

Development of animal models

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To establish an animal model of fatigue, we kept rats in a cage filled with water to a height of 1.5 cm. We selected a weight-loaded forced swimming test for evaluation of the extent of fatigue. Animals kept in the wet cage for 5 days showed a reduction in 2-[¹⁸F]fluoro-2-deoxy-D-glucose ([¹⁸F]FDG) uptake into their brain. The session for 1 day showed significantly increased 5-hydroxyindoleacetic acid (5-HIAA)/5-hydroxytryptamine (5-HT) and [3,4-dihydroxyphenylacetic acid (DOPAC) + homovanillic acid (HVA)]/dopamine (DA) ratios in all brain regions, but the session for 5 days showed the restoration of the 5-HIAA/5-HT ratio in the hippocampus and hypothalamus and in the (DOPAC + HVA)/DA ratio in the striatum and hypothalamus. After the fatigue session, they were returned to their home cage. Rats resting for 15 min or 2 hr showed reduced [¹⁸F]FDG uptake in their brain. Rats resting for 1 hr showed a significantly increased ratio of 5-HIAA/5-HT in the frontal cortex, hippocampus, and cerebellum; and the ratio of (DOPAC + HVA)/DA tended to be increased as compared with the control. Our data suggest that decreased glucose uptake and insufficient serotonin and dopamine turnover introduced by deprivation of rest were correlated with central fatigue and that improvement of glucose uptake and increased serotonergic and dopaminergic neuronal activities are associated with recovery from central fatigue.

Published Papers

M. Tanaka, F. Nakamura, S. Mizokawa, A. Matsumura, K. Matsumura, Y.

Watanabe. Role of acetyl-L-carnitine in the brain: revealed by Bioradiography. *Biochem Biophys Res Commun.* 2003 Jul 11;306(4):1064-9.

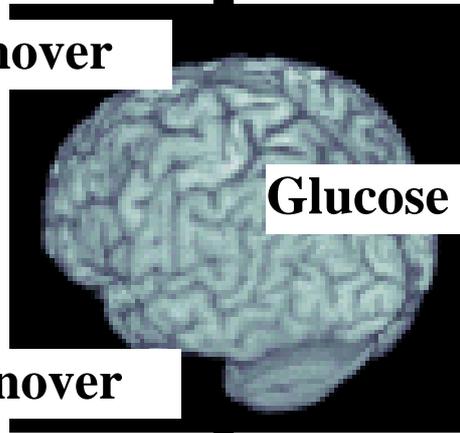
M. Tanaka, F. Nakamura, S. Mizokawa, A. Matsumura, K. Matsumura, T. Murata, M. Shigematsu, K. Kageyama, H. Ochi, Y. Watanabe. Role of lactate in the brain energy metabolism: revealed by Bioradiography. *Neuroscience Research*, submitted.

M. Tanaka, F. Nakamura, S. Mizokawa, A. Matsumura, S. Nozaki, Y. Watanabe. Establishment and assessment of a rat model of fatigue. *Neuroscience Letters*, submitted.

S. Mizokawa, M. Tanaka, A. Matsumura, S. Nozaki, Y. Watanabe. Recovery from fatigue: changes in local brain [¹⁸F]FDG utilization measured by autoradiography and in brain monoamine levels of rat. *Neuroscience Letters*, submitted.

Deprivation of rest

Serotonin Turnover

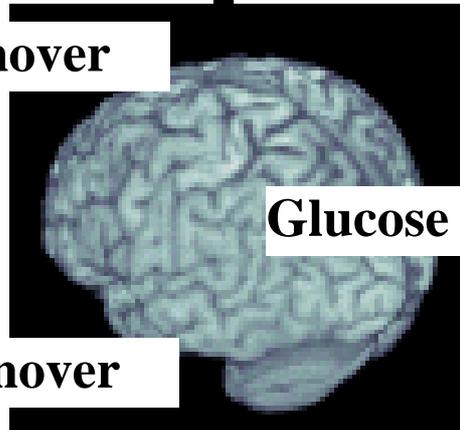


Glucose metabolism

Dopamine Turnover

Central fatigue

Serotonin Turnover



Glucose metabolism

Dopamine Turnover

Recovery from fatigue