### Abstract

Physiological measures of exercise performance provide reference points for physical health and fitness. They allow to evaluate the progression of improvements in work capacity with training in the active sportsman or the injured with rehabilitation. Tests are now established in many Sports Clinics to document task-specific exercise performance. Major developments in the area of the molecular health sciences highlight options to reinforce current performance testing with molecular diagnosis. In the following, a personal view of the perspectives of exercise testing at the molecular level is given with respect to endurance performance. The case is developed that local, biopsy-based measures of the transcript response of exercised muscle to endurance work may be used to estimate specificity, pace, and possibly magnitude of adaptation with repeated endurance stimuli. This expression profiling of muscle's adaptive response to an exercise stimulus complements non-invasive, genomic methodologies that have identified the association of exercise performance with modifications in heritable elements (gene polymorphisms). Research applying these tools highlights the possibility that the molecular analysis of sample collected with minimally invasive methodology from peripheral muscle tissue and blood serum can enhance the diagnostic power of current physiological tests, and lend to a future use in predicting the progression and variability of endurance performance with training.

#### Keywords

Skeletal muscle– biopsy– serum– gene– prognosis

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Leistungsdiagnostik auf Ebene der Genexpression des Muskels in den Ausdauersportarten

### REVIEW

# Diagnostics of endurance performance on the level of gene expression

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Llassical exercise physiology has provided valuable tools to quantify maximal work capacity over a large spectrum of power output and forms of physical activity. This covers labbased tests measuring force production and power output of single, isolated contractions, as well as field tests assessing energy expenditure of repeated contractions in relation to discipline specific performance (Table 1). A major benefit of these tests is that the conversion of metabolic energy into mechanical output is assessed in an integrated manner in a whole body context.

# Limitations in current performance testing

A major drawback of functional tests into work capacity is that these are often too coarse to resolve improvements or bottlenecks in the processes that conspire to set maximal performance. Maximal performance depends on a number of interrelated biological pathways/organ systems (Fig. 1). However these do only demonstrate minute adjustments with each bout of exercise. In consequence standard performance tests such as ergospirometry do not typically resolve the individual processes [21,50,48]. In consequence they cannot provide specific answers on functional

improvements before an important period of training has passed. This limits their use in the selection and fine-tuning of training and probably explains why experienced coaches prefer to explore psychological options to maximize performance through motivating the recruitment of functional reserves in Athletes. Recent additions to exercise testing involve the assessment of genetic constitution through the measure of gene variants, or polymorphisms, being associated with performancerelated phenotypes. According to leading experts, however, current genetic testing has zero predictive power on talent identification [35].

### **Endurance training**

The ultimate purpose of endurance training is to increase the duration during which force production of repeated contractions can be maintained. Classically this is achieved through the completion of a protocol of repeated exercise sessions with a high number of contractions at low load. Thereby the distinction to power sports is typically drawn based on soft parameters respective to the individual maximal values of power output during a workout and the duration during which this can be performed (such as a VO2max test).

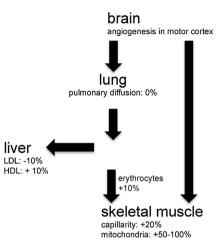
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### Zusammenfassung

Die Ermittlung der aeroben Ausdauerleistung liefert physiologische Eckdaten zur körperlichen Gesundheit und Fitness. Dies erlaubt die Verbesserungen aeroben der Leistung und Ermüdungresistenz im Verlauf eines Trainings im aktiven Sportler oder mit der Rehabilitation beim Verletzten festzuhalten. Physiologische Tests werden heute routinemäßig in Sport-Kliniken angeboten, um die sportspezifische Leistungsfähigkeit zu dokumentieren. Entwicklungen im Bereich der molekularen Gesundheitswissenschaften zeigen weiterführende Ansätze zur Diagnostik der Ausdauerleistung. Im folgenden Beitrag wird eine persönliche Perspektive der Möglichkeiten molekularer Methodik, in der Diagnostik der Ausdauerleistung, entwickelt. Es wird gezeigt, dass die Vermessungen der Umschreibung von Geninformation in Boten-Ribonukleinsäuren in Muskelbiopsien nach einer Trainingslektion Aufschluss über Spezifität, Tempo und Ausmaß muskulärer Anpassungen an ein Trainingsparadigma erlaubt. Die Vermessung des Expressionsprofils der muskulären Antwort auf einen Trainingsreiz ergänzt nichtinvasive, genomische Methoden, welche erbliche Faktoren (Gen-Polymorphismen) der körperlichen Leistungsfähigkeit aufzuzeigen vermögen. Ergebnisse der neueren Grundlagenforschung unterstreichen, dass die biochemische Analyse minimal-invasiv gewonnenen Probenmaterials aus peripherem Muskelgewebe und Blutserum erlaubt, die Aussagekraft der aktuellen Leistungsdiagnostik zu verbessern. Die Kombination von sportphysiologischer Leistungsdiagnostik und molekularbiologischer Methodik bietet sich an, die Trainierbarkeit der Ausdauerleistung durch Einbezug konstitutioneller und erblicher Faktoren individuell zu optimieren und in bedingtem Maße vorherzusagen.

#### Schlüsselwörter

Skelettmuskel – Biopsie – Blutserum – Gen – Prognose



#### Figure 1

Drawing illustrating the interrelationship between adaptations in organs that set endurance performance. The typical range of improvement for selected parameters related to endurance performance in untrained subjects after 6-10 weeks of endurance training is indicated.

Improvements in endurance performance of running type exercise for instance can be assessed via the measure of running economy, peak velocity and time-to-exhaustion in time trials [43,27]. The adequacy of these measures is amply demonstrated for elite athletes [30,9,8] but they are rarely performed in routine diagnosis. At best maximal oxygen uptake (VO2max) is assessed in an incremental test, which allows, when accompanied with measures of mechanical work, to estimate the economy of a given exercise. VO2max, however, is a steady state measure of maximal exercise performed at relatively short duration. This parameter, while reporting maximal aerobic performance, does not necessarily document fatigue resistance, which is probably more relevant to characterize performance of long distance events, which rely on the capacity to maintain substrate metabolism and metabolic stores. This distinction is also important because the improvement in endurance performance with training is more pronounced for factors reflecting the time-to-exhaustion or velocity at a high metabolic strain, than for VO2max, which typically only improves moderatelv [30,9]. Towards a representative diagnostics of endurance performance it therefore appears sensitive to target the tests as close as possible to the muscle groups being trained and quantify both the maximal capacity for aerobic work and the time-toexhaustion.

# Myocellular underpinning of exercise performance

As pointed out in a number of research papers, measures comparing structure-function relationships in the effector organ of mechanical work, skeletal muscle, can reveal unprecedented detail on the features that set the endurance training state. For instance, muscles of endurancetrained subjects have been shown to differ to un-trained subjects in terms of muscle size and fat content, slow fiber type composition and myocellular constituents of mitochondrial lipid metabolism [19,22]. The theme of these adaptations is the promotion of aerobic substrate pathways that increased the economy of muscle contractions.

Performance in most individual sports disciplines has its foundation in two, partially exclusive traits that reflect the maximization of power output or fatigue-resistance of a motor task, i.e. strength vs. endurance (reviewed in [15]). Skeletal muscle contributes in a specific way to the furthering of both traits with training. It has been appreciated that this is mostly explained by the composition in motor units [29]. Three major motor unit types are described based on

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