Carnitine-deficient JVS (juvenile visceral steatosis) mice as a fatigue model

Takeyori Saheki, Meng Xian Li, Masahisa Horiuchi, Goichiro Yoshida, Department of Biochemistry, Faculty of Medicine Kagoshima University

Carnitine deficiency might be related to chronic fatigue syndrome as reported by Kuratsune et al.[1] In this study we use carnitine-deficient JVS mice which are generalized carnitine deficiency caused by a defect of Octn2, plasma membrane carnitine transporter[2,3], if they show some fatigue-related symptoms and if so, what is the mechanism underneath especially at central nervous system.

Homozygous JVS (j/j) mice showed much lower locomotor activity (LA) in the night under fasted conditions, while they were as active as the heterozyote (+/j) and wild type (+/+) mice under fed conditions. Since JVS mice were active with a synthetic diet containing no carnitine and with sugar cube only, carnitine is not directly related to the low LA of fasted JVS mice. The blood glucose and free fatty acid levels were varied among the mice with various dietary conditions, but seemed not to be determinants of the LA. After withdrawal of food for 24 h, the JVS mice ate much less diet as compared with the control mice, suggesting they were anorexic. Administration of carnitine once at the beginning or twice a day normalized the lower LA and food intake.

Serum leptin was decreased to a lower level under fasting in control mice, but was not significantly decreased in JVS mice. Proportion of c-Fos expressed cells in orexin neurons detected by double immunostaining method was increased under fasting in control mice, but decreased in JVS mice. These results strongly suggest that disturbance of central nervous system is involved in pathogenesis of these symptoms of JVS mice under fasted conditions. Very similar symptoms were also found in wild-type mice in which fatty acid oxidation was inhibited by administration of methyl palmoxirate, an inhibiter of carnitine palmitoyltransferase 1 (CPT1), indicating the low LA and anorexia found in JVS mice under fasted conditions are not directly related to carnitine deficiency but related to disturbance of fatty acid oxidation in general.

References

1. Kuratsune H, Yamaguti K, Takahashi M, et al. Acylcarnitine deficiency in chronic fatigue syndrome. Clin Infect Dis (1994) 18, S62-67.
2. Horiuchi M, Kobayashi K, Yamaguchi S, et al. Primary defect of juvenile visceral steatosis (jvs) mouse with systemic carnitine deficiency is probably in renal carnitine transport system. Biochim Biopys Acta (1994) 1226, 25-30.

3. Nezu J, Tamai I, Oku A et al. Primary systemic carnitine deficiency is caused by mutations in a gene encoding sodium ion-dependent carnitine transporter. Nat Genet (1999) 21, 91-94.