

Spineless tales provide strong backbone to human brain research

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University of Oregon biologist Nathan Tublitz talked about moths, flies and cephalopods, telling an audience of scientists meeting in Australia this week that research on these spineless creatures is unveiling the mechanics of how the brain regulates behavior.

Among his tales of three invertebrates were details of his discoveries, published in two papers this year, that two specific brain chemicals (glutamate and FMRFamide-related peptides), residing in a specific location, allow a cuttlefish (cephalopod) to change skin color or skin patterns in less than a second. In a paper that appeared online July 25 ahead of regular publication in the journal *Integrative and Comparative Biology*, Tublitz and colleagues announced that the quick-change machinery resides primarily in the posterior subesophageal mass of the cuttlefish brain.

Color change in cuttlefish skin is caused by pigments in star-shaped cells known as chromatophores. Upon certain inputs, pigment granules spread outward in cells, causing human skin, for instance, to tan or a chameleon's skin to turn between green and brown. However, such changes take hours in humans and minutes in lizards. Cephalopods have some two million chromatophores that are directed by chemical signals originating in a central brain location. They change colors for camouflage or to communicate with like or different species, Tublitz said.

"The region we've identified is similar to the human motor cortex,"

Tublitz said in his presentation Tuesday morning in Sydney at the Association of Pacific Rim Universities' Brain & Mind Research Symposium. "There is a similar mapping of the cuttlefish brain onto the body as in the homunculus of the human motor cortex. Once we understand that similarity, we can start to understand how these cuttlefish brain cells receive different inputs that cause different types of complex body patterns. We want to know how muscles are being activated to generate such complicated behavior."

Such knowledge is important because it provides clues as to how the far more complex human brain acts to alter behaviors, he said. One of the goals of his research at the Institute of Neuroscience at the University of Oregon is to understand the intricacies of brain signaling that allow people, such as athletes, to repeat and adjust tasks they perform repeatedly.

Cephalopods, which also include octopuses and squids, have 100 million nerve cells compared to the 10,000 in insects and the some one trillion in humans. "The idea is to look at simpler brains to allow us to generalize broad concepts that are applicable to humans," Tublitz said in an interview. "Much of what we've learned about the human brain at the cellular level has come from the study of invertebrates," he said.

His findings involving the European cuttlefish (*Sepia officinalis*) provide an example of system-level brain activity, he said in his presentation. Tublitz also discussed his lab's earlier findings involving cellular plasticity in the tobacco hornworm (*Manduca sexta*), also known as the hawk moth.

"We have identified a set of nerve cells in the moth whose properties are completely altered during metamorphosis," he said. "The biochemistry is altered. The translators that they use are altered. The shapes of the cells are altered, and their physiology is altered. The dogma is that most cells

don't change their characteristics, but here's a case of nerve cells changing not only one characteristic but almost all of them."

The driving force of these changes is naturally occurring steroid hormones, he said.

Insects are fascinating because they accomplish complex behaviors with relatively few nerve cells. Moths, in particular, have easy-to-study nerve cells that are 10 to 20 times as large as those in humans, and they go through three distinct body states, each with its own set of behaviors, with the same brain, "which must adjust and be modified to work in each body state," Tublitz said.

As for flies, Tublitz outlined a tantalizing question, as yet unanswered, that has continued to take flight out of his lab for the last decade. Scientists for years, he said, have held "one hard rule" about what constitutes a neuron – that a neuron cell always arises from the ectoderm of a developing embryo. However, a discovery in *Drosophila* – fruit flies – has softened that assumption.

Cells arising from the mesoderm rest in a layer on top of the fruit fly's nervous system, Tublitz explained. "These cells have all of the properties of nerve cells." A slide shown during his talk displayed a long list of characteristics most often applied, with only few exceptions, to neurons. "Are these mesodermal cells nerve cells? I can't answer that question conclusively, but we have generated data that suggest the answer may be 'yes'."

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