

Brain regions involved in fatigue sensation: reduced acetylcarnitine uptake into the brain.

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Fatigue is an indispensable sense for ordering rest. However, the neuronal and molecular mechanisms of fatigue remain unclear. Chronic fatigue syndrome (CFS) with long-lasting fatigue sensation seems to be a good model for studying these mechanisms underlying fatigue sensation. Recently, we found that most patients with CFS showed a low level of serum acetylcarnitine, which well correlated with the rating score of fatigue, and that a considerable amount of acetyl moiety of serum acetylcarnitine is taken up into the brain. Here we show by metabolite analysis of the mouse brain that an acetyl moiety taken up into the brain through acetylcarnitine is mainly utilized for the biosynthesis of glutamate. When we studied the cerebral uptake of acetylcarnitine by using [2-(11)C]acetyl-L-carnitine in 8 patients with CFS and in 8 normal age- and sex-matched controls, a significant decrease was found in several regions of the brains of the patient group, namely, in the prefrontal (Brodmann's area 9/46d) and temporal (BA21 and 41) cortices, anterior cingulate (BA24 and 33), and cerebellum. These findings suggest that the levels of biosynthesis of neurotransmitters through acetylcarnitine might be reduced in some brain regions of chronic fatigue patients and that this abnormality might be one of the keys to unveiling the mechanisms of the chronic fatigue sensation.

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