To fix diabetic nerve damage, blood vessels and support cells may be the real targets of treatment

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Blood vessels and supporting cells appear to be pivotal partners in repairing nerves ravaged by diabetic neuropathy, and nurturing their partnership with nerve cells might make the difference between success and failure in experimental efforts to regrow damaged nerves, Johns Hopkins researchers report in a new study.

About 20 percent of diabetics experience neuropathy, a painful tingling, burning or numbness in the hands and feet that reflects damage to nerves and sometimes leads to infections and amputation of the toes, fingers, hands and feet over time. Current treatments for diabetic neuropathy focus on relieving symptoms, but don't address the root cause by repairing nerve damage. Previous research has shown that nerve cells' long extensions, known as axons, regenerate slowly in diabetics, scuttling various experiments to regrow healthy nerves, explains study leader Michael Polydefkis, M.D., M.H.S., associate professor of neurology at the Johns Hopkins University School of Medicine.

Searching for the reasons behind this slow regeneration, Polydefkis, along with Johns Hopkins assistant professor of neurology Gigi Ebenezer, M.B.B.S., M.D., and their colleagues recruited 10 patients with diabetic neuropathy and 10 healthy people of similar ages and took tiny (3 millimeters) "punch" biopsies from the skin of each participant's thigh. Several months later, they took 4 mm biopsies from the same site to see how the nerves, blood vessels and nerve-supporting cells, called

Schwann cells, were growing back into the healing biopsy site.

In both the neuropathy patients and the healthy individuals, results reported in the June issue of *Brain* showed that the first to grow into the healing skin were blood vessels, followed soon after by Schwann cells and then axons, which appeared to use the blood vessels as scaffolds. However, the entire process was significantly delayed for the neuropathy patients. Not only was axon regeneration slower compared to the healthy patients, as expected, but blood vessel growth rate was also slower, and fewer Schwann cells accompanied the growing axons into the healing skin.

"Our results suggest that regenerative abnormalities associated with diabetes are widespread," Polydefkis says. "They're not just affecting nerves—they're also affecting blood vessel growth and Schwann cell proliferation."

Additionally, he says, the findings could explain why blood vessel-related problems, such as heart attacks and strokes, often accompany diabetes. Slowed regeneration of damaged blood vessels could contribute to these conditions as well, he explains.

Polydefkis says the findings provide potential new targets for treating neuropathy and vascular problems. By promoting blood vessel and Schwann cell growth, researchers might be able to speed up axon regeneration and successfully repair damaged nerves and blood vessels, potentially combating diabetic neuropathy and vascular complications simultaneously.

Provided by Johns Hopkins Medical Institutions

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