Evidence that reduced skeletal muscle recruitment explains the lactate paradox during exercise at high altitude

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The studies of Amann et al. (1, 2) provide the final evidence necessary to solve the ‘lactate paradox’ that has haunted the exercise sciences since first described in 1936 (4) and which was the recent focus of a Point-Counterpoint debate (25, 26).

In its simplest form the paradox describes the finding of lower than expected blood lactate concentrations during maximal exercise at altitude, especially extreme altitude (26). This is naturally paradoxical according to the model, which holds that skeletal muscle lactate production should be increased and not reduced in the presence of profound hypoxia.

But there are two additional components of the paradox that are seldom addressed together. The first is the cause of the profound fatigue that develops at extreme altitude and that is even more incapacitating than that which develops at lower altitudes (13). For clearly low blood (and muscle; Ref. 5) lactate concentrations cannot cause such fatigue.

The second paradox is the finding that the maximal cardiac output falls progressively with increasing altitude (22) as again recently confirmed (12). This is paradoxical since if skeletal muscle hypoxia is the protected variable during maximal exercise at any altitude, then the cardiac output should be the highest when the oxygen content of the blood is the lowest (13, 15). Only in this way can the heart maximize oxygen delivery to those exercising muscles that are at risk of becoming severely hypoxic.

Nor can the lower than expected cardiac outputs at extreme altitude be explained by impaired myocardial function, which is highly preserved even at the greatest levels of environmental hypoxia yet studied (3, 6, 17, 20). Indeed coronary flow reserve exists during maximal exercise in hypoxia, confirming the absence of myocardial hypoxia (7, 8). These data prove 1) that cardiac function during exercise in hypoxia is not regulated to maximize blood flow to the exercising limbs and 2) that the progressively lower cardiac outputs during maximal exercise with increasing hypoxia cannot be due to myocardial failure. But to be complete, any explanation for the ‘lactate paradox’ in severe hypoxia must also reconcile why the peak power output is so low when blood lactate concentrations are also low and the cardiac output is submaximal.

Amann et al. (1, 2) report two findings that appear to confirm an earlier (11) explanation for the paradox. First that during 5-km cycling time trials at four different inspired oxygen fractions (FiO2; values of 1.0, 0.28, 0.21, and 0.15) skeletal muscle activation, measured with standard electromyographic (EMG) techniques, was reduced as a linear function of the hemoglobin oxygen saturation (HbO2) measured with a pulse oximeter (SPO2; Fig. 1 in Ref. 14). The opposite has also been shown: EMG activity (and power output) is increased during a 20-km time trial at an FiO2 of 1.0 compared with an FiO2 of 0.21 (24).

These findings are compatible with the original interpretation of Kayser and his colleagues (10, 11), who showed that EMG activity was reduced during maximal exercise at an altitude of 5,050 m but increased when subjects inhaled oxygen with an FiO2 of 1.0. The authors concluded that “... during chronic hypobaric hypoxia, the central nervous system may play a primary role in limiting exhaustive exercise and maximum accumulation of La (lactate) in blood” (11). Those authors also noted that hypoxia did not reduce either exercise performance or muscle lactate concentrations during exercise with a small (forearm) muscle group, an observation also made by Shephard et al. (19). While they concluded that this was because an adequate oxygen delivery was maintained to small muscle groups even in hypoxia, a more inclusive explanation would be that whole-body oxygen homeostasis is less disturbed during exercise with small than with large muscle groups.

Second, Amann et al. (2) found that the decision to terminate maximal exercise at an FiO2 of 0.10 occurred even though the extent of ‘peripheral’ fatigue was much less than in normoxia or moderate hypoxia. Thus they concluded that there was a “relatively minor involvement of peripheral fatigue in the decision to terminate exercise in severe hypoxia” (2; p. 400). Thus the choice to terminate exercise at an FiO2 of 0.1 was regulated by an altered central motor command.

When all these findings are considered together, this explanation for the ‘lactate paradox’ seems more probable: The allowable extent of skeletal muscle recruitment during “maximal exercise” falls progressively with increasing altitude perhaps as a function of a falling SPo2 or other more precise determinants of cerebral oxygenation (9, 16, 18, 21). As a result, progressively lower levels of skeletal muscle recruitment prevent the development of sufficient muscle power, leading to the termination of “maximal” exercise at progressively lower 1) work rates (5, 22), 2) blood and muscle lactate concentrations (4, 5), and 3) cardiac outputs (12, 22) with increasing altitude.

According to this explanation, the reasons for the lactate paradox should not be sought in an altered biochemistry in skeletal muscle as the result of adaptations to an (unproven) hypoxia, but may result from an altered behavioral response coordinated within the brain and that occurs within the first 10...
or so seconds of exposure to either a lower FiO2 or a reduced barometric pressure or both (1, 14). The function of this control is to regulate the extent of skeletal muscle recruitment probably to protect the brain from hypoxia (9, 13, 16, 18, 21), although some argue that the goal is to limit to which peripheral muscle fatigue develops (1, 2). There is some evidence that the former mechanism might also contribute to the termination of progressive maximal exercise at sea level (16, 18, 23).

Finally it is appropriate to acknowledge that this idea is not new. Already in 1994 Kayser et al. (11) concluded that “it appears that at high altitude heavy exercise involving large muscle groups may be limited by a reduced central drive. The latter phenomenon, possibly aimed at preventing the failure of vital systemic functions, like pulmonary ventilation, could therefore, at least in part, be responsible also for the so-called lactate paradox, i.e., the reduced size of anaerobic glycolysis at high altitude. By contrast, at high altitude small muscle groups appear to preserve their sea level capacity for maximum work” (p. 640).

REFERENCES