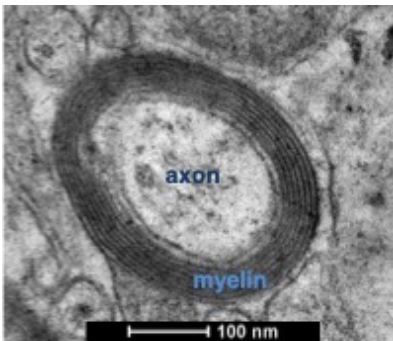


Changing the Brain Through Learning

Research at the University of Oregon



An electron microscope picture of a single axon (fibre that leads to another cell) surrounded by myelin rings (insulating the axon). Electron microscopy by Dr Denise Piscopo

role of attention and memory networks. Are there any special connections involved? Do they look similar in mice and in humans? And intriguingly, if we find out more about these pathways and the mechanisms behind them, could we manipulate them to improve learning?

The team was able to provide answers to several of these questions. Notably, they found that the evidence pointed towards the presence of two pathways in the brains of both animals and humans, serving to connect attentional networks with the hippocampus. The first pathway (anterior pathway) involves the brain structure nearer the front of the brain and includes the

anterior cingulate cortex. The second pathway (posterior pathway) involves the brain structures further back, including areas of the parietal lobe.

Because these pathways use different routes crossing many brain structures, the team speculated about the mechanisms that might underpin learning. Most specifically, they were interested in whether the anterior pathway could be significant for generalisation – a process that helps the brain demonstrate learning in situations different from the original learning. They further proposed that the posterior pathway might be complementary to this and may play a part in navigation in the rodent and retrieval of memories related to location in the human.

Manipulating Pathways Through Neuromodulation

Neuromodulation is a technique through which we can actively change the brain's nerve activity using mild electrical stimulation or drugs. Based on encouraging results from the field of epilepsy, where neuromodulation can reduce seizures, researchers were encouraged to study its potential application to other disorders, as well as the understanding of healthy brain processes.

For Dr Posner, neuromodulation presented a very promising candidate for improving learning outcomes. Based on his earlier research, he was eager to explore the anterior cingulate cortex and surrounding brain structures, particularly in relation to improving learning. To look at this directly, the team used lasers to manipulate neuronal activity in mice in the anterior cingulate cortex.

Neuromodulation Can Repair the Brain

Neuromodulation of the anterior cingulate cortex of mice by low-frequency stimulation resulted in several exciting results. First, they showed that the brain structure close to the stimulation became more strongly connected after neuromodulation. White matter is the tissue that allows communication from one part of the brain to another. Dr Denise Piscopo (lead author), was able to take pictures magnified 16,000 times to show an increase in the white matter surrounding the anterior cingulate, allowing information to travel more quickly and more effectively to and from this structure (see Figure 2).



This was excellent news – not least because neuromodulation might help to repair the protective sheet of white matter across many different neurological problems. For example, people who suffer from concussions or multiple sclerosis have damage to white matter in diverse brain regions. These findings suggest a possible way forward to help the recovery of patients with such neurological problems.

Neuromodulation and Meditation

Plenty of evidence supports the positive effects of meditation on the brain. Some work by Drs Posner and Rothbart in conjunction with Dr Yiyuan Tang has shown that brain connections strengthened after two to four weeks of meditation training. Could meditation have similar positive effects on the brain as neuromodulation? They identified several common patterns in the literature pointing to the role of the anterior cingulate cortex, stronger white matter, and better learning outcomes on different tests and tasks using meditation training in humans and stimulation in animals.

Neuromodulation and meditation seem to involve a specific brain rhythm that causes a cascade of molecular changes in the brain. Dr Pascale Voelker is investigating these molecular changes. Taken together, both neuromodulation and mental activity, such as meditation, are believed to improve information transportation by strengthening white matter connections. This impacts real-life behavioural outcomes, such as improving concentration and emotional regulation. But how?

Next Steps in Understanding Learning

Having ascertained that neuromodulation can improve

connections between structures, it is important to understand the mechanisms underlying the impact neuromodulation has on the two pathways involved in learning skills. One question is how to separate the direction of information flow in the two pathways. Understanding the direction of information flow will help determine the exact function of each pathway between attention and memory. Neuromodulation could then be targeted to help understand the function of each pathway. Hopefully, modulation can then be used to improve specific learning skills. In the long run, improved knowledge could repair white matter and thus help people to recover from neurological problems.

But, of course, very little is ever straightforward. As Dr Posner explains, 'The ability to determine the direction of information flow is critical to the design of new studies. It is hard to distinguish between memory-to-attention and attention-to-memory control in subcortical areas. Optogenetics using laser light can help them to accomplish some of these goals. By injecting the brains of mice with two different types of viruses, they will be able to separate the direction of two pathways. It is then possible to use laser light to stimulate these areas in a specific direction through surgically implanted optic fibres.

Future research could involve designing tasks for mice that would help in modulating each pathway separately. This experimental plan is similar to the researchers' previous studies looking at the contribution of different brain areas to learning. This will allow study of the specific roles these pathways have and how the information flows within them. Looking even further ahead, if successful, it may then be possible to apply similar non-invasive methods, such as stimulation from electrodes on the scalp of humans, to improve both neurological conditions and skill learning.



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Meet the researchers

Team profile

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This team began its collaboration in 2015 when after a lecture by Dr Posner, Dr Niell came forward to say that he could provide a test of Dr Posner's hypothesis that meditation could change through a frontal rhythm that might activate dormant cells. Dr Niell was using optogenetics to activate cells in the brain of mice. In addition to Dr Posner, who has studied the mechanisms of attention for more than 50 years, the team included Dr Mary K. Rothbart, a world-leading developmental psychologist with whom Dr Posner has worked for many years. Dr Denise Piscopo (working with Dr Niell) was instrumental in testing the hypothesis and developed the needed skill with electron microscopes to examine the change in white matter. Dr Aldis Weible worked with Dr Niell to train and test the mice, for which he received special recognition with a research award from the University. Dr Pacale Voelker, trained in molecular biology, added the molecular analysis to the team's work. The experiments reported in this article reflect a genuine collaboration and also build on the work of many other people in this field.

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FUNDING

This work was supported by grants from the Office of Naval Research to the University of Oregon. The team wishes to express its appreciation to the late Dr Ray Perez, who approached us with the goal of using our research to develop a model of skill acquisition. We also acknowledge the contribution of Dr Harold Hawkins, ONR, and Mr Rudy Chapa, who both contributed funding to our research.

FURTHER READING

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