

For a pragmatic approach to exercise studies

We are skeptical about the feasibility of defining a gold standard for exercise studies on animals with a huge variety in strain, age, gender, transgenesis or exercise paradigms (1). For example, the practical determination of exhaustion in rodents (and humans) is more difficult than implied by the simple theoretical definition. The criteria proposed by Booth et al. are invasive, disruptive, terminal or ethically difficult to justify. In contrast, electric shock stimulation, in particular in combination with computer-controlled break-off criteria, is a pragmatic, non-invasive solution for comparing endurance capacity between different experimental groups, even for longitudinal studies. Problems with running style and non-compliance can be overcome by appropriate acclimatization and group size.

Second, we certainly appreciate the historic, excellent work by our predecessors. However, novel complementary and interdisciplinary methods provide additional important details about the contractile and metabolic characterization of muscle (3). Even so, individual methods such as immunohistochemical staining of myosin heavy chains, or myosin ATPase activity staining for that matter, fail to provide a comprehensive picture. Therefore, a combination of methods, optimally less delicate than myosin ATPase activity determination, should be used and optimally combined with approaches that allow true determination of peak force generation and fatigue resistance (2, 4).

Finally, we think that instead of a dogmatic approach to exercise concepts (i.e., “no increase in type I fibers” vs. increase in (5) and other references), we should remain open to novel findings and continue to improve our animal-based exercise studies accordingly.

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References

1. **Booth FW, Laye MJ, and Spangenburg EE.** Gold standards for scientists who are conducting animal-based exercise studies. *J Appl Physiol* in press: 2009.
2. **Delbono O, Xia J, Treves S, Wang ZM, Jimenez-Moreno R, Payne AM, Messi ML, Briguet A, Schaerer F, Nishi M, Takeshima H, and Zorzato F.** Loss of

skeletal muscle strength by ablation of the sarcoplasmic reticulum protein JP45. *Proc Natl Acad Sci U S A* 104: 20108-20113, 2007.

3. **Keller P, Vollaard N, Babraj J, Ball D, Sewell DA, and Timmons JA.**

Using systems biology to define the essential biological networks responsible for adaptation to endurance exercise training. *Biochem Soc Trans* 35: 1306-1309, 2007.

4. **Lin J, Wu H, Tarr PT, Zhang CY, Wu Z, Boss O, Michael LF, Puigserver P, Isotani E, Olson EN, Lowell BB, Bassel-Duby R, and Spiegelman BM.**

Transcriptional co-activator PGC-1 alpha drives the formation of slow-twitch muscle fibres. *Nature* 418: 797-801, 2002.

5. **Russell AP, Feilchenfeldt J, Schreiber S, Praz M, Crettenand A, Gobelet C, Meier CA, Bell DR, Kralli A, Giacobino JP, and Deriaz O.**

Endurance training in humans leads to fiber type-specific increases in levels of peroxisome proliferator-activated receptor-gamma coactivator-1 and peroxisome proliferator-activated receptor-alpha in skeletal muscle. *Diabetes* 52: 2874-2881, 2003.