Calcium Channels Dwindle in Old Hearts

If grandmother can't get up the stairs the way she used to, she might long for stronger muscles and sturdier bones. New research suggests she could also use more doors in her heart nerves.

Scientists studying cardiac nerves have taken an important step toward explaining why aging diminishes the heart's ability to pump harder and faster under exertion. At this week's meeting of the American Society for Pharmacology and Experimental Therapeutics, held in Milwaukee, researchers described rat studies showing evidence of fewer calcium "gateways" in the aging heart's sympathetic nerves.

That gateway shortage probably diminishes the flow of calcium into those nerves, they say, impeding the transmission of signals that ordinarily would tell the heart muscle to speed and strengthen contractions as the body works harder.

"It is well known in the elderly that when they are put under stress you see failure of the [cardiovascular] system to respond," says pharmacologist Jay Roberts of the Medical College of Pennsylvania in Philadelphia. Those same older hearts may function fine under stress-free circumstances, he notes.

Secretion of the neurotransmitter norepinephrine in rat hearts decreases with age. Norepinephrine causes the heart to beat faster and more forcefully in response to increased physiological demands. However, norepinephrine's release depends on the influx of calcium ions into the sympathetic nerves.

When a nerve cell is stimulated, calcium-specific gateways, or channels, in its membrane open to allow an inrush of ions from the surrounding fluids where they are concentrated. Calcium's presence then causes the sympathetic nerve cell to release norepinephrine into a narrow gap, or synapse, between the stimulated cell and an adjacent nerve or muscle cell. Thus the signal travels from one cell to the next.

In an earlier experiment, described in the June JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Roberts and his co-workers tried to influence levels of norepinephrine excretion by using a calcium-binding chemical called an ionophore, which can transport calcium ions across cell membranes with or without gateways. In aging rat hearts, the ionophore boosted norepinephrine secretion to nearly youthful levels, they found. The restoration hints that a disappearance of calcium channels causes the decline.

New evidence seems to confirm the calcium-channel decrease. At the meeting, Roberts' co-worker Ajay M. Parikh reported that he has indirectly counted calcium channels in young and old rat hearts, finding significantly fewer channels in the older hearts.

The Philadelphia team began by removing the hearts of five 6-month-old rats and five 24-month-old rats. (Normally, these rats live for about 26 months.) By adapting a technique used in brain research, they processed each heart to isolate a purified nerve extract. Next they added a radioactively labeled snail venom, which binds to calcium channels. Measurements of radioactivity in each nerve sample consistently indicated fewer channels in older-heart nerves, Parikh says.

The researchers do not know why the gateways disappear. They concede that a reduced population of neurons could explain the finding, but then say this would not explain the restored norepinephrine levels induced by the ionophore. The answer may lie in how nerve cells produce the proteins that form the calcium channels, Roberts says.

The group's findings represent "a big step forward," comments Philip J. Scarpace at the Department of Veterans' Affairs Hospital in Gainesville, Fla. In particular, Parikh's work will allow researchers "to quantitatively assess one important factor in the regulation of norepinephrine release," Scarpace says.

Scarpace studies norepinephrine receptors on the receiving end of the synapse. Those receptors also change with age, suggesting that a variety of age-related factors contribute to the decline in heart responsiveness, he says. Nonetheless, he thinks the calcium-gate decrease "could be a very important one."

Parikh postulates that ionophores or similar chemicals might eventually emerge as a tonic for countering the age-induced decline in heart responsiveness. Cardiologist Asher Woldow at the Philadelphia Geriatric Clinic agrees that such drugs might prove valuable, but he doesn't foresee using them to intervene in the normal aging process.

Instead, Woldow thinks physicians would probably use ionophores as stimulants — like the digitalis and digoxin typically prescribed today — in cases of weak pumping due to congestive heart failure. He cautions, however, that only about half the U.S. cases of congestive heart failure respond well to stimulants, and that chemical stoking of damaged hearts increases the risk of fatal heart arrhythmias. — *P.L. Weiss*

Radar-mapper Magellan orbits Venus

The Magellan spacecraft climaxed its 15-month trip to Venus on Aug. 10 by entering a near-perfect orbit from which scientists expect to compile the most detailed maps yet of the cloud-covered planet's surface.

Magellan now orbits Venus every 3 hours and 15 minutes, following an elliptical orbit that ranges from 294 to 8,472 kilometers above the surface. It achieved an orbit so close to the one intended that engineers canceled a maneuver to "fine-tune" the satellite's flight track around Venus, says project manager Anthony J. Spear of NASA's Jet Propulsion Laboratory in Pasadena, Calif.

The craft's primary goal is to map the planet's surface, using synthetic-aperture radar and a radar altimeter that measures the ups and downs of Venus' topography. Magellan's orbit will carry it over the entire surface every 243 days, and scientists hope to get data from as many as five complete passes. The first pass should map 70 to 80 percent of the surface. Later passes should fill in the blanks. On these mappings, scientists will aim the radar at different angles to create stereographic, three-dimensional radar images and gain a more precise view of the planet's small-scale surface features.

Radar maps of Venus have also been made by the U.S. Pioneer Venus, mostly in 1979; by the Soviet Venera 15 and 16 craft in 1983; and by Earth-based instruments. Magellan scientists plan to check out its equipment and begin mapping about Sept. 1, Spear says.

An unexpected event occurred when Magellan jettisoned the solid-propellant rocket motor that had put it into orbit. Spear says the jolt apparently caused one set of gyros in Magellan's positioning system to switch off and another set to take over. The change posed no problem for the mission, he says, and the original gyros automatically switched back on and are available if needed.

A component failure in the memory of one of Magellan's computers should cause only limited problems, according to Spears. Engineers expect to radio Magellan instructions to work around the failed component, and Spear says the only loss will be 1,000 words of reserve capacity from the computer's 34,000-word memory. — *J. Eberhart*