# Researchers develop new method to map cholesterol metabolism in brain

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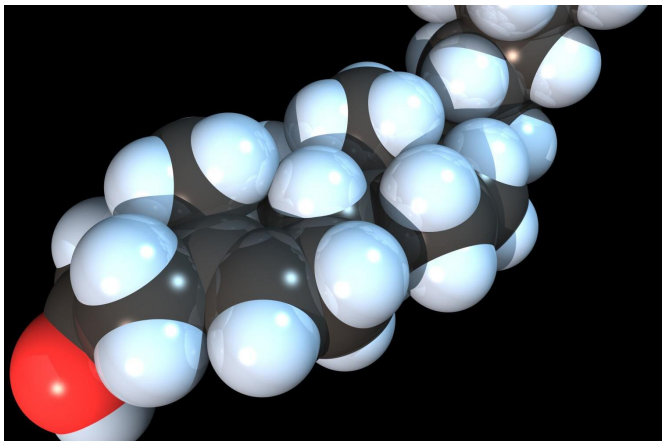

Space-filling model of the Cholesterol molecule. Credit: RedAndr/Wikipedia

A team of researchers led by Swansea University have developed new technology to monitor cholesterol in brain tissue which could uncover its relation to neurodegenerative disease and pave the way for the development of new treatments.

The research, published in the *Proceedings of the National Academy of Sciences*, shows the major locations of cholesterol in the brain and what molecules it can be converted to.

The brain is a remarkably complex organ, with cholesterol and its metabolites underpinning the brain's function. Dysregulated cholesterol metabolism is linked to a number of neurodegenerative disorders including Alzheimer's, Parkinson's, Huntington's disease, multiple sclerosis and motor neurone disease.

It is known that cholesterol is not evenly distributed across different brain regions; however, up until now there has been no technology available to map cholesterol metabolism in defined locations of the brain at microscopic levels, and to visualise how it changes in pathological niches in the brain.

Here, researchers describe an advanced mass spectrometry imaging platform to reveal spatial cholesterol metabolism in mouse brain at micrometre resolution from tissue slices. The researchers mapped not only cholesterol, but also biologically active metabolites arising from cholesterol turnover. For example, they found that 24S-hydroxycholesterol, the major cholesterol metabolite in the brain, is about ten times more abundant in striatum than in the cerebellum, two regions involved in different ways in voluntary movement and cognition.

The new technology comes from a decade of research at Swansea University where the team have worked out methods to reveal the different metabolites of cholesterol in very small quantities of the brain, as small as the tip of a ballpoint pen.

Professor William Griffiths, who co-led the study from Swansea University added: "Although our work was with a mouse, the technology can similarly be used in humans in a research lab or a clinical setting, and could have revolutionary value when linked to neurosurgery.

"Tissue excised during surgery could rapidly be profiled by our method in-clinic and used to distinguish healthy from diseased tissue, informing the surgeon on the next step of the operation."

Professor Yuqin Wang added: "This technology which precisely locates molecules in the brain will further our understanding of the complexity of brain function and how it changes in neurodegenerative disorders.

"Our results show that cholesterol turnover is particularly high in striatum, the area most affected in Huntington's disease. We will apply this method to find out how cholesterol metabolism is associated with this disease. This may lead to the

development of new therapies to a disease which currently has no cure."

**More information:** Eylan Yutuc et al, Localization of sterols and oxysterols in mouse brain reveals distinct spatial cholesterol metabolism, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1917421117

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