NEWS

Mitochondrial function disrupted in children with autism

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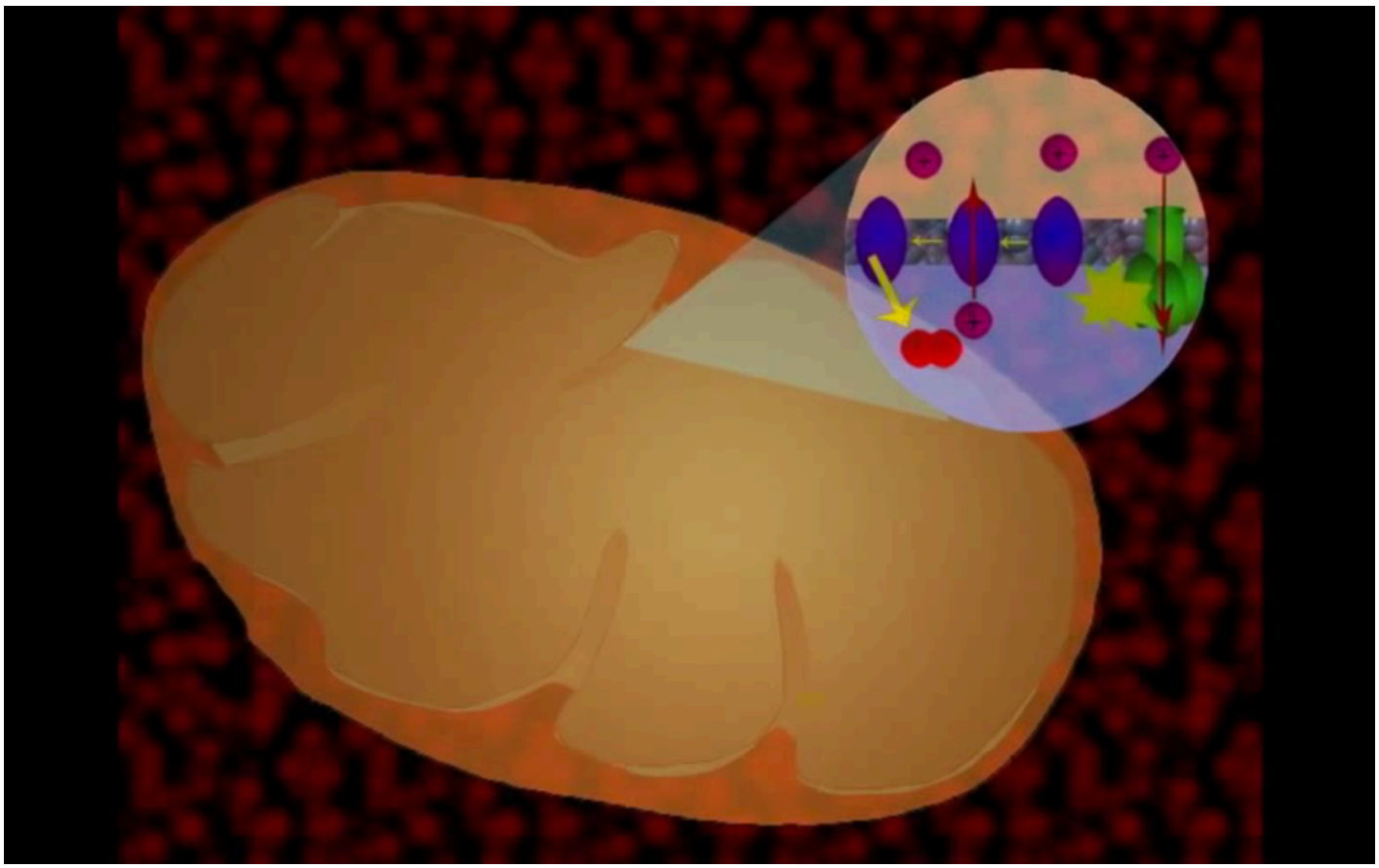

The first study to look at mitochondria — the powerhouses of the cell — in postmortem brain tissue taken from children with autism has found significant abnormalities in their function in some regions of the brain.

These findings, reported online in the *Journal of Neurochemistry* in January[1], are fueling discussion of the **role mitochondria may play in autism**.

The researchers discovered that in children with autism, protein expression in the electron transport chain — a chain reaction that drives energy production in the cell — is disrupted in mitochondria located in the cerebellum and in the frontal and temporal regions of the brain.

"These are the brain regions where neuropathological changes have also been observed in autism," says lead investigator **Abha Chauhan**, head of the developmental neuroscience laboratory at the New York State Institute for Basic Research in Developmental Disabilities.

Curiously, researchers observed these abnormalities only in the brain tissue of children with autism, not in that of adults with the disorder, or in age-matched controls.

In December, a different group of researchers reported finding mitochondrial defects in the white blood cells of children with autism[2]. That study found that key biomarkers of mitochondrial function are markedly lower in children who have the disorder compared with controls.

The small size of the sample — ten children — and the use of white blood cells rather than muscle tissue weakened the findings, according to some researchers. However, even critics admitted that the report added to a growing body of evidence identifying mitochondrial defects in a subpopulation of children with autism.

"There is now ample evidence that mitochondria are abnormal in some cases of autism," says **Salvatore DiMauro**, professor of neurology at Columbia University.

Provocative links:

The first suggestion that mitochondrial disease might be implicated in autism came in 1998[3]. In 2008, the **U.S. Court of Federal Claims Vaccine Program**, dubbed the 'vaccine court,' ruled that vaccination had aggravated a pre-existing mitochondrial disorder in a 9-year-old girl, leading to her degenerative brain disease with features of autism.

Though research has found no link between vaccination and autism, some researchers estimate that at least ten percent of children with regressive autism have an underlying mitochondrial disorder[4].

In the new study, researchers honed in on the electron transport chain, which is a key element of mitochondrial function, and generates both energy and free radicals — molecules that disrupt cellular processes. Normal cellular operations create a certain amount of oxidative stress, caused by free radicals and reactive oxygen species. Cellular breakdown caused by oxidative stress is thought to be involved in many diseases as well as in normal aging.

"Our previous studies had shown that there is oxidative stress in autism and we found brain region-specific increases in oxidative stress," says Chauhan. "That was the reason we started looking at mitochondria."

The researchers looked at the five stages of the electron transport chain — complexes I through V — in brain tissue samples from the **Brain and Tissue Bank for Developmental Disorders** at the University of Maryland.

When they divided the samples by age into one group of samples ranging in age from 4 to 10 years and another ranging from age 14 to 39, they found that 60 percent of the first group have significantly lower levels of the complexes in the cerebellum, frontal cortex and temporal cortex.

These results are not surprising, says **Richard Kelley**, director of the division of metabolism at the Kennedy Krieger Institute in Baltimore. Kelley says most of the children who have regressive autism that he sees at the clinic have mitochondrial abnormalities. Many of those anomalies appear in the same part of the electron transport chain — Complex I — identified in the new study.

Still, Kelley says he is puzzled by the fact that defects uncovered in the new study are specific to certain brain regions. "What we find is clearly a systemic abnormality," he says.

It's clear that mitochondrial dysfunction is far more common than previously suspected, says DiMauro: a 2008 paper reported, for instance, that 1 in 200 healthy children carry one of the most common mutations[5]. "Many of these children look healthy and will likely remain healthy throughout life," he says.

Kelley says a second 'hit' — possibly an environmental or dietary factor layered on the existing genetic vulnerability — may be needed to tip the individual into a disease state.

"We really have to get down to the pathophysiology of the process," Kelley says. "Genetics alone is not going to do it."

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