Fatigue biomarker index: An objective salivary measure of fatigue level

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ABSTRACT

Fatigue changed the composition of the small-molecular weight (sMW) proteome of saliva during a 10 h session of moderate (70% of maximum ventilatory threshold) physical exertion. Saliva samples were collected from nine recreationally trained cyclists participating in a cross-over study designed to simulate prolonged manual labor, a military operation or wildfire-suppression work. During each hour of the study, participants performed an exercise program that included upper and lower body exercises separated by short periods of recovery. Over the course of the study, fatigue level increased as suggested by a significant increase in the participants’ relative perceived exertion. The composition of the sMW proteome was investigated using reversed-phase liquid chromatography with mass-spectrometric detection. Isotopes of acetic anhydride were used for mass-specific labeling of samples and subsequent identification of ions with significant changes in intensity. Cluster analysis was used to identify a pair of peptides with concentrations that changed in opposite directions with fatigue level, i.e. concentration of one peptide increased while concentration of the other decreased. The sequences of the two peptides were determined by high-resolution mass spectrometry. The ratio of the ion intensities of these two peptides, referred to as the fatigue biomarker index, was calculated for subjects throughout the study. The FBI values from the start of the study likely arose from a different distribution than the FBI values measured at the end of the study (Mann–Whitney test, P < .05). While this study is restricted to a small population of recreationally trained cyclists performing exercise under controlled conditions, it holds promise for the development of an objective salivary measurement of fatigue that is applicable to a much broader population performing in uncontrolled environments.

1. Introduction

Fatigue degrades both physical and cognitive performance. The impact of fatigue is best exemplified by its position as the leading identifiable and preventable cause of accidents in transportation operations, surpassing even alcohol and drugs (Akerstedt, 2000). While fatigue levels are frequently assessed by self-reporting, an individual’s perception of fatigue is not a robust predictor of the ability to perform (Van Dongen, 2004). Moreover, compensation practices within some industries motivate individuals to distort their self-reported fatigue levels, even though the consequences of an error in those industries impact the lives of many others besides that of the impaired operator (Akerstedt, 2000). Clearly, there is a need for objective measures of fatigue, especially in situations when individuals are motivated to distort their self-reported level of fatigue (Caldwell et al., 2009).

Fatigue is caused by many different factors, including sleep deprivation, persistent mental activity and prolonged physical exertion. In the case of a sustained physical effort, fatigue is associated with a loss of power in peripheral muscles, as well as a perception of fatigue mediated by signaling pathways in the central nervous system (CNS) (Ament and Verkerke, 2009). The former is associated with the depletion of glycogen stores, the accumulation of metabolites and a perturbation in ionic balances within myocytes. The mechanism for the latter remains a topic of research, although the CNS-mediated perception of fatigue is associated with changes in levels of cytokines and/or neurotransmitters, such as interleukin (IL) 1, IL-6, tumor necrosis factor (TNF), serotonin, dopamine and tyrosine (Cannon and Kluger, 1983; Cannon et al., 1989; National Research Council, 2009). Prolonged physical exertion also triggers changes in the autonomic nervous system (ANS) marked by a simultaneous withdrawal of the parasympathetic nervous system (PSNS) and activation of the sympathetic nervous system (SNS) (Klein and Corwin, 2002). All of these physiological changes offer potential targets for monitoring fatigue level objectively, thereby removing the reliance on self-reporting of fatigue.

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