Astroglia zip the two halves of the brain together

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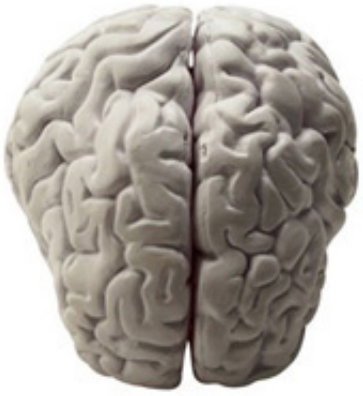

Scientists have identified the cellular origins of the corpus callosum, the 200 million nerve fibers that connect the two hemispheres of the brain. A study of mice and human brains published on October 11 in *Cell Reports* shows that during development, astroglia, the main supporting cells of the brain, weave themselves between the right and left lobes, and form the bridge for axons to grow across the gap. Without these astroglia, the corpus callosum doesn't form correctly, causing a condition called callosal agenesis—which affects 1 out of 4,000 people—and a range of developmental disorders.

"Very little is known about the cause of callosal agenesis, and there hasn't been a satisfactory explanation for how it occurs," says first author

Ilan Gobius, a postdoctoral research fellow at the Queensland Brain Institute, University of Queensland in Australia. "We believe we've finally discovered one of the major causes for this group of disorders."

During development, the hemispheres of the brain are separated by a gap filled with fibroblasts—and other non-neural cells. In order to see how callosal axons navigated around this area to connect the hemispheres, the researchers used mice embryos to observe the growth of individual axons. They observed that the axons cannot grow through this gap, and instead grow down and around it to connect the two hemispheres of the brain. However, they don't do this on their own; instead they rely on astroglial cells to guide their path.

Using the mice embryos and human brain scans, the team lead by Linda Richards, Deputy Director of the Queensland Brain Initiative found that these astroglial cells are initially located beneath the area filled with fibroblasts, but during fetal development a molecular pathway signals the astroglia to migrate forward and mature, allowing them to weave together into a thick column along the center of the brain, which pushes back against the gap and causes it to shrink. This column of astroglia acts as a bridge for callosal axons and allows them to cross between the two sides of the brain. As this bridge grows, the gap between the hemispheres shrinks until only a small portion of it remains, and the corpus callosum begins to form.

The researchers saw that when there was an issue with molecular signaling, the astroglial cells didn't change into multipolar cells. This prevented the formation of the callosal tract and resulted in callosal agenesis. "This midline area is one of the first places in the brain that you normally start to see these astroglial cell changes," says Gobius. "And we found that if these cells don't make this transition, the remodeling process that you need to form the corpus callosum doesn't get started."

Moving forward, the team hopes to use this knowledge to help make better diagnostic tests for callosal agenesis. As of now, doctors can only diagnose the disorder during fetal development using an ultrasound or MRI, but since the condition can range in severity, the lack of an accurate genetic test makes it difficult to council parents about what developmental issues to expect in their child.

"The field is desperate for a genetic test for this disorder," says Richards. "This opens up the possibility for testing for genes like those that Dr. Gobius identified. Identifying the cellular process that causes this range of disorders is very important for looking to the future and finding new genes for possible therapeutic targets."

More information: *Cell Reports* Gobius, Morcom, Suárez, Bunt, Richards, et al: "Astroglial-mediated remodeling of the interhemispheric midline is required for the formation of the corpus callosum" www.cell.com/cell-reports/full … 2211-1247(16)31255-4 , DOI: 10.1016/j.celrep.2016.09.033

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