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Correspondence

Nerve–muscle specificity

A correspondence item entitled 'A warning against revival of the classic tenets of gross anatomy related to nerve–muscle specificity' was recently published in the *Journal of Anatomy* (Shinohara, 1996*a*). The present correspondent fully agrees with some aspects of his opinion, in particular, the 3 laws about applications which he described, and he also appreciates his approach to the argument based on the results of embryology and experimentation. However, his denial of morphological interpretations based on the theory of nerve–muscle specificity may be due to an incomplete understanding of the current status of the theory.

My main point is not that Shinohara evaluated the studies listed in his correspondence as irrelevant, but rather that he did not offer any direct or concrete support for his argument against nerve-muscle specificity. Shinohara stated that 'Your correspondent is concerned that this will give readers an erroneous impression that this provides confirmation for the correctness of such tenets.' I think, on the contrary, it is his argument that will not only give readers a biased impression, but will also impede the current movement of the reexamination of applications of the specificity using new techniques by gross anatomists.

As pointed out by Shinohara, the classic theory of nerve–muscle specificity has certainly lost its scientific validation. Developmental studies have indeed demonstrated that connections between muscles and supply nerves are not established in the early stage of development. The evolution and history of the classic theory was detailed in the review by Straus (1946). I also recognise there have been many studies in which the theory was applied too strictly.

In contrast, for example, the study of gluteus and piriformis muscles by Akita et al. (1994) appears reliable, because the interpretation of muscle differentiation in that study corresponds with the results of a developmental study (Lance-Jones, 1979). Moreover, Yamada (1986, 1992) showed that the branching pattern of the teased median nerve accords with the phylogeny of the forearm flexors. Indeed, certain stable relationships between muscle phylogeny and innervation can be identified.

Reports by Lance-Jones & Landmesser (1980), Lewis et al. (1981), Ferguson (1983), Landmesser (1984), Keynes et al. (1987), Tosney (1987), Phelan & Hollyday (1990) and others have demonstrated that nerve pathways are formed according to information from the neurons themselves and guidance cues from mesodermal or mesenchymal structures. In other words, certain specific relations between supply nerves and target muscles are consequently present during development, although the process and mechanism of morphogenesis are still not completely clarified.

Considering the above background, my colleagues and I are examining relationships between muscle arrangement and phylogeny, innervation (ramification patterns of supply nerves) and the locations of motoneuron pools. We have already reported that the trunk muscle arrangement, the ramification pattern of supplying nerves, and the locations of motoneuron pools correspond with each other in the cat (Tani et al. 1994; Kida et al. 1995). Our recent experiments (unpublished) also show that the same relation is seen in the rat. Moreover, with respect to the spinal nerve development, Nakao & Ishizawa (1994) have demonstrated that the primary ramification consists of the principal branches excluding the anterior cutaneous branch, and that the primary ramification pattern is established in the middle stage (E12) of the mouse.

When the above-mentioned results are compared with trunk muscle phylogeny, the primary ramification pattern of the thoracic spinal nerves generally corresponds with the phylogenetic muscle classification of Seiho Nishi (Nishi, 1938, 1961). However, this classification must be partly revised based on our findings (Yamada & Kida, 1995). Thus the external intercostal and external abdominal oblique muscles cannot be classified in the same group, since the locations of the motoneuron pools supplying these muscles are clearly different in the ventral horn, and the pool for the abdominal muscle is situated in the area corresponding with that of the pool for the internal intercostal muscle. In this respect, the functional homology is not detectable in the differentiation of locations of the motoneuron pools.

Although Shinohara maintained a conservative interpretation concerning the origins of the external intercostal and external abdominal oblique muscles in a related paper (Shinohara, 1996*b*), our experiments support the new interpretations proposed by Sato (1973) and Kodama (1986). These interpretations were presented on the basis of the findings obtained for the gross and comparative anatomy of the spinal nerves. I think, therefore, that we cannot completely discount speculations based on nerve–muscle specificity.

Concerning the limb muscles, they have been examined in more detail in both classic and modern morphological studies than the trunk muscles. Nevertheless, the branching patterns of nerves (e.g. median or radial) examined by nerve teasing have not been studied widely in many species. Thus we have recently reported that there are both consistent and inconsistent ramification patterns of tested radial nerves in a comparative anatomical study of 25 species (Numata et al. 1996). Although further studies are required to elucidate this issue, the presence of the consistent (almost 100%) pattern reminds us that there is a possibility of certain genes sharing in the production of common guidance cues in many species. Therefore, stable ramification patterns of spinal nerves might become one of the standards which will help us reach appropriate interpretations on morphogenesis.

Shinohara (1966*b*) also referred to the issue of the formation of the pocket of the pectoralis major muscle, and indicated that Horiguchi (1981) supported the explanation given by Zuckerkandl (1910). However, Horiguchi explained the formation of the pectoral muscles based on the ramification pattern of the pectoral ansa from the standpoint of the differentiation of its anlage, and this apparently differs from the interpretation by Zuckerkandl. In this respect, the interpretations of Shinohara and Horiguchi are not essentially different. As shown by the evolution of the concepts on this problem, it probably cannot be resolved by reliance solely on human dissection. One problem is whether the pocket is homologous both in marsupials and primates, including man. Another is why a constant innervation pattern is observed in the pocket portion for man and other species. Experimental and embryological studies as well as human and comparative anatomical exploration are therefore required.

Some stable and definite relationships are in fact recognisable between a group of muscles and their innervation pattern, as mentioned above. Molecular biology will probably reveal the process and mechanism of the establishment of such a relationship. At present, however, it is an entirely different matter to interpret the phylogeny of each muscle and/or variation in individual animals or in various species. In the sense of contributions to discussion of issues in comparative anatomy, molecular biology still has limited force and this situation will probably continue for the foreseeable future.

Considering the above-mentioned progress in the understanding of the theory of nerve-muscle specificity, I believe it is important to examine comprehensively the issue of specificity from the viewpoints of gross anatomy, comparative anatomy, experimental investigations, and embryology to clarify exactly how and to what degree we can apply the theory (Yamada & Kida, 1995). My colleagues and I are therefore performing both human and comparative anatomical investigations and experiments, and have also begun embryological studies. Many gross anatomists are already aware that they must decide on the applications of the theory on a case-by-case basis. Only a small number of gross anatomists maintain that the theory is universally applicable to studies of muscle phylogeny.

MASAHIKO Y. KIDA
Department of Anatomy,
Iwate Medical University School of Medicine,
19-1 Uchimaru, Morioka 020,
Japan

REFERENCES

Akita K, Sakamoto H, Sato T (1994) Arrangement and innervation of the glutei medius and minimus and the piriformis; a morphological study. *Anatomical Record* **238**, 125–130.

Ferguson BA (1983) Development of motor innervation of the chick following dorsal–ventral bud rotations. *Journal of Neuroscience* **3**, 1760–1772.

Horiguchi M (1981) A comparative anatomical study of the pectoral muscle group in brindled bandicoot (*Isoodon macrourus* Gould, 1842), an Australian marsupial. *Acta Anatomica Nipponica* **56**, 375–399.

Kida MY, Tani M, Akita K, Nakano M (1995) The arrangement of motor nuclei in the ventral horn of the cat spinal cord in relation to the innervation of trunk muscles. *Journal of Anatomy* **187**, 509.

Keynes RJ, Stirling RV, Stern CD, Summerbell D (1987) The specificity of motor innervation of the chick wing does not depend upon the segmental origin of muscles. *Development* **99**, 565–575.

Kodama K (1986) Morphological significance of the supracostal muscles, and the superficial intercostal nerve—a new definition. *Acta Anatomica Nipponica* **61**, 107–129.

Lance-Jones C (1979) The morphogenesis of the thigh of the mouse with special reference to tetrapod muscle homologies. *Journal of Morphology* **162**, 275–310.

Lance-Jones, Landmesser L (1980) Motoneurone projection patterns in the chick hind limb following early partial reversals of the spinal cord. *Journal of Physiology* **302**, 581–602.

Landmesser L (1984) The development of specific motor pathways in the chick embryo. *Trends in Neurosciences* **6**, 336–339.

Lewis J, Chevallier A, Kieny M, Wolpert L (1981) Muscle nerve branches do not develop in chick wings devoid of muscle. *Journal of Embryology and Experimental Morphology* **64**, 211–232.

Nakao T, Ishizawa A (1994) Development of the spinal nerves in the mouse, with special reference to innervation of the axial musculatures. *Anatomy and Embryology* **189**, 117–138.

Nishi S (1938) Muskeln des Rumpfes. In *Handbuch der vergleichenden Anatomie der Wirbeltiere* (ed. Bolk L, Göppert E, Kallius E), vol. 5, pp. 351–446. Berlin: Urban and Schwarzenberg.

Nishi S (1961) Typological anatomy of muscles. *Nissin Igaku* **48**, 137–145 (in Japanese).

Numata N, Kida MY, Kudoh H (1996) Ramification patterns of the nerves innervating the forearm extensors in mammals and reptiles. *Okajimas Folia Anatomica Japonica* **73**, 55–64.

Phelan KA, Hollyday M (1990) Axon guidance in muscleless chick wings: the role of muscle cells in motoneuronal pathway selection and muscle nerve formation. *Journal of Neuroscience* **10**, 2699–2716.

Sato T (1973) On the homology of the obliquus externus abdominis with the intercostales externi, preliminary report. *Proceedings of the Japan Academy* **49**, 271–275.

Shinohara H (1996*a*) A warning against revival of the classic tenets of gross anatomy related to nerve–muscle specificity. *Journal of Anatomy* **188**, 247–248.

Shinohara H (1996*b*) Does the nerve supply to both the superficial and deep surfaces of pectoralis major imply two separate developmental origins? *Journal of Anatomy* **188**, 263–268.

Straus, Jr WL (1946) The concept of nerve–muscle specificity. *Biological Reviews* **21**, 75–91.

Tani M, Kida MY, Akita K (1994) Relationship between the arrangement of motoneuron pools in the ventral horn and ramification pattern of the spinal nerve innervating trunk muscles in the cat (*Felis domestica*). *Experimental Neurology* **128**, 290–300.

Tosney KW (1987) Proximal tissues and patterned neurite outgrowth at the lumbosacral level of the chick embryo: deletion of the dermamyotome. *Developmental Biology* **122**, 540–558.

Yamada TK (1986) Re-evaluation of the flexor digitorum superficialis. *Acta Anatomica Nipponica* **61**, 107–129.

Yamada TK (1992) Phylogenetic implications of prosimian forearm flexors. In *Topics in Primatology* (ed. Matano S, Tuttle RH, Ishida H, Goodman M), pp. 119–126. Tokyo: University of Tokyo Press.

Yamada TK, Kida MY (1995) Recent advances in the study of peripheral nerve pathways. Gross anatomical assessments toward the understanding of the peripheral nervous system. Is there still more to be done? In *An Active Direction to the Future of Peripheral Nerve Research* (ed. Kida MY, Horiguchi M), pp. 1–30. Sapporo: Kyobunsha.

Zuckerkandl E (1910) Zur Anatomie und Morphologie der Musculi Pectorales. *Sitzungsberichte der Kaiserlichen Akademie der Wissenschaften in Wien, Mathematisch-Naturwissenschaftliche Klasse, Abt. 3, Anatomie und Physiologie des Menschen und der Tiere* **119**, 469–558.