Biologists announce unique spinal nerve cell activity discovery

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This is a picture of a zebrafish embryo, similar to the ones used in this study. Credit: University of Leicester

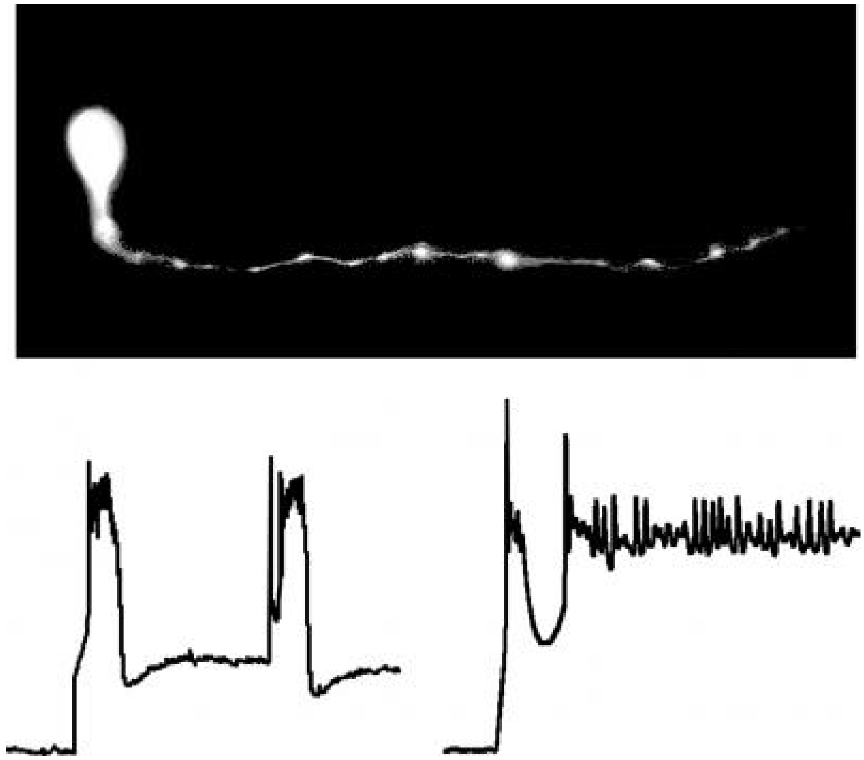
Scientists from the University of Leicester have hit upon unique forms of spinal nerve activity that shape output of nerve cell networks controlling motor behaviours.

The breakthrough in the Department of Biology at the University of Leicester is announced today (Nov 8) in the journal Current Biology. The three- year study was funded by the Biotechnology and Biological Sciences Research Council (BBSRC).

Although the neural basis of motor control has been studied for over a century, the processes controlling maturation of locomotor behaviours – like walking and swimming - are not fully understood.

The University of Leicester research into nerve cells responsible for motor behaviours was carried out on fish. The team aimed to understand how spinal networks produce rhythmic activity from a very immature stage - and how such activity changes during maturation.

The team used zebrafish, a freshwater fish native to northern India and Bangladesh, because their motor networks are similar to humans. However, as they are fertilized outside the mother and their embryos are transparent, scientists can readily monitor motor network development from its onset - something that is very difficult to do in mammals.



Three panels show: The upper panel is a micrograph of a fluorescently labelled IC cell of the zebrafish embryo spinal cord. The neuron was dialysed with the fluorescent dye sulforhodamine during physiological recording. The lower panels depict rhythmic (left hand panel) and sustained (right hand panel) recorded from early embryonic and swimming stage zebrafish respectively. Credit: University of Leicester

Lecturer in Neurobiology, Dr Jonathan McDearmid, who led the research, said: "What's unique about our work is the observation that a group of spinal nerve cells generate unusual forms of electrical activity that adapt to meet the changing requirements of the developing motor network. Whilst these cells had been previously identified, their excitable properties had not been studied in detail. We found that these cells produce age-specific activity patterns: in early life they have "autorhythmic" properties that are likely to drive embryonic movements. However, as fish develop towards more mature swimming stages, they switch firing activity to generate sustained impulses that appear to be necessary for maintenance of swimming.

"Our work is important because it sheds light on the mechanisms by which spinal nerve cells shape activity in the maturing of motor network. This is basic research that allows us to better understand how vertebrate motor activity emerges. However, in the long term, understanding of this process might help determine what goes wrong in diseases that affect spinal cord function."

Dr McDearmid said the identification of the activity generated by this group of cells –termed IC cells- happened as quite a surprise:

"It was two days after Christmas when we first observed IC cells generating these unusual patterns of activity. I was conducting a few routine experiments for a related study we were running in parallel. Whilst monitoring electrical responses in different nerve cells I hit on a cell that did some very unusual things. It was a very exciting finding indeed. The only problem was that subsequent attempts to find this "magic cell" didn't prove straightforward. Because these cells change location as the fish develops, it initially proved challenging to track them down for further study. Still, in time we figured out where these cells were and that very first recording turned out to be one of the best Christmas presents we've ever had."

Researchers say they have a long way yet to go in the study – and many questions remain unanswered. Dr McDearmid said:

"We have many questions that we want to ask next. Are there other cells in the developing spine that display similar types of activity? Also, we currently have no idea how IC cells function at more mature stages, such as in adult fish. Our next aim is to determine whether IC cells retain their unusual firing characteristics at older stages."

More information: Background information:

The University of Leicester research team was interested in how nerve cells networks dedicated to production of rhythmic motor behaviour (such as walking and swimming) form. These networks assemble within the spinal cord from a very early age, and they often start to generate behaviour before birth. However, they must undergo an intense period of maturation before being able of generate behaviours that we typically associate with adult life. Their work was aimed at understanding how spinal networks produce rhythmic activity from a very immature stage and how such activity changes during maturation.

The Leicester research team use the zebrafish because, like mammals, their motor maturation follows a stereotyped sequence of behavioural transitions that occur prior to the emergence of mature behaviour. This begins with rhythmic, periodic trunk contractions, akin to foetal movements that occur in mammals. Subsequently, as fish mature their motor networks switch output to generate swimming activity which, although quite simple, is a blueprint for adult behaviour.

The Leicester biologists aimed to shed light on the physiological mechanisms underpinning this process. They aimed to address two issues:

First - to understand how zebrafish spinal networks produce activity at very immature stages, when they contain very few nerve cells.

Second - to understand the maturation processes underpinning the progression from embryonic trunk contractions to more mature swimming behaviour.

Using a specialised technique ("patch clamp electrophysiology") the biologists monitored electrical properties of different nerve cell types in the developing zebrafish spinal cord.

The researchers found that most cells were unremarkable: when stimulated they produced brief, arrhythmic electrical discharges called "action potentials". However, one group of cells (the "IC cells") generated a very different form of activity. Stimulating these cells triggered prolonged, rhythmic "bursts" that closely resembled activity that drives embryonic trunk movements. Moreover, when IC cells were prevented from generating this activity, motor behaviour was abolished, suggesting the activity produced by these cells drive embryonic behaviour.

When biologists looked at more mature stages, when fish acquire the capacity to swim they saw that IC cells produced very different, yet equally unusual, forms of activity. On the transition to swimming, IC cells switched firing mode to produce powerful and sustained bursts that plateaued for tens of seconds. When the biologists blocked these discharges, fish could no longer swim for prolonged periods, a finding that suggests IC cells become important for maintenance of sustained swimming activity.

Provided by University of Leicester