

## ESSAYS ON APS CLASSIC PAPERS |

## Nature vs. nurture: can exercise really alter fiber type composition in human skeletal muscle?

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This essay looks at the historical significance of two APS classic papers that are freely available online:

**Gollnick PD, Armstrong RB, Saubert CW IV, Piehl K, and Saltin B.** Enzyme activity and fiber composition in skeletal muscle of untrained and trained men. *J Appl Physiol* 33: 312–319, 1972 (<http://jap.physiology.org/cgi/reprint/33/3/312>).

**Gollnick PD, Armstrong RB, Saltin B, Saubert CW IV, Sembrowich WL, and Shepherd RE.** Effect of training on enzyme activity and fiber composition of human skeletal muscle. *J Appl Physiol* 34: 107–111, 1973 (<http://jap.physiology.org/cgi/reprint/34/1/107>).

IT IS WELL RECOGNIZED TODAY that mammalian skeletal muscle has a remarkable potential to alter its phenotype. Since the publication of the classic 1960 paper by Buller et al. (2) demonstrating the reversal of contractile characteristics in fast- and slow-twitch muscles after cross-innervation in cat, the plasticity of skeletal muscle has been demonstrated at the molecular and cellular levels using a variety of animal models and experimental treatments. Chronic electrical stimulation, synergistic muscle ablation, hindlimb suspension, and hormone manipulation have all been used to document changes in metabolic enzymes, Ca<sup>2+</sup> handling proteins, myosin isoforms and regulatory proteins of skeletal muscle, as well as alterations in muscle fiber type and size. Moreover, John Holloszy's classic 1967 paper (6) demonstrating the remarkable adaptation of the energy metabolism system in rat skeletal muscle to chronic exercise training indicated that the malleability of muscle could also be observed with a simple physiological stimulus. However, whether a stimulus such as exercise training could produce not only metabolic adaptations, but also transform fiber types in human skeletal muscle, is a question that has been long debated.

The first prospective research study that addressed this question using a fiber type classification system based on histochemical staining of myosin ATPase activity was published in the *Journal of Applied Physiology* in 1973 by Phil Gollnick (Fig. 1), Bob Armstrong, Bengt Saltin, Carl Saubert, Walt Sembrowich, and Ray Shepherd from the Department of Physical Education for Men at Washington State University ("Effect of training on enzyme activity and fiber composition of human skeletal muscle" Ref. 4). The initial interest in this question arose from the early work of Reggie Edgerton and colleagues at UCLA, whose work was critical for the development of fiber type classification systems. Furthermore, Edgerton's doctoral dissertation at Michigan State University in-

duced exercise physiologists to the idea of exercise-induced fiber type transformation in rodent muscle (3). To address the idea of fiber type plasticity in human skeletal muscle, Gollnick needed expertise in the techniques of fiber typing and needle biopsy of muscle. Therefore, Bob Armstrong, a National Science Foundation Predoctoral fellow in Gollnick's laboratory, spent the summer of 1971 learning fiber type techniques from Reggie Edgerton at UCLA. It was also at this time that Gollnick initiated his life-long research collaboration with Bengt Saltin, an Associate Professor in the Department of Applied Physiology at the Karolinska Institute in Stockholm Sweden, with expertise in the needle muscle biopsy technique and nearly 80 exercise science publications (an impressive publication record considering that he received his PhD in 1964!).

Gollnick and coworkers initially applied these techniques in a classic study published in the *Journal of Applied Physiology* in 1972 ("Enzyme activity and fiber composition in skeletal



Fig. 1. Philip D. Gollnick. Courtesy of Biomedical Communications Unit, College of Veterinary Medicine, Washington State University.

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muscle of untrained and trained men" Ref. 5). This may be the first study to document the distribution of slow- and fast-twitch fibers (i.e., based on myosin ATPase staining) in skeletal muscles from trained athletes from a variety of sporting disciplines (e.g., cycling, running, swimming, weight lifting). Gollnick and coworkers reported that skeletal muscle from trained endurance athletes was predominated by slow-twitch fibers with relatively high oxidative capacity, an observation that has been confirmed in numerous subsequent cross-sectional studies. The authors stated, "The question arises as to whether the percentage distribution of a specific fiber type in skeletal muscle can be altered by training" or whether "this [high percent distribution of slow-twitch fibers in trained endurance muscle] could be due to a selection of these activities by individuals possessing the natural endowment." Recognizing the limitation of their 1972 study, Gollnick and coworkers then embarked on a study in which muscle fiber type distribution would be examined before and after long-term, high-intensity endurance training.

Besides being the first study to address the idea of exercise-induced fiber type plasticity in human skeletal muscle, the 1973 *Journal of Applied Physiology* article (4) is noteworthy for several reasons. First, the duration and intensity of exercise training are truly remarkable for a human research study. Six subjects exercised on a cycle ergometer for 1 h per day, 4 days per week, for 5 mo. At the completion of the study, most of the subjects were exercising for 1 h at 85–90% of the maximal aerobic power! All of the subjects were either graduate students or the lab director, and five of the six subjects were authors/coauthors on the paper. Considering the commitment of time and intensity of physical effort required by this long-term study, it's astonishing that this research group was still able to publish nine articles in 1973! Presumably, the reason that Saltin did not participate in the study as a subject, as he was usually accustomed to, was because the long duration of the study kept him from other academic responsibilities and that he was too well trained. Second, the first time that the myosin ATPase-based fiber type system was applied to muscle biopsy samples from humans was in the studies from 1972 (5) and 1973 (4). Although J. B. Peter, R. J. Barnard, and Edgerton had refined the myosin ATPase-based fiber type technique to document three basic fiber types (i.e., type I, slow-twitch, oxidative; type IIa, fast-twitch, oxidative and glycolytic; and type IIb, fast-twitch, glycolytic) in muscles from laboratory animals, the histological approach used by Gollnick and coworkers at the time only allowed them to discriminate between fast- and slow-twitch fibers in human muscle. Third, the conclusion that chronic exercise training does not significantly alter the distribution of fast- and slow-twitch fibers in human skeletal muscle has been a source of debate for years. It should be noted that the magnitude of the mean change in the percent of slow-twitch fibers (32% to 36%) reported by Gollnick et al. has been consistent with numerous subsequent studies that have (e.g., Ref. 7) and have not (e.g., Ref. 1) reported statistically significant alterations in slow-twitch fiber distribution after exercise training. A small sample size ( $n = 6$ ) and relatively high sampling variance may have precluded Gollnick et al. from observing statistically significant changes. Today, it is generally accepted that exercise training can promote

changes within the population of fast-twitch fibers (i.e., type IIb to IIa) and to a lesser extent changes from fast- to slow-twitch fibers. To this end, it is interesting to note that the two subjects (R. B. Armstrong and W. L. Sembrowich) in the Gollnick study with the lowest distribution of slow-twitch fibers before training were the same two subjects that exhibited the greatest absolute increase in slow-twitch fiber percentage (23% to 32%), succinate dehydrogenase (SDH) activity (3.5 to 10.3  $\mu\text{mol}\cdot\text{g}^{-1}\cdot\text{min}^{-1}$ ), and maximal aerobic power (4.1 to 5.0 l/min) after training. Fourth, other observations made in this study have helped fuel exercise science questions over the last 30 years. Gollnick and coworkers reported that endurance training resulted in supercompensation of muscle glycogen storage (153% increase). Furthermore, the disproportionate increase (95%) in muscle SDH activity compared with the small increase (13%) in maximal aerobic power suggested that whole body  $\dot{V}\text{O}_{2\text{max}}$  was not limited by changes in muscle oxidative potential.

It is now generally recognized that skeletal muscle fibers do not exist in three discrete forms at the subcellular level, but rather in a continuum based on the multitude of combinations of myosin heavy and light chain isoforms, polymorphic expression of protein isoforms, metabolic potential, and  $\text{Ca}^{2+}$  handling characteristics. Moreover, it is clear that all of these cellular characteristics exhibit some degree of plasticity in response to exercise training. The seminal work of scientists such as Edgerton, Holloszy, Ken Baldwin, Frank Booth, Dirk Pette, Saltin, and Gollnick over the years has been critical in shaping our understanding of exercise-induced plasticity of the muscle fiber phenotype. Although all the authors of the 1973 paper have gone on to respectable careers in and out of academia, three deserve special mention. According to the Thomson ISI Web of Knowledge index, Saltin, Gollnick, and Armstrong have published over 600 exercise science articles. Over 90 of these publications have been referenced more than 100 times, and 7 papers have been cited over 400 times. The 1972 and 1973 *Journal of Applied Physiology* papers have been referenced 554 and 397 times, respectively, making them both true classic papers in exercise physiology.

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