Virtual reality allows researchers to measure brain activity during behavior at unprecedented resolution

May 9 2012

Researchers have developed a new technique which allows them to measure brain activity in large populations of nerve cells at the resolution of individual cells. The technique, reported today in the journal *Nature*, has been developed in zebrafish to represent a simplified model of how brain regions work together to flexibly control behaviour.

Our thoughts and actions are the product of large populations of nerve cells, called neurons, working in harmony, often millions at a time. Measuring brain activity during behaviour at detailed resolution in these groups of cells has proved extremely challenging. Currently, scientists are restricted to measuring their activity in individual brain areas of, for example, moving rats, typically in less than a few hundred neurons.

Dr Misha Ahrens, a Sir Henry Wellcome Postdoctoral Fellow based at Harvard University and the University of Cambridge, worked with colleagues to develop a technique which allows neuroscientists to study as many as 2,000 neurons simultaneously, anywhere in the brain of a transparent zebrafish. Their work was funded by the Wellcome Trust and the National Institutes of Health.

Dr Ahrens and colleagues created a virtual environment for zebrafish, which allowed them to measure activity in the neurons as the fish 'moved'. In reality, the zebrafish was paralysed to allow the researchers to image its brain; the fish perceived to 'move' through the virtual environment by activating their motor neuron axons, the cells responsible for generating movement.

Zebrafish are often used as a simple organism to study genetics and characteristics of the nervous system that are conserved in humans . They are genetically modifiable, so by manipulating the fish's genetic make-up, Dr Ahrens and colleagues created a fish in which all neurons contained a particular protein that increases its fluorescence when the cells are active. The fish are transparent and so the team were able to use a laser-scanning microscope, to see activity in any neuron in the brain of the fish, and up to 2,000 neurons simultaneously.

Dr Ahrens explains: "Our behaviour is determined by thousands, possibly millions, of nerve cells working in harmony. The zebrafish performs complex behaviors, with a brain of about 100,000 neurons, almost all of which are accessible to optical recording of neural activity. Our new technique will help us examine how large networks mediate behaviour, while at the same time telling us what each individual cell is doing."

Using the technique, Dr Ahrens and colleagues asked the question: do zebrafish adapt their behaviour in response to changes in their environment? To do this, they manipulated the virtual environment to simulate the fish suddenly becoming more "muscular". This served as a simplified version of what happens when the brain needs to adapt the way it drives behavior, for example, when water temperature changes the efficacy of the muscles, or when the fish gets injured.

Dr Ahrens adds: "The paralyzed fish in the virtual world do indeed adapt their behaviour, by adjusting the amount of impulses the brain sends to the muscles. They also 'remember' this change for a while. Imaging the brain everywhere during this behaviour, we identified certain brain regions that were involved, most notably the cerebellum and related structures. This technique opens the possibility that eventually, the behaviour may be used to gain insights into human motor control and motor control deficits.

"Our own motor control is continuously recalibrating itself in a similar way to the fish's to cope with ever changing conditions of our body and environment, such as when we injure a leg, or if we're walking on a slippery floor or carrying a heavy bag. The zebrafish's behaviour is an ultra-simplified version of this and we have been able to gain some insight into how its brain structures drive behaviour. This might someday help us understand how damage to certain brain regions in humans affects the way in which the brain integrates sensory information to control body movements."

Understanding the brain is one of the Wellcome Trust's five strategic challenges.

More information: Ahrens, MB, Li, JM, Orger, MB, Robson, DN, Schier, AF, Engert, F and Portugues, R. Brain-wide neuronal dynamics during motor adaptation in zebrafish. *Nature*; 9 May 2012 [Epub ahead of print]. DOI: 10.1038/nature11057

Provided by Wellcome Trust