MedicalXpress

Feet first? Old mitochondria might be responsible for neuropathy in the extremities

March 3 2011

The burning, tingling pain of neuropathy may affect feet and hands before other body parts because the powerhouses of nerve cells that supply the extremities age and become dysfunctional as they complete the long journey to these areas, Johns Hopkins scientists suggest in a new study. The finding may eventually lead to new ways to fight neuropathy, a condition that often accompanies other diseases including HIV/AIDS, diabetes and circulatory disorders.

Neuropathies tend to hit the feet first, then travel up the legs. As they reach the knees, they often start affecting the hands. This painful condition tends to affect people who are older or taller more often than younger, shorter people. Though these patterns are typical of almost all cases of neuropathy, scientists have been stumped to explain why, says study leader Ahmet Hoke, M.D., Ph.D., a professor of neurology and neuroscience at the Johns Hopkins University School of Medicine.

He and his colleagues suspected that the reason might lie within mitochondria, the parts of cells that generate energy. While mitochondria for most cells in the body have a relatively quick turnover — replacing themselves every month or so — those in nerve cells often live much longer to accommodate the sometimes long journey from where a cell starts growing to where it ends. The nerve cells that supply the feet are about 3 to 4 feet long in a person of average height, Hoke explains. Consequently, the mitochondria in these nerve cells take about two to three years to travel from where the nerve originates near the spine to where it ends in the foot.

To investigate whether the aging process during this travel might affect mitochondria and lead to neuropathy, Hoke and his colleagues examined nerve samples taken during autopsies from 11 people who had HIV-associated neuropathy, 13 who had HIV but no neuropathy, and 11 HIV-negative people who had no signs of neuropathy at their deaths. The researchers took two matched samples from each person — one from where the nerves originated near the spine and one from where the nerves ended near the foot.

They then examined the DNA from mitochondria in each nerve sample. Mitochondria have their own DNA that's separate from the DNA in a cell's nucleus.

The researchers report in the January Annals of Neurology that in patients with neuropathy, DNA from mitochondria in the nerve endings at the ankle had about a 30-fold increase in a type of mutation that deleted a piece of this DNA compared to mitochondrial DNA from near the spine. The difference in the same deletion mutation between the matched samples in people without neuropathy was about threefold.

Since mitochondria quit working upon a person's death, the scientists looked to a monkey model of HIV neuropathy to see whether these deficits affected mitochondrial function. Tests showed that the mitochondria from the ankles of these animals didn't function as well as those from near their spines, generating less energy and producing faulty proteins and damaging free radicals.

Hoke explains that as mitochondria make the trek from near the spine to the feet, their DNA accumulates mutations with age. These older mitochondria might be more vulnerable to the assaults that come with disease than younger mitochondria near the spine, leading older mitochondria to become dysfunctional first. The finding also explains why people who are older or taller are more susceptible to neuropathies,

Hoke says.

"Our mitochondria age as we age, and they have even longer to travel in tall people," he says. "In people who are older or taller, these mitochondria in the longest nerves are in even worse shape by the time they reach the feet."

Hoke notes that if this discovery is confirmed for other types of neuropathy, it could lead to mitochondria-specific ways to treat this condition. For example, he says, doctors may eventually be able to give patients drugs that improve the function of older mitochondria, in turn improving the function of nerve cells and relieving pain.

Provided by Johns Hopkins Medical Institutions