# Mitochondria defects linked to social behavior and spatial memory

4 December 2007

Respiration deficiencies in mitochondria, the cell's powerhouses, are associated with changed social behavior and spatial memory in laboratory mice, report scientists at the American Society for Cell Biology 47th Annual Meeting.

This research, conducted by Atsuko Kasahara and colleagues at the University of Tsukuba, Kyoto University, and the Fujita Health University in Japan, may open the door to understanding the connection in humans between mitochondrial breakdowns and mental illness.

Previous studies have shown that mitochondrial "cytopathies" can underlie conditions as diverse as muscle weakness, lactic acidosis, mental retardation, stroke, diabetes, or heart disease. Significant mitochondrial genetic defects have been found in patients diagnosed with neurodegenerative diseases like Alzheimer's and Parkinson's. It also has been reported that mutated mtDNAs are associated with mood disorders and schizophrenia.

Since the brain's normal functioning depends on a large amount of the ATP energy that mitochondria harvest from food through aerobic respiration, Kasahara and colleagues theorized that pathogenic DNA in mitochondria -- mtDNA mutations -- and decreased ATP could affect behavior. The researchers had previously generated a trans-mitochondrial mouse model. Their "mito-mouse" model, B6COXI, had the nuclear genome of a standard lab mouse, C57BL/6 (B6WT), but a missense mutation in the COXI gene of its mtDNA. The blocked COXI gene is involved in the last stage of the mitochondrial energy processing cycle called oxidative phosphorylation.

Without active COXI, the mito-mouse had lower ATP output from mitochondria and a build-up of lactic acid as glycolysis compensated for the lost energy. Otherwise the B6COXI mice looked healthy and without any other signs of serious mitochondrial disease. The researchers wondered if their B6COXI mice could be models for less-visible mental disorders, and set out to find out whether this showed up in tests of social behavior and spatial memory.

The researchers evaluated the ability of the mice to remember locations in a maze. Surprisingly, the spatial memory of the B6COXI mice was actually elevated compared with controls. However, in tests to measure the social behavior of mice toward unfamiliar mice, the B6COXI mice did poorly. Kasahara and colleagues believe their results demonstrate that mitochondrial respiration deficiencies are associated with changed social behavior and spatial memory.

Source: American Society for Cell Biology