation in total energy consumption. Variation in energy consumption is also directly or indirectly influenced by individual variation in the metabolic properties of the skeletal muscle tissue, such as fiber type composition. In humans, the limb and trunk skeletal muscles consist of different proportions of three main muscle fiber types, type 1, 2A, and 2X, classified on basis of the myosin heavy chain (MyHC) they express. Most human muscles also contain a variable number of hybrid fibers that express either both type 1 and 2A MyHC (type 1/2A) or both type 2A and 2X MyHC (type 2A/X). Studies of mono- and dizygotic twins in humans[1,2] and breeding studies of rodents,[3,4] horses,[5] and pigs[6] have shown that the proportions of fiber types in single muscles are dependent on heritable factors. Under normal physiological conditions in humans the type 1 fibers seem to be resistant to change and do not switch into type 2, even when exposed to long-term training[7–13] or a long-term reduction in physical activity.[8,13–17] In contrast, a switch between the type 2 fiber subsets (2A and 2X in humans) is induced by changes in physical activity.[8,11,13,14,17]

The fiber type proportions of a single muscle have been associated with outcomes of various physical performance tests[18,19] and are also linked to several cardiovascular risk factors in humans.[20,21] It has been demonstrated that a high proportion of type 1 fibers in the vastus lateralis muscle is associated with low blood pressure,[22] increased insulin sensitivity,[23] and other indicators of a low risk of cardiovascular disease.[21,24] Conversely, a low proportion of type 1 fibers in single muscles is associated with the presence of diabetes mellitus type 2,[25] peripheral artery disease,[26] coronary artery disease,[27] and chronic heart failure.[28] These relationships between the fiber type proportions of one single skeletal muscle alone and cardiovascular risk factors and human performance raise the question of whether there is a systematic relationship between the fiber type proportions of different muscles in the same individual. This hypothesis was proposed by Saltin et al. in a review from 1977,[29] but we have not found any studies that address this in a systematic fashion in humans. The main purpose of this study was to determine whether some individuals consistently display predominantly type 1 fibers or predominantly type 2 fibers in different muscles. In addition to presenting new empirical data, we have reanalyzed three previously published, independent data sets with respect to this hypothesis.[30–32]

METHODS

Approach to the Problem. To test the hypothesis that the distribution of fiber types in different skeletal muscles is interrelated at the individual level we completed an autopsy study of 12 subjects. Five muscles with presumably diverse patterns of activity were excised: the sternocleidomastoideus (SCM); splenius; scalenus medius; trapezius; and vastus lateralis. Fiber type composition was assessed by immunohistochemistry and muscle fiber cross-sectional area (CSA) was completed by tracing the cell borders. In addition to our data, we tested the

Abbreviations: CSA, cross-sectional area; CVD, cardiovascular disease; MyHC, myosin heavy chain; SCM, sternocleidomastoideus

Key words: human striated muscle, immunohistochemistry, intermuscular correlations, MyHC, skeletal muscle phenotype

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hypothesis by reanalyzing three different published data sets on human fiber type proportions in different muscles from the same individual.[30–32]

Our study was approved by the Regional Committee for Medical and Health Research Ethics.

Muscle Sampling. Muscle specimens were excised between 24 and 72 hours postmortem from 12 cases of sudden death [1 car accident, 1 accidental poisoning, 3 suicides (1 carbon monoxide poisoning and 2 drug overdoses), 6 coronary-related deaths, and 1 hemorrhage]. The cases (11 men and 1 woman) ranged from 18 to 65 years of age (mean ± SD: 45.3 ± 15.8 years). Inclusion of cases was based on pathologist evaluation and medical records. None had a history of bed rest or hospitalization in the final 24 hours prior to death. Cachectic or severely obese cases were excluded. We also excluded cases in which the medical record or autopsy revealed neurological, rheumatological, or endocrinological disorders; alcoholism or drug abuse; or other severe diseases, including malignancy. The general lifestyle or physical activity levels of the cases were not known. Samples were taken from one muscle in the thigh (vastus lateralis), one in the shoulder girdle (trapezius), and three in the neck (SCM, scalenus medius, and splenius muscle). To our knowledge, the scalenus medius and splenius muscle have not been studied previously for fiber type proportions in presumably normal subjects. From the knee extensor vastus lateralis muscle, samples were taken in the superficial portion, midway between trochanter major and the lateral epicondyle of the knee. Samples from the trapezius were collected from the lower descending portions of the muscle, and for the scalenus medius and SCM at their midpoints. The samples from the lateral portion of the splenius were excised at approximately the C4–C5 level. From the muscle tissue excised, smaller samples with lengths of approximately 2 cm and 0.5 cm in diameter were dissected free from fat and connective tissue, and superficial blood was removed. The samples were snap frozen in melting isopentane cooled with liquid nitrogen and stored at −80°C until further preparation.

Immunofluorescence and Microscopy. The muscle samples were oriented and mounted on metal disks using an embedding medium (Tissue-Tek OCT compound), and serial cross-sections of 10 μm were cut in a cryostat (HM 560M; Microm International), put on glass microscope slides, and air dried at room temperature. Muscle fiber types were visualized by immunofluorescence using a series of antibodies against different myosin heavy chains, including BA-D5 (type 1 MyHC), SC-71 (type 2A MyHC), BF-35 (all non-2X MyHC), which were donated by Stefano Schiaffino (University of Padova, Italy[33]), and 6H1 (type 2X MyHC), which was donated by Joseph Hoh (University of Sydney, Australia).[34] Anti-laminin (L-9393; Sigma) was used to stain the basement membrane. The specificity of the myosin antibodies in human muscles has been tested in previous studies using Western blots (BA-D5, SC-71, and BF-35 by Wu et al.[35] and 6H1 by Li et al.[36]). Primary antibodies were diluted with 1% bovine serum albumin in 1 × phosphate buffer saline to final concentrations of 1:2000 (BA-D5, SC-71, and BF-35), 1:700 (anti-laminin), and 1:3 (6H1). The cryosections were incubated with the primary antibodies using an overnight protocol at 4°C. The secondary antibodies used included goat anti-mouse IgM, fluorescein isothiocyanate (FITC)-conjugated (F9259; Sigma) against the 6H1 antibody and rabbit anti-mouse IgG, and FITC-conjugated (F9137; Sigma) against the other MyHC primary antibodies. Goat anti-rabbit IgG and tetramethyl-rhodamine isothiocyanate (TRITC)-conjugated (T6778; Sigma) antibodies were used against the anti-laminin antibody. All incubations of secondary antibodies were completed in a humid chamber at 37°C for 1 hour. The muscle cross-section samples were then placed in a microscope (BX50WI; Olympus) connected to an SIT camera (C2400-08; Hamamatsu), magnified using a 10× water immersion objective (UMPLFL10XW; Olympus), and photographed. The images were digitized by an image processer (Argus-20; Hamamatsu) and transferred to a MacIntosh G3 computer. Composite photomontages of the images were then assembled in Adobe Photoshop CS3.

Fiber Type Proportions. For determination of fiber type composition, two to four separate areas containing approximately 200–400 fibers, each with good cell integrity, were first chosen randomly in the laminin staining images. Each area contained fibers with intact cell borders and that appeared cross-sectionally cut. The fiber identities of these cells were then determined on the basis of the four MyHC staining patterns using the following criteria: cells that stained positively for BA-D5 and BF-35, but not SC-71 nor 6H1, were type 1 fibers; cells that stained positively for SC-71 and BF-35, but neither BA-D5 nor 6H1, were type 2A fibers; and cells that stained for 6H1, but not BF-35, BA-D5 nor SC-71, were classified as type 2X fibers. Any muscle cell that stained for BA-D5, SC-71, and BF-35 either strongly or weakly and did not stain for 6H1 was classified as a hybrid 1/2A fiber. Cells that stained SC-71, 6H1, and BF-35 strongly or weakly, but not BA-D5, were classified as hybrid 2A/X (Fig. 1). A total of of 880 ± 161 (mean ± SD) cells per muscle were analyzed.

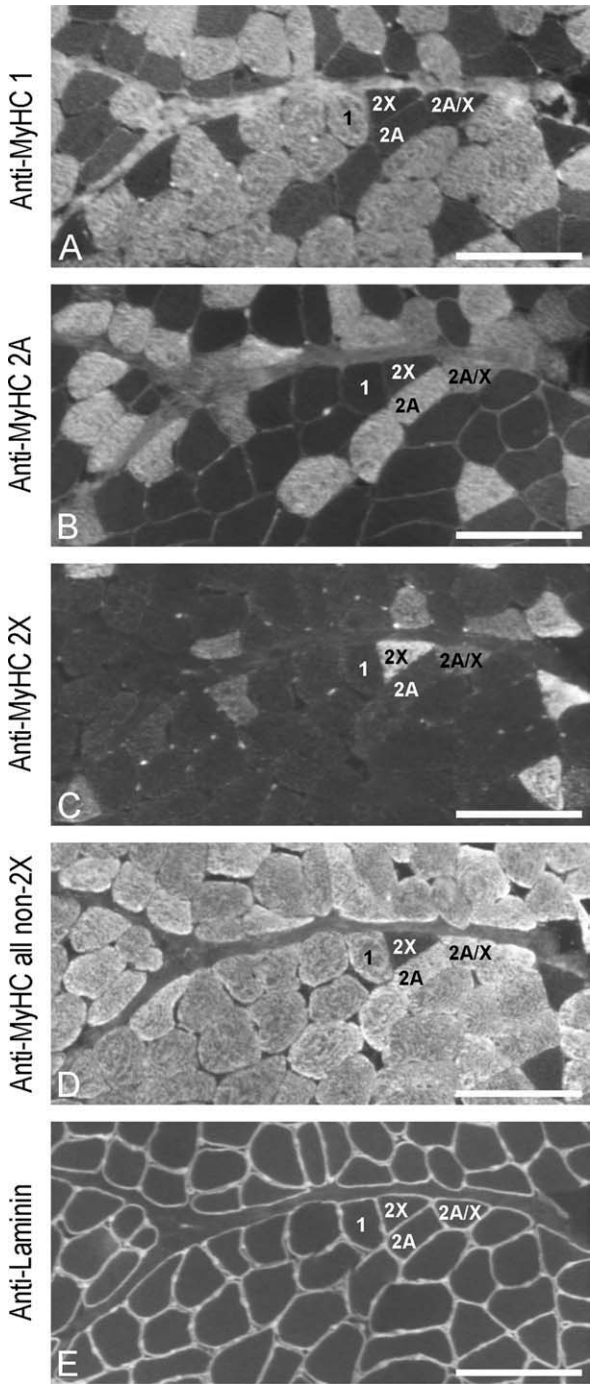

FIGURE 1. Serial cross-sections from the trapezius muscle from 1 subject **(A–E)**. Sections were stained using immunofluorescence with antibodies **(A)** BA-D5 (MyHC 1), **(B)** SC-71 (MyHC 2A), **(C)** 6H1 (MyHC 2X), **(D)** BF-35 (all non-2X MyHC), and **(E)** anti-laminin. 1, type 1 fibers; 2A, type 2A fibers; 2A/X, type 2A/X fibers; 2X, type 2X fibers. Scale bars = 200 μm.

Muscle Fiber Type Cross-Sectional Area. After inspection of cell integrity the cross-sectional area (CSA) was measured by manually tracing the inner laminin border of the cells. The CSA of at least 50 and up to a maximum of 100 cells of each fiber type, evenly distributed in the muscle samples, were measured.[37] All measurements were completed using ImageJ software, version 1.31 (W.S. Rasband, National Institutes of Health, Bethesda, Maryland). On average, we measured a CSA of 100 ± 2 type 1, 95 ± 13 type 2A, and 89 ± 16 type 2A/X cells. Because of the low proportion of 2X and 1/2A fibers, they were not analyzed in detail.

Reanalysis of Previously Published Data. Three earlier studies,[30–32] containing information on the individual fiber type proportions in several skeletal muscles of the same subject, were reanalyzed with respect to the hypothesis. If samples had been taken from more than one site within the same muscle, we used the average values in the analysis. Weber et al.[32] reported fiber type proportions in biopsies from neck muscles SCM and omohyoideus of 11 male and 10 female patients [age 52 years ± 14 (mean ± SD)] with cervical dysfunction. The second study was an autopsy investigation by Garrett et al.,[31] which included samples taken from 9 hip and thigh muscles from 7 men and 3 women (mean age 60 years, range 37–76 years). Their causes of death included myocardial infarction, lymphoma, or cerebrovascular accident, and thus the inclusion criteria deviated from those of the primary data set. Finally, we reanalyzed data from the autopsy study by Johnson et al.[30] (also reanalyzed by Medbø[38]) in 6 young men (age 21.8 ± 5.7 years, weight 78.5 ± 12 kg, height 186 ± 6 cm), all of whom had died suddenly. Samples were taken from 54 different sites of 36 different muscles across the body, which included a wide variation in location, size, and presumably activity patterns (see Fig. 4). No information was given regarding the subjects' general lifestyle or level of physical activity in these three studies. The myofibrillar ATPase protocols employed in these three studies provides results of the proportions of type 1 and 2 fibers that are indistinguishable from those of immunohistochemical methods.[33]

Statistics. All data are given as mean ± SD. To examine the effects of subject and muscle on fiber type composition, both subject and muscle were entered simultaneously in an analysis of variance model. This implies that the large variation between muscles with regard to fiber type composition is taken into account when comparing subjects. The same model was used for analysis of muscle fiber CSA and in the reanalysis of type 1 fiber proportions in the studies by Johnson et al.[30] and Garrett et al.,[31] which included 36 and 9 muscles, respectively. The Pearson correlation coefficient was used to explore the relationship between pairs of muscles and in one muscle and the mean of the others in our primary data set. This test was also used in the reanalysis of the type 1 fiber proportions in the two muscles reported by

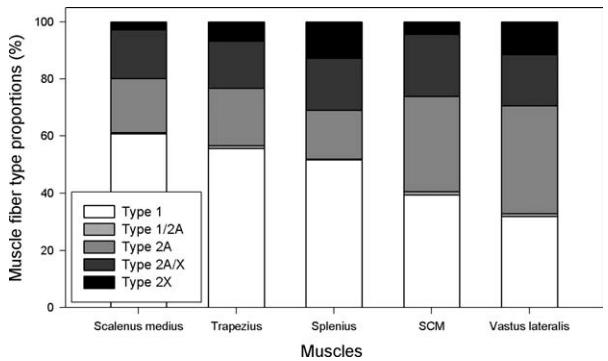

FIGURE 2. Mean fiber type proportion (%) in the five different muscles. Muscles are ordered from the highest to the lowest mean proportion of type 1 muscle cells, starting from the left.

Weber et al.[32] The *t*-tests were used for evaluating pairwise differences. $P < 0.05$ (all tests two-sided) was considered statistically significant. All analyses were performed using JMP (version 8.0) statistical software.

RESULTS

Muscle Fiber Type and Size. The muscles in the primary set of data displayed a marked difference in the proportion of the fiber types ($P < 0.0001$; Fig. 2). Type 1 fiber proportion was relatively low in our samples from vastus lateralis (mean ± SD: 31.9 ± 11.0%) and SCM (39.5 ± 14.5%). Both muscles were composed of fewer type 1 fibers than the splenius (51.6 ± 11.5%, $P < 0.01$), the trapezius (55.6 ± 10.2%, $P < 0.001$), and the scalenus medius (60.8 ± 13.4%, $P < 0.001$). Only a small fraction of the cells in the muscles were hybrid 1/2A fibers (0.3–1.2%). The mean proportion of type 2A fibers also differed between muscles ($P < 0.01$). The vastus lateralis and the SCM muscles had the highest proportions of type 2A fibers (37.6 ± 8.2% and 33.2 ± 14.1%, respectively) and were significantly different ($P < 0.01$) from trapezius (20.1 ± 6.5% type 2A), scalenus medius (18.9 ± 6.4%), and splenius muscles (17.2 ± 7.6%). All muscles were comprised of a relatively high proportion of hybrid 2A/X fibers, with no significant difference between muscles. The vastus lateralis was comprised of 18.1 ± 7.6%, the SCM 21.6 ± 10.4%, and trapezius 16.5 ± 6.8% of type 2A/X fibers. The scalenus medius and splenius muscle had 17.2 ± 9.0% and 18.3 ± 7.6% type 2A/X fibers, respectively. The proportions of 2X fibers also differed somewhat in the muscles. The vastus lateralis and splenius displayed 11.4 ± 7.4% and 12.7 ± 12.3% type 2X fibers, respectively and were significantly different ($P < 0.01$) from the trapezius, SCM, and scalenus medius (6.7 ± 7.0%, 4.3 ± 6.7%, and 2.7 ± 5.2% 2X fibers, respectively). The results from the single female and from the 2 oldest cases (age 65 years) did not deviate from those of the other cases in our material and, more generally, no association was found between the overall mean type 1 fiber proportions and age or cause of death.

Table 1. Mean fiber type CSA (μm^2) of the different muscles.

Muscles	Fiber type		
	Type 1	Type 2A	Type 2A/X
Scalenus medius	2275 ± 694	1918 ± 682	1821 ± 661
Trapezius	3173 ± 1115	2369 ± 993	2206 ± 874
Splenius	1971 ± 546	1845 ± 706	1645 ± 660
SCM	2503 ± 880	2788 ± 894	2397 ± 821
Vastus lateralis	3926 ± 1188	3583 ± 1065	2654 ± 1255

Results are presented as mean ± SD. Significant differences between muscles in the mean fiber type CSA are given in the text (n = 12).

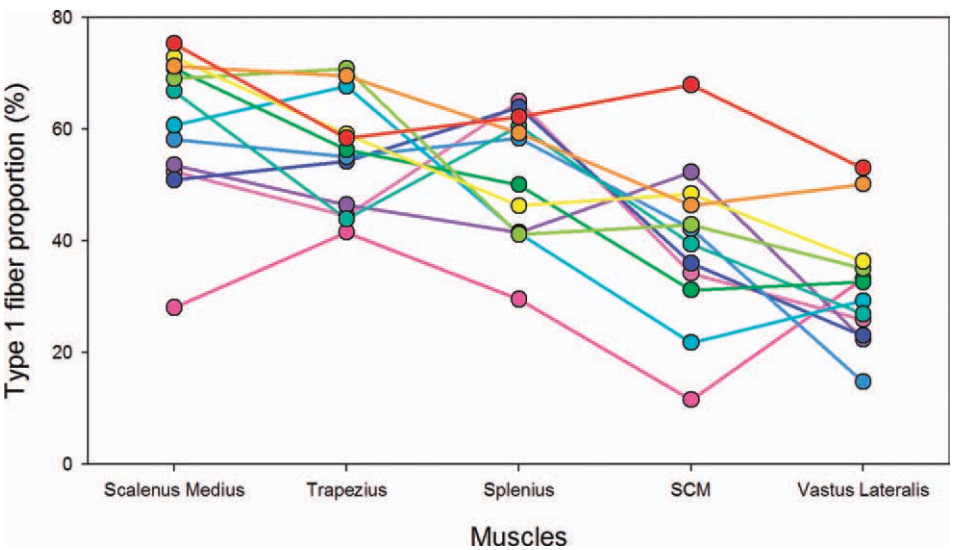

FIGURE 3. Type 1 fiber proportion (%) in 5 different muscles and 12 individuals. Each individual is represented by a unique color in all muscles. Muscles are ordered according to mean type 1 fiber proportion (see Fig. 2).

Table 2. Relationship between type 1 fiber proportions (%) of the different muscles, and between each muscle and the mean of the other muscles.

	Muscles				
Muscles	Scalenus medius	Trapezius	Splenius	SCM	Vastus lateralis
Trapezius	0.62*	–			
Splenius	0.39	−0.03	–		
SCM	0.67*	0.23	0.46	–	
Vastus lateralis	0.47	0.45	0.03	0.38	–
Mean other muscles	0.80*	0.43	0.32	0.64*	0.45

Pearson correlation coefficient was used ($n = 12$).
**P < 0.05.*

The leg muscle vastus lateralis was comprised of cells with larger CSA than the other muscles for all fiber types (Table 1), whereas the neck muscles scalenus medius and splenius generally had small CSAs. The difference between vastus lateralis and the two neck muscles is clearly significant ($P < 0.01$).

Intermuscular Relationship. As displayed in Figure 3, subjects demonstrated an overall high or low proportion of type 1 fibers for the muscles examined in our primary set of data. Some deviation from this general pattern is seen in Figure 3, but the overall difference between individuals was statistically significant ($P < 0.001$). Accordingly, the proportions of type 1 fibers were positively correlated between pairs of muscles and between one muscle and the mean of the other muscles (Table 2). Although only four correlations were significantly different from zero, all except one displayed a positive relationship for the type 1 fiber proportion. Taken together, the data point to a clear correlation between the proportion of type 1 fibers in the muscles, although there may be differences in the strength of this correlation.

To test the hypothesis further, we also reanalyzed three independent sets of published data on human fiber type proportions in multiple muscles.[30–32] As for our primary set of data, we found an overall significant difference between subjects with respect to the type 1 fiber proportions across muscles in the studies by Johnson et al.[30] ($P < 0.0001$; Fig. 4) and Garrett et al.[31] ($P < 0.001$), who assessed 36 and 9 muscles, respectively. Finally, the type 1 fiber proportions for the two muscles (SCM and omohyoideus) reported by Weber et al.[32] correlated significantly ($r = 0.52$, $P < 0.02$; Fig. 5).

DISCUSSION

The most important finding from our study is that there seems to be an intermuscular relationship in human muscle fiber type composition. Subjects who express a high proportion of type 1 fibers in one muscle are likely to express a comparably high proportion of type 1 fibers in other muscles as well. This result was observed for muscles covering a wide range of functional demands and fiber type proportions.

Muscle Fiber Type and Size. In general, the mean type 1 fiber distribution and variation of the five examined muscles in our primary data set were similar to those of previously published studies. Only for vastus lateralis were our results for type 1 fiber proportion (32%) somewhat in the lower range of typical findings.[39] This may reflect the fact that our samples were taken in the superficial part of the muscle.[40] The proportion of type 1 fibers of the shoulder girdle muscle trapezius in this study was found to be about 10–15% lower than in some studies,[41,42] yet similar to others.[30,43] There are fewer comparable studies of human neck muscles. We found 39.5% type 1 fibers in the SCM, which is similar to findings by Johnson et al.[30] and among patients with cervical disorders.[32,43] The splenius was comprised of 52% type 1 fibers in our data set, which is comparable to the 55% found in subjects with neck complaints.[43] In our data set, the scalenus medius had a mean of 61% type 1 fibers (Fig. 2). We are not aware of other studies of fiber type proportions of this muscle.

As expected, there were some differences in the mean fiber type proportions between the muscles. The vastus lateralis and SCM were composed of significantly fewer type 1 fibers and, reciprocally, more type 2A fibers than the other muscles studied (Fig. 2). Conversely, proportions of hybrid (1/2A and 2A/2X) fibers were very similar between muscles. Because we were among the first investigators to study humans using a specific antibody against type 2X MyHC (6H1), we were able to positively detect large fractions (17–22%) of hybrid 2A/X fibers in all muscles examined. In accordance with prior studies, only small portions (0.3–1.2%) of hybrid 1/2A fibers were found.[11,12,39,44]

Compared with the other muscles, the leg muscle vastus lateralis had the greatest cell areas and the neck muscle splenius had the smallest cell areas for all fiber types (Table 1). As muscle fibers readily increase or decrease in cell CSA in response to training or inactivity,[13–15,17,44] such use-dependent change may explain a significant fraction of the intermuscular and interindividual variation in the muscle fiber CSA.

Intermuscular Relationship. We tested and found a significant overall difference between individuals in the proportion of the type 1 fibers across muscles both in our primary set of data and for

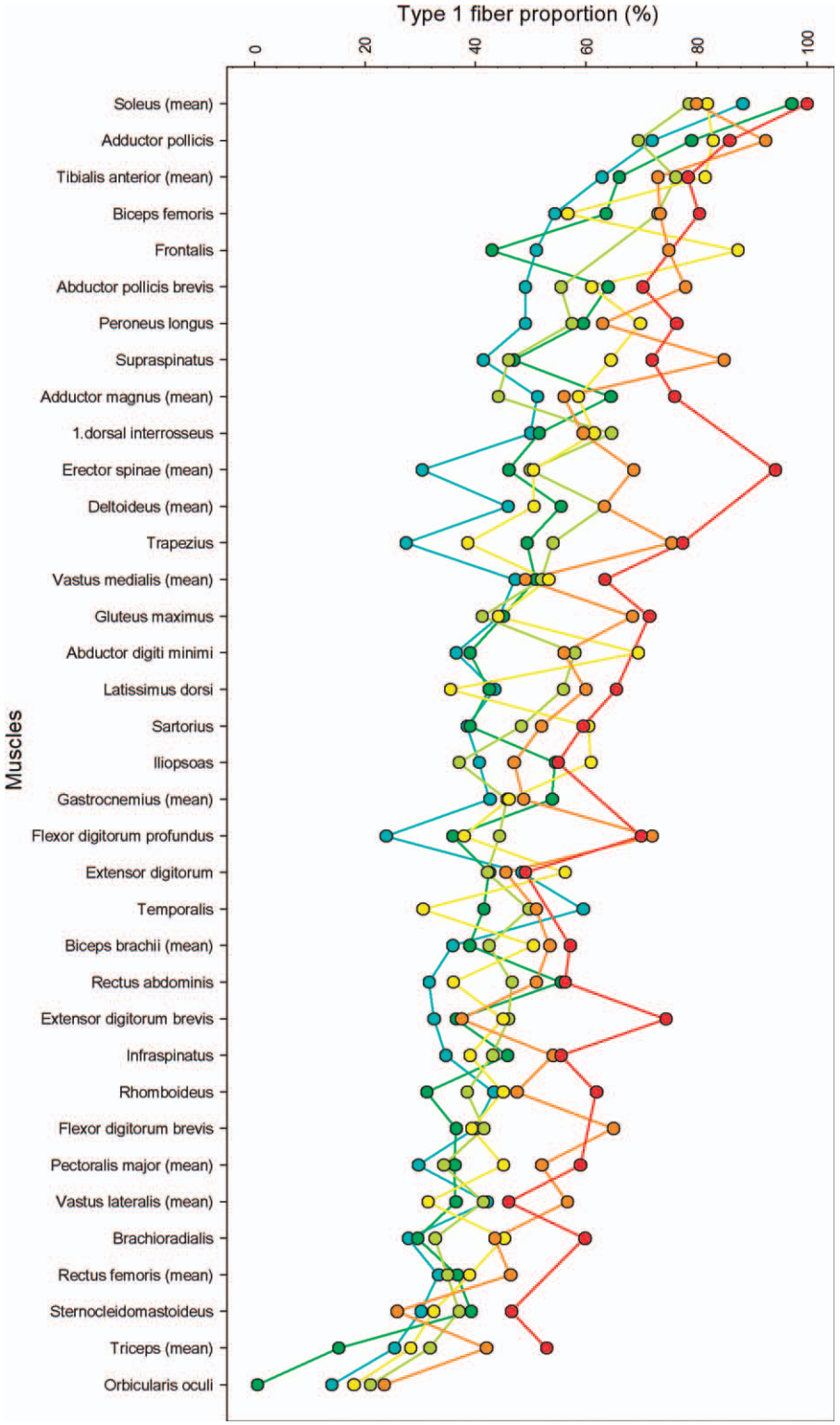

FIGURE 4. Individual type 1 fiber proportion (%) of 6 subjects in 36 different muscles. The 'mean' given in parentheses in 12 of the muscles depicts the average fiber type proportion taken from two or three separate samples in these muscles. Each subject is given a unique color and muscles are ordered according to mean type 1 fiber proportion (%). All reanalyzed data are from Johnson et al.[30]

the data sets of Johnson et al.[30] and Garrett et al.[31] Also, the bivariate analyses of the type 1 fiber proportions showed positive correlations for the two muscles in the study by Weber et al.[32] and in pairs of muscles from our primary set of data. Thus, the results of four independent sets of data consisting of a wide range of muscles, with presumably a large variation in activity patterns and fiber type proportions, suggest that the individual type 1 fiber proportions in different muscles are not

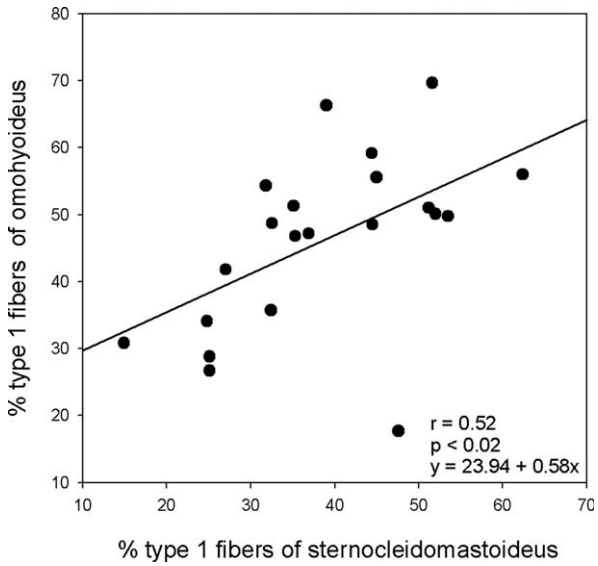

FIGURE 5. Relationship between type 1 fiber proportions (%) of SCM and omohyoideus in 21 subjects. The data were reanalyzed from Weber et al.[32] $r = 0.52$, $P < 0.02$.

random, but instead subject to an overall across-muscle regulation. Accordingly, subjects who express a relatively high proportion of type 1 fibers in one muscle will also express a relatively high proportion of type 1 fibers in other muscles, which supports the proposal made in 1977 by Saltin and colleagues.[29] Hence, these results point to the existence of an individual, across-muscle phenotype with respect to fiber type proportions.

As illustrated in Figures 3 and 4 there are discrepancies in the general pattern of an intermuscular relationship because subjects do not display a fully consistent interindividual difference for all muscles. These deviations from the overall pattern may be due to some individual biological variation and to the uncertainty of the method for estimating the true, unknown fiber type proportion for a whole muscle.[45] In this study, all four sets of data were, in general, based on one muscle sample from each muscle and, for two of the data series,[30,31] only 200 cells per sample. It is thus unreasonable to regard each single, small muscle sample to be truly representative of the whole muscle. Blomstrand and Ekblom[46] found a mean variation of 6.2% in the type 1 fiber proportions between two muscle samples at the same site in the vastus lateralis muscle. In the data analyzed from Johnson et al.,[30] the absolute difference in type 1 fiber proportion between a deep and a superficial sampling site in 11 muscles was, on average, 9.6%-point (range 0–36%-points). Thus, the uncertainty of the method for estimating the true, mean fiber type proportion of the muscles is likely to explain a significant fraction of the deviation among subjects from the general pattern of an intermuscular relationship. Despite such measurement errors and the likelihood of some biological deviations from the overall pattern, the hypothesis was supported in all four sets of data.

If the fiber type proportions of various muscles of an individual are interrelated, the proportion of one muscle may also be indicative of the general fiber type proportions of the total muscle mass. Our findings therefore offer a possible explanation for the observation that the type 1 fiber proportion of one single skeletal muscle alone seems to correlate with more global phenomena such as the presence or absence of risk factors for cardiovascular disease (CVD)[20–25,47] and CVD itself[26–28] or athletic performance.[19] Breeding studies in rats offer strong support for the existence of an across-muscle phenotype. Suwa et al.[4] first demonstrated that selective breeding over several generations for a large proportion of fast fibers in the medial gastrocnemius increased the fast fiber proportions in the gastrocnemius in each brood of rats. Concurrently, they observed that the proportion of fast fibers in the synergistic slow soleus muscle increased as well, indicating that selective breeding for a large proportion of fast fibers in one muscle may have a response among the fiber type proportions of skeletal muscles in general. In a later study they confirmed this proposition after analyzing a series of skeletal muscles in each individual rat.[48]

There are several possible genetic and non-genetic factors that may cause the intermuscular relationship. At the adult age, it is well known that physical activity can affect the metabolic and contractile properties of a muscle[49] and cross-sectional studies of elite athletes and sedentary subjects imply that physical activity may also influence the fiber type proportions.[50] For the three data sets based on samples taken at autopsy there is no information about lifestyle, including habitual physical activity. An evaluation of the possible impact of such factors is therefore not possible. However, causal relations are more suitably examined by an experimental study design. Thus, under normal physiological conditions, data from long-term, controlled experimental studies demonstrate that increased physical activity, such as long-term endurance training[7,11] or strength training,[8,9] sprint training,[12] or extreme endurance activity,[10] has a limited effect on the fraction of type 1 fibers in human muscles. Comparable observations were made for reduced muscle activity, such as continued bed rest[15] or detraining.[8,13,14,16,17] Furthermore, similar conclusions could also be drawn from long-term exercise experiments in rodent muscles under otherwise normal physiological conditions.[51] In contrast, the proportions of 2A and 2X fibers are readily changed due to modulation in physical activity in humans.[8,11,13,14,17]

The hybrid fibers (1/2A and 2A/X) have been suggested to be intermediate or transitional between muscle cells expressing only one MyHC and may indicate the state of fiber type alteration at a given time-point. In this study we found a large number of hybrid 2A/X fibers in all muscles but only minute fractions of 1/2A fibers. Thus, the existing experimental evidence does not suggest that any substantial activity-dependent transition occurs between type 1 and type 2 fibers under normal physiological conditions in adulthood. Therefore, it appears unlikely that the findings in the four sets of data presented herein simply reflect individual differences in physical activity at an adult age. We cannot, however, rule out that the fiber type proportions may be more changeable during prenatal or early postnatal periods. It has been suggested that the intrauterine milieu may affect the postnatal skeletal muscle fiber type proportions, and thus it may influence the intermuscular relationship. Both low birth weight,[52] a marker for suboptimal intrauterine milieu, and a protein-restricted diet during pregnancy[53] are associated with changes in postnatal fiber type proportions. It seems, however, that both in humans[52] and rodents[53] such alterations mainly occur within the type 2 fiber subsets, whereas the fraction of type 1 fibers is more stable. The results from the rat breeding studies of Suwa et al.[4,48] suggests a clear role for heritable factors in the intermuscular relationship of fiber type proportions. Such genetic influence is also supported by studies of single muscles in mono- and dizygotic human twins.[1,2] Our study had a cross-sectional design, and the results are compatible both with an influence of genetic factors and possibly early milieu on the development of the intermuscular relationship in fiber type proportions. Similar investigations should be done with younger subjects to strengthen and extend our findings.

In conclusion, we suggest the existence of an across-muscle phenotype with respect to fiber type proportions; some individuals display generally faster muscles and some individuals slower muscles compared with others.

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