

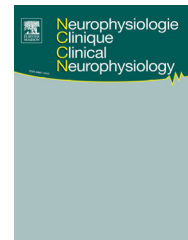


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COMPREHENSIVE REVIEW/REVUE GÉNÉRALE

# Neuromuscular fatigue during exercise: Methodological considerations, etiology and potential role in chronic fatigue



*La fatigue neuromusculaire au cours de l'exercice : considérations méthodologiques, étiologie et rôle potentiel dans la fatigue chronique*

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## KEYWORDS

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Transcranial magnetic stimulation

**Summary** The term fatigue is used to describe a distressing and persistent symptom of physical and/or mental tiredness in certain clinical populations, with distinct but ultimately complex, multifactorial and heterogenous pathophysiology. Chronic fatigue impacts on quality of life, reduces the capacity to perform activities of daily living, and is typically measured using subjective self-report tools. Fatigue also refers to an acute reduction in the ability to produce maximal force or power due to exercise. The classical measurement of exercise-induced fatigue involves neuromuscular assessments before and after a fatiguing task. The limitations and alternatives to this approach are reviewed in this paper in relation to the lower limb and whole-body exercise, given the functional relevance to locomotion, rehabilitation and activities of daily living. It is suggested that under some circumstances, alterations in the central and/or peripheral mechanisms of fatigue during exercise may be related to the sensations of chronic fatigue. As such, the neurophysiological correlates of exercise-induced fatigue are briefly examined in two clinical examples where chronic fatigue is common: cancer survivors and people with multiple sclerosis. This review highlights the relationship between objective measures of fatigability with whole-body exercise and perceptions of fatigue as a priority for future research, given the importance of exercise in relieving symptoms of chronic fatigue and/or overall disease management. As chronic fatigue is likely to be specific to the individual and unlikely to be due to a simple biological or psychosocial explanation, tailored exercise programmes are a potential target for therapeutic intervention.

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**MOTS CLÉS**

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**Résumé** Le terme fatigue est utilisé pour décrire un symptôme pénible et persistant de fatigue physique et/ou mentale dans certaines populations cliniques, avec une pathophysiologie distincte, mais finalement complexe, multifactorielle et hétérogène. La fatigue chronique a des répercussions sur la qualité de vie, réduit la capacité d'effectuer des activités de la vie quotidienne et est généralement mesurée à l'aide d'outils subjectifs d'auto-évaluation. La fatigue se réfère également à une réduction aiguë de la capacité à produire une force ou puissance maximale au cours de l'exercice. La mesure classique de la fatigue induite par l'exercice implique des évaluations neuromusculaires avant et après une tâche fatigante. Les limites et les solutions de rechange à cette approche sont revues dans cet article en rapport avec l'exercice du membre inférieur et corps-entier, étant donné la pertinence fonctionnelle de cela en ce qui concerne la locomotion, la réadaptation et les activités de la vie quotidienne. Nous suggérons que les altérations des mécanismes centraux et/ou périphériques de la fatigue au cours de l'exercice puissent être liées aux sensations de fatigue chronique. Ainsi, les corrélats neurophysiologiques de la fatigue induite par l'effort sont brièvement examinés dans deux exemples cliniques : les survivants du cancer et les personnes atteintes de sclérose en plaques. Cette étude met en évidence la relation entre les mesures objectives de fatigabilité liée à l'exercice corps-entier et les perceptions de fatigue comme une priorité de recherche pour le futur, étant donné l'importance de l'exercice pour soulager les symptômes de la fatigue chronique et/ou la gestion globale de la maladie. Comme la fatigue chronique est susceptible d'être spécifique à l'individu et qu'il est peu probable qu'elle est due à une simple explication biologique ou psychosociale, des programmes d'exercices adaptés représentent une stratégie potentielle de traitement.

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## Introduction

The term fatigue is defined by the Oxford Dictionaries as "extreme tiredness resulting from mental or physical exertion or illness" and originates from the Latin *fatigare*—"to weary, to tire out" [182]. In this context, the effects of fatigue have received attention in occupations where extreme tiredness can have serious consequences, such as in pilots [79], military personnel [205], fire-fighters [39] and surgeons [183]. In addition, the term fatigue is used to describe a non-specific but debilitating symptom in a range of chronic diseases and disorders such as cancer [129], multiple sclerosis [101], stroke [32] and depression [11]. The subjective nature and severity of fatigue in healthcare is assessed using psychometric tools such as self-report questionnaires and scales [48,207]. There is no all-inclusive definition of clinical fatigue but the distinction from other uses of the term is that the symptom is the result of an underlying pathophysiology or its associated treatment. The term fatigue is also used in relation to a decline in performance induced by exercise, where exercise is defined inclusively as muscle activity with the potential to disrupt homeostasis [209]. Understanding fatigue in the context of the limitations to exercise performance has been a major research agenda for exercise physiologists for over a century [78,133]. Lively debate continues to enrich the literature and has provoked consideration across the entire discipline of exercise science [9,19,112,144].

The relative merit of objective and subjective measures of fatigue is dependent on the theoretical framework of study. For example, in a clinical population where fatigue may be chronic and have a devastating impact on quality of life (QoL) and/or physical function, a multidimensional approach is clearly warranted. In contrast, investigation

of the mechanisms of fatigue following a specific exercise task may primarily rely on objective physiological measures [125]. It follows that generic use of the term fatigue without explicit definition or consideration of fatigue-related phenomena in different populations or contexts can be problematic. This highlights the inadequacy of the single term "fatigue" for concepts which are readily acknowledged by both exercise scientists and clinicians as being multifactorial, interactive and complex. A taxonomy was suggested for use in clinical research using two domains: perceptions of fatigue and performance fatigability [97] and it was recently proposed that this framework should be implemented as a foundation to unify research in human performance [50]. There is certainly value in adopting a cohesive nomenclature and the emphasis in this review is on describing fatigue according to the application and the techniques used to measure it.

An early model of exercise-induced fatigue proposed that exercise is limited by muscle lactate accumulation secondary to an inadequate supply of oxygen due to a limited cardiac output [78]. In opposition to this model where exercise termination was considered the result of skeletal muscle anaerobiosis, the central governor/complex systems model proposes that exercise is regulated in an anticipatory manner, to ensure exercise terminates before catastrophic biological failure [102,142]. The latter model involves feed forward motor output to recruit an appropriate number of motor units (based on numerous physiological and psychological factors), continuous modification of pace via feedback from conscious sources and allows for the presence of an end-spurt in closed-loop tasks [143]. There are multiple models of fatigue [1,141] but a crucial divide is whether fatigue is studied with respect to a change in motor performance (for example, a decrease in the ability to

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