Evidence that brains re-wire themselves following damage or injury

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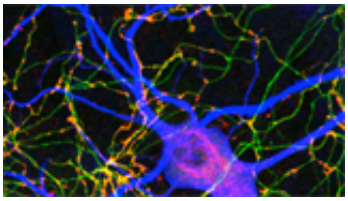

(Medical Xpress)—Scientists from the United States and Australia have advanced our understanding of brain plasticity by showing that the brain forms complex new circuits after damage, often far from the damaged site, to compensate for lost function.

A new study by Drs Moriel Zelikowsky and Michael Fanselow from the University of California Los Angeles (UCLA), in collaboration with Dr Bryce Vissel, from Sydney's Garvan Institute of Medical Research, identified the exact regions of the brain that take over when a learning and memory centre, known as the 'hippocampus', is damaged.

Their breakthrough, the first demonstration of such circuit plasticity, is published today in the early online edition of the *Proceedings of the National Academy of Science* (*PNAS*).

Learning theorists Drs Michael Fanselow and Moriel Zelikowsky

conducted studies in the lab showing clearly that rats were able to learn new tasks after damage to the hippocampus. While they needed more training, the rats nonetheless learned from their experiences, a surprising finding.

After performing these behavioural experiments, Dr Zelikowsky came to Australia and collaborated with Dr Bryce Vissel to analyse the anatomy of the changes that had taken place in rat brains. Their analysis identified significant functional changes in two regions of the pre-frontal cortex.

"Interestingly, previous studies had shown that these pre-frontal cortex regions also light up in the brains of Alzheimer's patients, suggesting that similar compensatory circuits develop in people," said Dr Vissel.

Vissel, who examines the potential for hippocampal regeneration and repair in Alzheimer's patients, believes that the finding will radically change the ways in which scientists think about the brain. He said "we've constrained ourselves by the idea that specific parts of the brain are dedicated to specific functions, and that if regeneration were to take place it would have to do so near the damaged site."

"Until now, we've been trying to figure out how to stimulate repair within the hippocampus. Now we can see other structures stepping in, and whole new brain circuits coming into being. That's truly exciting."

Dr Zelikowsky finds it interesting that subregions in the pre-frontal cortex compensate in different ways, with one subregion – the infralimbic cortex – silencing its activity and another subregion – the prelimbic cortex – increasing its activity.

"If we're going to harness this kind of plasticity to help stroke victims or people with Alzheimer's, we first have to understand exactly how to

differentially enhance and silence function, either behaviourally or pharmacologically," she said.

"It's clearly important not to enhance all areas. The brain works by silencing and activating different populations of neurons. To form memories, you have to filter out what's important and what is not – in other words, you need to keep the background noise down in order to detect similar patterns."

Dr Michael Fanselow explained that whenever a complex behaviour develops, it always involves multiple parts of the brain talking to each other, one region's message affecting how another region will respond. These molecular changes produce our memories, feelings and actions.

"The brain is heavily interconnected – you can get from any neuron in the brain to any other neuron via about 6 synaptic connections," he said.

"So there are many alternate pathways the brain can use – but it normally doesn't use them unless it's forced to. Once we understand how the brain makes these decisions, then we're in a position to encourage pathways to take over when they need to, especially in the case of brain damage."

"I expect that the brain probably has to be trained through experience. In this case we gave animals a problem to solve."

"Behaviour creates molecular changes in the brain – so if we know the molecular changes we want to bring about, then we can try and facilitate those changes to occur through behaviour and drug therapy. I think that's the best alternative we have – future treatments are not going to be all behavioural or all pharmacological, but a combination of both."

"While it's probable that the brains of Alzheimer's sufferers are already compensating for damage, this discovery has significant potential for

extending that compensation and improving the lives of many," added Dr Vissel.

Provided by Garvan Institute