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LAB NOTES

One Brainy Fish

An electric fish from the Congo may hold the key to how we move

For decades neuroscientists have been building theories of brain function despite a near total lack of data on the most numerous neurons of all: cerebellar granule cells. Making up 70 billion of the nearly 86 billion neurons in the human brain, these relatively simple cells are tightly packed into the cerebellum, a broccoli-shaped structure tucked under the back of our brain. Cerebellar granule cells form part of a brain circuit with a strikingly regular, almost crystalline, structure.

Yet the purpose of this straightforward anatomical arrangement has baffled researchers. In the 1960s a team of neuroscientists, computer scientists and mathematicians theorized that these cells played an important role in the cerebellum's ability to learn motor skills. Several groups of researchers set out to put the theory to the test, imagining that, shortly, our understanding of the brain would take a giant leap forward. But gathering data on granule cells turned out to be not so easy. Their dense packing, small size and location deep in the brain make them difficult to reach with traditional experimental techniques. The theory has gone unresolved for 40 years, casting a shadow over the efforts of cerebellum researchers.

One possible road to discovery has recently come from an unusual source: the electric fish *Gnathonemus petersii,* which has long fascinated neuroscientists because it has a monstrously large cerebellum. By painstakingly recording the activity of individual granule cells with microelectrodes in a living electric fish, neuroscientist Nate Sawtell of Columbia University's Kavli Institute for Brain Science, where I am currently a Ph.D. candidate, has uncovered some of the first direct evidence in support of the 1960s theory that granule cells may enhance the cerebellum's ability to learn skills such as fine movements. Sawtell showed that neurons receiving input from these cells were able to predict the position of the fish's tail based on a combination of motor and sensory signals, a crucial step in the learning of motor skills. Sawtell is one of only a handful of neuroscientists working with this fish, but his results suggest the fish's potential in helping to solve this long-standing mystery.

Knowing the function of cerebellar granule cells could lead to further important discoveries. In humans, the cerebellum's extensive connectivity with the rest of the brain suggests it does far more than learn motor skills: it has been shown to have a part in both perception and cognition, with recent work linking cerebellar dysfunction to such complex diseases as schizophrenia and autism. It's time to start listening to the silent majority of 70 billion, which we are now starting to do thanks to a little electric fish with a huge cerebellum.

—Tim Requarth