Human Brain Neurons Grown in Culture

For the first time, neuroscientists have maintained mature, human brain neurons in long-term cultures, achieving a feat that many researchers thought lay a decade away. Beyond facilitating unprecedented studies of the human central nervous system, the accomplishment may provide an ethical end-run around controversial transplants of fetal brain cells.

"One of the issues in brain research has always been that neurons of the brain and spinal cord don't divide and don't live long in culture," says Solomon H. Snyder of the Johns Hopkins University School of Medicine in Baltimore. The failure of neurons to engage in further cell division after reaching maturity severely limits the body's ability to recover from damage to the central nervous system. And in the laboratory — where researchers would like to study the chemical messenger systems through which neurons communicate, and apply that information to drug development — human brain neurons "might last a few hours, then that's it," Snyder says.

Gabriele V. Ronnett, working with Snyder and three other colleagues, saw an opportunity to break through that research barrier when an 18-month-old girl arrived at Johns Hopkins to undergo surgery for unilateral megalencephaly. The rare disorder, in which one side of the brain grows substantially larger than the other, occurs when neurons in that hemisphere undergo too many cell divisions before they mature. The neuronal imbalance in the girl's brain was causing seizures, and surgeons successfully removed the enlarged hemisphere — a treatment that has proved helpful in several similar cases.

Snyder's group took neurons from the excised gray matter and placed them in a blood-rich culture medium. After 21 days, nearly all the cells had died, but a few continued growing well and dividing. In the 19 months since, the team has subcultured these colonies of neurons onto new culture plates more than 20 times, with no significant changes in cellular appearance or growth characteristics, they report in the May 4 SCIENCE.

Nobody knows what triggers the extra proliferation of immature neurons in unilateral megalencephaly or what made the girl's cells amenable to life in a culture dish. But unlike neurons taken from central nervous system tumors — which scientists can maintain in culture but which are generally considered poor models of normal neurons — these cells are not cancerous in appearance or behavior, Snyder says.

For example, when his group exposes the cultured cells to brain chemicals called nerve growth factors, the cells divide normally until they fill the culture dish, gradually differentiating into mature neurons. In the absence of growth factors, the cells "de-differentiate" into what Snyder tentatively calls "cortical neuronal stem cells" — immature neurons not yet committed to a particular line of development. Such cells, until now unavailable for study, have the potential to become any of the several varieties of mature neurons that together make up the cerebral cortex, the brain structure responsible for cognition and the interpretation of sensory impressions. Each mature neuron variety in the brain secretes and responds to its own combination of chemical messengers, or neurotransmitters.

Snyder says the cultured neurons should prove valuable for studies of brain cell development, differentiation and neurotransmitter systems, and should help pharmacologists design drugs for various neurological diseases. "Pretty much anything you want to know about the brain you can find out better with the availability of an *in vitro* system," he says.

Moreover, he says, the cultured cells may someday preclude the need for human fetal cells in experimental treatments for neurological disorders. Fetal nerve-cell transplants have shown some promise in patients with Parkinson's disease, and scientists have proposed using them to treat other diseases such as Alzheimer's. But an inability to culture these cells, which researchers instead must obtain from aborted fetuses, has stirred a national debate about the ethics of the procedure (SN: 12/5/88, p.296).

Although the cultured neurons maintained by the Hopkins team do not secrete dopamine — the neurotransmitter lacking in Parkinson's patients — Snyder says scientists could almost certainly genetically engineer them to do so. He notes that non-nerve cells have already proved amenable to the insertion of a dopamine gene, with therapeutic effects in rats (SN: 12/9/89, p.378). — *R. Weiss*

Antenna jam delays Hubble's first light

A few days after astronauts eased the Hubble Space Telescope into orbit from the shuttle Discovery, Earth-bound engineers still struggled cautiously to get the costly instrument working. Before seeing even a glimmer of light from space, the telescope automatically put itself on "safe hold" when a cable apparently jammed the swivel mounting of one of its two principal antennas.

These antennas will relay observations of stars and other astronomical objects through a pair of tracking satellites to the ground (SN: 1/6/90, p.8). After analyzing the problem, however, Jean Olivier, the telescope's deputy project manager at NASA's Marshall Space Flight Center in Huntsville, Ala., said the effect on the telescope's overall science mission will probably prove "very small."

Hubble's principal, or "high-gain," antennas are designed to turn through an angle of plus or minus 93° in each of their two swivel directions. To prevent recurrence of the jamming difficulty, engineers tentatively decided early this week to limit the antennas to plus or minus 78°. In this way they hope to avoid having the telescope "safe itself" again, shutting down its various systems while engineers analyze a problem.

The telescope "has many more levels of safety systems than any vehicle we've ever flown," says David R. Skillman, the project's chief engineer at NASA's Goddard Space Flight Center in Greenbelt, Md. "The safe-mode systems have been tested and exercised very well. It's pretty idiot-resistant."

The limited antenna motion may mean that the telescope cannot always send its data directly to Earth through the satellites, says Michael M. Harrington of Marshall. He notes, however, that a possible alternative may be to store the information on one of three onboard tape recorders and transmit it to Earth at more convenient times.

After engineers finish checking out the antenna system, the next big event on the schedule is "first light" — the space telescope's first observation of a light source in the heavens. Astronomers plan to target a portion of a star cluster known as NGC 3532 in a Milky Way constellation called Carina, about 1,500 light-years from Earth and readily visible to the naked eye in the southern sky.

The space telescope's first look at an astronomical object will come via the wide-field planetary camera, one of five scientific instruments onboard. The date of "first light" will depend on when the engineers manage to move the telescope past its initial difficulties, but it could come as early as May 5.

— *J. Eberhart*