Experimentally evolving exercise endurance: one step at a time

WITHIN THIS ISSUE IS A STUDY from Gonzalez and colleagues (4) presenting an update on a long-term selective breeding investigation in rats, originally initiated by Koch et al. (8) to study the genetic basis for inherent exercise endurance. The present study reports new findings suggesting that as rats were selectively bred for high and low intrinsic exercise endurance, the mechanisms responsible for differences in exercise capacity between the two lines have evolved at differing rates. These findings are important not only because of their relationship to the ongoing literature that is attempting to understand the role that genetic factors play in determining the inherent variability in exercise capacity, but also because of their implications in the continuing appreciation of the importance of aerobic capacity toward general health.

There is a plethora of evidence that increased exercise endurance or maximal aerobic capacity is linked with several positive health outcomes (1). These suggestions include recent findings from Britton and Koch’s group (13) that rats bred for low exercise endurance exhibited impaired mitochondrial biogenesis and functioning that was linked with several cardiovascular risk factors. Thus the investigation and understanding of the causal factors underlying maximal exercise endurance are no longer just germane to those exercise physiologists interested in increasing athletic performance; rather, understanding the multiple factors that underlie an individual’s aerobic capacity and exercise endurance may provide information useful in preventing and ameliorating a large number of inactivity-related diseases.

Scientifically, it has been a relatively short time since the estimates for the heritability of exercise endurance ranged from “negligible” (10) to 93.4% (7). However, from both human and animal models it has become generally accepted that ~50% of the variability in exercise endurance is related to genetic factors (e.g., Refs. 2, 9). Several approaches ranging from large-scale human studies (2) to the use of inbred mouse and rat strains (9, 12) to the selective breeding model of the present study (4) are being used in an attempt to discern the identity of the nonenvironmental factors primary in the determination of the variability of exercise endurance. Selective breeding studies are important because they provide the opportunity to observe phenotypically linked physiological traits to determine whether these traits evolve at a similar rate as does the phenotype (e.g., exercise endurance). Interestingly, the study presented by Gonzalez et al. (4) suggests that these phenotypically linked physiological traits evolve at differing rates, resulting in a continuous evolution of exercise capacity.

It is well accepted that aerobic capacity is controlled by a multitude of factors, loosely grouped under two headings: central mechanisms that deliver O2 to the skeletal muscle and peripheral mechanisms that transport and use the O2 in the skeletal muscle to induce ATP production and movement. Previous studies from Britton and Koch’s laboratory group with the seventh generation (G7) of rats selectively bred for high and low exercise endurance found that the high-capacity runners (HCR) differed from their low-capacity (LCR) brethren not in central O2 delivery (e.g., cardiac output), but primarily because of an increased tissue O2 diffusive conductance, greater capillary density, and an increased oxidative enzyme activity, i.e., changes in the peripheral mechanisms (5, 6). However, in the present study (4) when the investigators considered the physiological differences between the LCR and HCR after 15 generations (G15) of selective breeding, they found that even though tissue O2 diffusive conductance increased in the HCR, the overall tissue O2 extraction was not different from the LCR owing to an increase in peripheral blood flow in the HCR. Thus, overall, unlike the G7 rats, the differences in exercise endurance were not explained by variance between the LCR and HCR in peripheral factors; rather, the G15 rats differed in the rate of O2 delivery to the tissues. Specifically, these authors noted that the cardiac output and stroke volume of the HCR rats were significantly higher than the LCR rats, with the increased stroke volume of the HCR rats being attributed to both larger hearts and a greater stroke volume produced per gram of heart tissue (4).

The implication of these findings is that as an organism is selectively bred (i.e., experimentally evolved; see Ref. 3) for a certain phenotype, the different mechanisms that control the phenotype evolve at differing rates. This implication, although not completely new [a similar observations has been made by Garland and Kelly (3) in relation to the evolution of daily wheel running activity across 36 generations of mice] is original to the study of the genetically controlled mechanisms of exercise endurance. Thus researchers concerned with understanding the genetics that control exercise endurance must now take into account the “evolutionary” progress of the model they are studying before being able to make conclusive statements regarding the physiological mechanisms through which the genetic controlling factors actually work.

On a broader scale, the findings by Gonzalez et al. (4) give further contextual background and add new data to the long-term debate regarding the primacy of either central or peripheral mechanisms in determining maximal exercise endurance and aerobic capacity. It could be suggested from the presented data that the primacy of either the central or peripheral mechanisms in determining the inherent maximal aerobic capacity depends on the stage of “evolution” that the organism is in. Although it would be difficult to apply these suggestions to understanding a human model of exercise responses, these results will speed progress toward understanding the genetic factors underlying exercise endurance in animal models (e.g., Ref. 12), which in the long term will be translated to the human model.

Maybe the most important contributions of this study are the questions that these findings raise that will give direction to future research. The importance of determining whether exercise endurance and aerobic capacity will continue to diverge as the rats are experimentally evolved and whether the divergence continues, what mechanisms are augmented in the HCR animals and inhibited or depressed in the LCR animals, could have great implications for human health. Furthermore, if there is continued divergence, it will be interesting to observe whether there will be a continuing augmentation of the peripheral and/or central mechanisms or whether other mechanisms, such as lipid metabolizing capability [a capability suggested recently to have a primary role in influencing exercise capacity (11)] will be altered to further change exercise endurance in
these animals. If nothing else, perhaps the findings of Gonzalez and coworkers (4) prove the old axiom that “good science generates more questions than answers.”

REFERENCES

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