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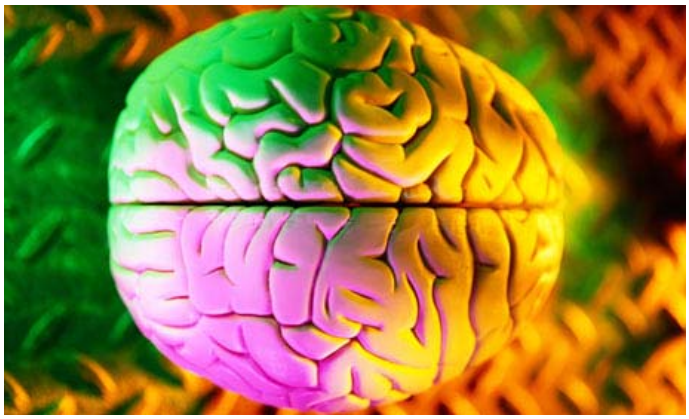
DISPATCHES FROM THE SCIENCE DESK

Light switches on the brain

A new technique called optogenetics that uses light to control the activity of nerve cells is ushering in a world of remote-controlled animals, light-regulated genes and wireless brain implants



Wireless, optogenetic implants containing light-emitting diodes could switch on specific brain regions. Photograph: Nick Koudis/Getty

Leading lights in optogenetics presented the latest developments in their field during a mini-symposium at the 40th annual meeting of the Society for Neuroscience in San Diego at the weekend.

Optogenetics has emerged in the past decade as a high-precision tool for monitoring and controlling the activity of nerve cells. It is based on light-sensitive proteins called rhodopsins, which are isolated from algae and bacteria and are related to the proteins found in the human retina.

When rhodopsins in the human eye's photoreceptors are struck by light, they initiate a cascade of biochemical reactions, causing the cells to send signals to the brain via the optic nerve. But the microbial rhodopsins behave differently – they alter the electrical properties of neurons directly, and it is these properties that make them so useful.

When introduced into neurons, they insert themselves into the membrane, making the cells sensitive to light. Pulses of laser light can then be used to activate or silence specified groups of neurons on a millisecond-by-millisecond timescale.

From the beginning, this technique proved to be extremely powerful. The earliest optogenetic experiments involved using the microbial proteins to control the movements of small organisms such as nematode worms and fruit flies.

More recently, the technique has been used to control increasingly complex behaviours in mammals. In the past few years, it has been used to restore vision in blind mice, to rescue nerve function in mice with spinal cord injuries, and to control the signalling

pathways involved in reward, motivation, and fear conditioning.

Ed Boyden of MIT Media Lab, who has been instrumental in developing the technique, described how tinkering with the optogenetic toolkit is leading to further refinements. Using genetic engineering, researchers are making the microbial rhodopsins more sensitive to light, improving their on/off rate and speeding up their recovery after activation, all of which are enabling them to control the activity of complex neuronal circuits with unprecedented and increasing precision.

Typically, optogenetics in mammals involves inserting optical fibres into the brain to deliver laser light to the areas being targeted. Boyden described new "multi-wave" arrays that emit light at multiple points, allowing larger areas of the brain to be targeted.

Until now, the microbial rhodopsins have only been expressed in the cell membrane, but Anselm Levskaya of the University of California, San Francisco, described how he is developing ways of using optogenetics to interrogate the computational processes that take place within cells.

Neurons process information by means of intricate networks containing hundreds of different enzymes and signalling molecules. Levskaya is now using optogenetics to study how the components of these networks interact with each other. The technique is so precise that it can be used to monitor these interactions in single dendritic spines, the tiny finger-like projections on nerve cell branches at which signalling takes place.

He also described how optogenetics can be used to control gene transcription, the process by which genetic information is transcribed during the early stages of protein synthesis. This "gene painting" is now enabling researchers to regulate patterns of gene expression at high spatial and temporal resolution, using light.

John Lin of the Howard Hughes Medical Institute described how genetically encoded calcium sensors can monitor nerve activity. These sensors can be used to visualise the tiny localised increases in calcium ion concentration that are characteristic of nerve cell activity. A recent paper published in the journal Nature Neuroscience shows how useful these sensors can be. A team of researchers led by David Tank of the Lewis-Sigler Institute for Integrative Genomics at Princeton used such a sensor in mice navigating a virtual reality environment. They were able to image the activity of the animals' place cells, which encode spatial information, in real time and at cellular resolution.

Eventually, optogenetics will enable the cumbersome neural implants used in humans today to be replaced with wireless implants containing miniature light-emitting diodes. Early pre-clinical trials conducted in primates show that the technique is safe and does not elicit an immune response.

There are, however, technical problems, including the poor penetration of light into deep tissues. One reason for this is that blood absorbs blue and green light, the wavelengths most commonly used to activate the microbial rhodopsins in optogenetic studies. Michael Lin of the University of California, San Diego, described how this can be overcome by "redshifting" the proteins, engineering them to be sensitive to bright red light instead of blue or green.

Mo Costandi *writes the Neurophilosophy blog*

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BxGt

17 November 2010 6:31PM
Sounds like science fiction!
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CrewsControl

17 November 2010 8:13PM
Very interesting, haven't been able to access the Tank paper yet.
Is it possible to monitor/stimulate single spines (diameter ~[illegible]μm)? Or a local group of spines? Is the site of stimulation important? Are distant spines less important than proximal spines? Does sequential input activation lead to a different output? Does the light sensitive protein alter the behaviour of the dendritic spine in the absence of light?
First impression is that it does seem quite a crude mechanism of activation when compared to the likely complex patterns of synaptic input to a dendritic tree. Look forward to getting hold of the paper
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atgrimeandreason

17 November 2010 10:36PM
Wow. Just wow.
I mean, a science article that doesn't sensationalise or dumb down the content.
Double wow... a sub-editor showing some restraint in writing the headline!
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dirkbruere

18 November 2010 12:23AM

One interesting fact not mentioned - the skull is reasonably transparent to infrared light.
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anewstart
18 November 2010 2:34AM
You can beat an egg but you can't beat science.
Recommend? (1)
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cactiform
18 November 2010 12:15PM
Excellent stuff !
How long before we can apply this to keeping the proles under control ?
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flanger
18 November 2010 1:48PM
Eventually, optogenetics will enable the cumbersome neural implants used in humans today to be replaced with wireless implants containing miniature light-emitting diodes. Early pre-clinical trials conducted in primates show that the technique is safe and does not elicit an immune response.

thats overegging it a bit. Non-optical wireless implants have already been demonstrated and are (for instance) cochlear implants really that "cumbersome"?
Plus how many people really want their nervous system genetically engineered? And why would it be a good idea to have an implant using electricity to generate light, just so a nerve can translate that back into an electrical impulse?
This research is very interesting, but its just one approach to the problem
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