

Myelin vital for learning new practical skills

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Image shows the complex shape of individual oligodendrocytes (OLs) and myelin in adult mice injected with tamoxifen. OLs formed before tamoxifen injection are red, newly-forming OLs have a yellow 'cell body' containing the nucleus surrounded by a green 'bundle of sticks' which are short stretches of myelin wrapped around thread-like axons. Axons are not visible but there are many of them running across the image right to left. Credit: Sarah Jolly, UCL



New evidence of myelin's essential role in learning and retaining new practical skills, such as playing a musical instrument, has been uncovered by UCL research. Myelin is a fatty substance that insulates the brain's wiring and is a major constituent of 'white matter'. It is produced by the brain and spinal cord into early adulthood as it is needed for many developmental processes, and although earlier studies of human white matter hinted at its involvement in skill learning, this is the first time it has been confirmed experimentally.

The study in <u>mice</u>, published in *Science* today, shows that new <u>myelin</u> must be made each time a skill is learned later in life and the structure of the brain's <u>white matter</u> changes during new practical activities by increasing the number of myelin-producing cells. Furthermore, the team say once a new skill has been learnt, it is retained even after myelin production stops. These discoveries could prove important in finding ways to stimulate and improve learning, and in understanding myelin's involvement in other brain processes, such as in cognition.

For a child to learn to walk or an adult to master a new skill such as juggling, new brain circuit activity is needed and new connections are made across large distances and at high speeds between different parts of the brain and <u>spinal cord</u>. For this, electrical signals fire between neurons connected by "axons" – thread-like extensions of their outer surfaces which can be viewed as the 'wire' in the electric circuit. When new signals fire repeatedly along axons, the connections between the neurons strengthen, making them easier to fire in the same pattern in future. Neighbouring myelin-producing cells called oligodendrocytes (OLs) recognise the repeating signal and wrap myelin around the active circuit wiring. It is this activity-driven insulation that the team identified as essential for learning.



The team demonstrated that young adult mice need to make myelin to learn new motor skills but that new myelin does not need to be produced to recall and perform a pre-learned skill. They tested the ability of mice to learn to run on a complex wheel with irregularly spaced rungs. The study looked at thirty-six normal mice and thirty-two mice with a drugcontrolled genetic switch to prevent new OLs and myelin from being made. They found the mice that were prevented from producing new myelin could not master the complex wheel, whereas those that could produce myelin did learn, with differences between the two groups' abilities seen after only two hours of practice.

A second experiment looked at mice that were first allowed to learn to run on the complex wheel before being treated with the drug to prevent further myelin production. When the mice were later re-introduced to the complex wheel, they were immediately able to run at top speed without having to spend time re-learning. This shows that the inability to make new myelin did not affect the mouse's running ability and that new myelin is not required to remember and perform a skill once learned; it is required only during the initial learning phase.

Lead researcher, Professor Bill Richardson, Director of the UCL Wolfson Institute for Biomedical Research, said: "From earlier studies of human white matter using advanced MRI technology, we thought OLs and myelin might be involved in some way in skill learning, so we decided to attack this idea experimentally. We were surprised how quickly we saw differences in the ability of mice from each group to learn how to run on complex wheel, which shows just how fast the brain can respond to wrap newly-activated circuits in myelin and how this improves learning. This rapid response suggests that a number of alternative axon pathways might already exist in the brain that could be used to drive a particular sequence of movements, but it quickly works out which of those circuits is most efficient and both selects and protects its chosen route with myelin.



"We think these findings are really exciting as they open up opportunities to investigate the role of OLs and myelin in other brain processes, such as cognitive activities (like navigating through a maze), to see if the requirement for new myelin is general or specific to motor activity. I'm keen to find out the precise sequence of changes to OLs and myelin during learning and whether these changes are needed more in some parts of the brain than others, which might shed light on some of the mysteries still surrounding how the brain adapts and learns throughout life."

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