Centers of Advanced Medicine
Center for Medical Science of Fatigue

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General Summary

The Jikei Center for Medical Science of Fatigue (JCMSF) was established in 2014 with support from the Ministry of Education, Culture, Sports, Science and Technology-Supported Program for the Strategic Research Foundation at Private Universities. The JCMSF is aimed at contributing to human welfare through developing novel methods for the diagnosis, prevention, and care of fatigue-related diseases. For this aim, our research focuses on the mechanism of fatigue and fatigue-related diseases.

Resulting from work-related or other stress or insomnia, fatigue is something that everyone experiences. Long-term fatigue can cause cardiovascular dysfunction, mental disorders such as depression, and occupational sudden death (karoshi). Fatigue is therefore a major social problem. People recover from physiological fatigue with rest. Pathological fatigue, however, persists for 3 months or more and greatly affects QOL. As the latter requires therapeutic interventions, we must distinguish between physiological and pathological fatigue.

Research Activities

Human herpesvirus 6 and 7 are biomarkers for fatigue, which distinguish between physiological fatigue and pathological fatigue

Fatigue is frequently assessed by self-reporting using the Checklist Individual Strength, Profile of Mood States or visual analog scales. However, its perception is influenced by negative or positive work events and compensation practices can motivate workers to distort self-reported fatigue levels, which therefore may not be a correct indicator. We focused on human herpesvirus (HHV-) 6 and HHV-7, which are reactivated by fatigue. These viruses cause exanthem subitum and establish latency in almost all individuals. Frequently reactivated and shed in saliva, they are potentially a useful fatigue biomarker. HHV-6 is useful for monitoring cognitive function, and adverse reactions in cancer chemotherapy and HHV-7 for assessing fatigue in end-stage renal disease.

Everyone experiences physiological fatigue and recovers with rest. Pathological fatigue, however, greatly reduces quality of life and requires therapeutic interventions. It is therefore necessary to distinguish between the two but there has been no biomarker for this. We report on the measurement of salivary human herpesvirus (HHV-) 6 and HHV-7 as biomarkers for quantifying physiological fatigue. They increased with military training and work and rapidly decreased with rest. Our results suggested that macrophage activation and differentiation were necessary for virus reactivation. However, HHV-6 and HHV-7 did not increase in obstructive sleep apnea syndrome (OSAS), chronic fatigue syndrome (CFS) and major depressive disorder (MDD), which are thought to cause path-

ological fatigue. Thus, HHV-6 and HHV-7 would be useful biomarkers for distinguishing between physiological and pathological fatigue. Our findings suggest a fundamentally new approach to evaluating fatigue and preventing fatigue-related diseases.

Caregiver burden and fatigue in caregivers of people with dementia: Measuring human HHV-6 and HHV-7 DNA levels in saliva

Purpose: We examined chronic fatigue, which has not been investigated in detail, in caregivers for family members with dementia.

Methods: The subjects of this study were 44 community-dwelling family caregivers and 50 elderly persons who were not caregivers. We measured salivary levels of HHV-6 and HHV-7 DNA and used the Chalder Fatigue Questionnaire (CFQ) to assess levels of fatigue; we also used the Center for Epidemiologic Studies Depression Scale, the Physical Activity Scale for the Elderly, the Zarit Caregiver Burden Interview, the Mini-Mental State Examination, the Assessment of Motor and Process Skills, and the Dementia Behavior Disturbance Scale.

Results: The salivary HHV-6 DNA levels and the CFQ scores were significantly higher in caregivers than in elderly persons. The salivary HHV-6 DNA levels in caregivers were significantly correlated with depressive symptoms, the cognitive function of the family members with dementia, and the activities of daily living/instrumental activities of daily living abilities of the patients. The CFQ scores in caregivers significantly correlated with caregiver burden, depression symptoms, leisure physical activity, the number of other family caregivers, the hours spent by caregiving per week, behavior disturbances, and activities of daily living/instrumental activities of daily living abilities.

Conclusions: The salivary HHV-6 DNA level is a new biomarker for caregiver exhaustion. To estimate the burden of caregivers of family members with dementia, fatigue assessments should be performed with a questionnaire, such as the CFQ, and the search for a biomarker, such as the salivary HHV-6 DNA level.