Tracing Earliest Neurons' Migration

In a vertebrate embryo, the brain develops when neurons are generated along the lining of the brain's innermost cavities, the ventricles, and migrate to the outer rim of the brain. There they settle, gradually building up the many layers of the mature brain.

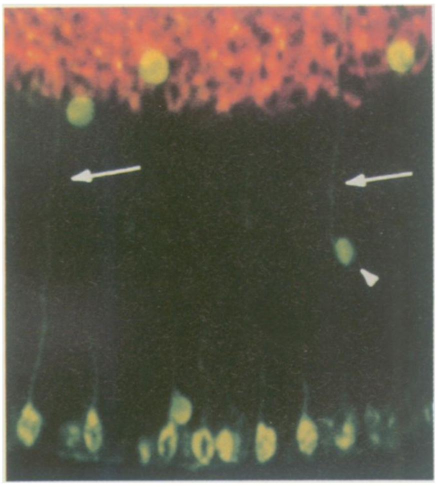
Scientists know little about the earliest stages of this process. Lacking a way to identify very young neurons, researchers could not tell them from nonneuronal brain cells, known as glia.

Now, researchers at Case Western Reserve University in Cleveland have found an antibody that labels these earliest neurons in rat embryos. By attaching a fluorescent tag to the antibody, the scientists can light up immature neurons as they arise in the ventricles and move away from their birthplace.

"We think that this antibody labels an unknown and newly discovered population [of neurons] that is very widespread throughout the central nervous system," says Jerry Silver, a Case Western neuroscientist. These cells occur in the retina, the spinal cord, and the brain's cortex, Silver's team reported at the annual meeting of the Society for Neuroscience, held this week in Washington, D.C.

The immature neurons first appear around the 11th day after gestation, when the embryo is about the size of a grain of rice, explains Silver. Previously, researchers could not visualize neurons until a day later, when many were well on their way to their destinations.

Earlier studies had discovered that neurons leave the ventricles by crawling along slender cells, called radial glia, that span the brain from center to surface, like the spokes of a wheel. Other studies showed that some neurons cross the brain obliquely rather than heading straight for the outer regions.



Earliest phase of neuronal migration in the cortex, 15 days after gestation. Emerging neurons (green, at bottom) extend thin arms upward (arrows). A slightly older neuron is ascending along its arm (arrowhead); three neurons have already arrived in the upper cortical zone (red).

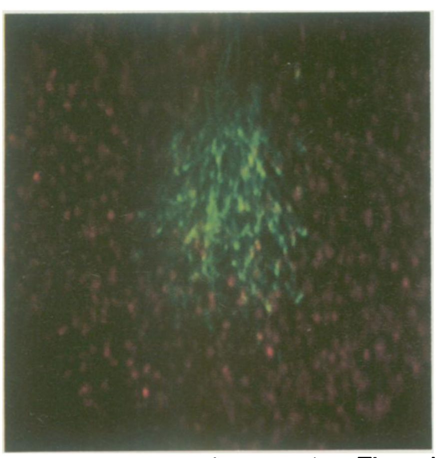
However, Perry A. Brittis, Silver's co-worker, observed that the youngest neurons do neither. Instead, each cell sends out a thin process to the brain's rim and transfers its nucleus and cellular material along that thread, much as a yo-yo moves up on its string. As the cells move, they lose these trailing processes. First described in 1970, this kind of cell migration had almost been forgotten, Silver notes.

"At that very early stage, it seems to us, this 'yo-yoing' is the easiest way for the neurons to reach the brain's surface," holds Brittis. "Days later, as the brain becomes more complex, they wander along the radial glia or in oblique directions, as was demonstrated earlier. Our antibody also captures that."

"It's a neat study," comments Dennis D. M. O'Leary, a neuroscientist at the Salk Institute for Biological Studies in La Jolla, Calif. "It shows very convincingly something that several researchers have suspected for a long time."

As cells leave the ventricles, new ones take their place, says Silver, continually replenishing the supply of immature neurons to populate the developing brain.

– G. Strobel



Photos: Brittis/Silver

Rat retina 13 days after gestation. The red cells, scattered throughout, are neuronal precursors – immature cells that until now could not be visualized as neurons this early in development. The green cells are more advanced neurons.

How to get order out of stirring things up

It's not unusual to mix up a batch of batter and still find unpalatable lumps of dry flour or baking powder embedded in the finished pancakes. Similar problems sometimes bedevil the mixing of ingredients, whether solid or liquid, in the chemical and pharmaceutical industries.

Now, researchers suggest that a simple mechanism may underlie many of the situations in which coherent structures – lumps – persist in the midst of the turbulent flows that surround them.

"Our work implies that coherent structures are in fact generic in any flow generated by stretching and folding," says Troy Shinbrot of the chemical engineering department at Northwestern University in Evanston, Ill. "Moreover, the work tells us exactly how to perturb a given system to create, manipulate, or destroy these structures."

The notion that mixing can be regarded as the stretching and folding of a material originated with British physicist Osborne Reynolds, who first described this process in 1894. The idea was revived in the 1980s by Northwestern's Julio M. Ottino, who used stretching and folding to model how disorder can emerge out of a simple mixing process.

As any mixture is stirred, the material is first stretched out – elongating like a wad of taffy – then folded over into a horseshoe shape. With each successive stretch and fold, any two particles along the horseshoe's legs get farther apart, eventually ending up separated by some random distance.

Shinbrot, working with Ottino, wondered whether the same stretching and folding process can also preserve coherent structures. He noticed that particles very close to a fold move only a short distance apart. Thus, after an initial stretch and fold, the movement of these particles can be minimized by getting the second fold to occur at roughly the same point as the first. By keeping successive folds near a specific point in a mixture or a stirred fluid, the material near the fold remains intact.

To demonstrate the effect, Shinbrot and Ottino turned to an apparatus consisting of two cylinders, one inside the other but placed off center. By pouring a thick liquid into the space between the cylinders, then slowly rotating the inner and then the outer cylinder back and forth, the researchers could induce flows in the liquid that produce patterns characteristic of stretching and folding.

Typically, a sequence of rotations would rapidly distribute a drop of dye injected into the body of the liquid throughout the material. But by adjusting the sequence of rotations to keep the