Early protein processes crucial to formation and layering of myelin membrane

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New findings from an international team of researchers probing the nerve-insulating myelin sheath were bolstered by the work of Boston College biologists, who used x-rays to uncover how mutations affect the structure of myelin, a focal point of research in multiple sclerosis and other neurological disorders.

The findings were central to the group's broader conclusion that a set of protein processes required in the early-stage conversion of glucose into fatty acids are critical to the proper formation and layering of myelin membrane, the researchers report in the Proceedings of the National Academy of Sciences.

Boston College Professor of Biology Daniel Kirschner, Senior Research Associate Hideyo Inouye, graduate student Adrienne Luoma, and undergraduate Michelle Crowther partnered with Dutch, Italian, Swiss and Japanese scientists. The research group looked at the composition of myelin lipids for clues about their role in myelin structure and stability, Kirschner said. Myelin sheaths surround the axons of neurons and are considered critical to the proper functioning of the nervous system.

"Myelin is a stack of membranes providing insulation to the axon and with that insulation comes rapid nerve conduction," said Kirschner. "If myelin becomes defective, the membranous insulator becomes leaky and the nerve doesn't conduct as well. If myelin is totally missing along part of an axon, the nerve conduction is blocked."

Using x-ray diffraction, Kirschner's group captured a view of the dynamic membrane assembly in whole nerve samples taken from mice engineered to mimic myelinic diseases. Compared to other microscopy techniques used in the study of myelinated tissue, x-ray diffraction delivers clearer, cleaner and quicker results about the structural integrity of internodal myelin, Kirschner said.

"We were able to tell that the packing of the membranes was abnormal, which could affect the electrophysical properties of myelin," said Kirschner. "We also saw that the packing of the lipids in the myelin lipid bilayers was more disordered in samples from the transgenic mice used here."

Other types of microscopy introduce chemical modifications to the tissue under study. These agents and the time involved in preparing and analyzing such samples can alter the molecular structure and mask the dynamic interactions of myelin. X-ray diffraction requires no chemical treatments and can be completed in about an hour, Kirschner said.

"The advantages of x-ray diffraction are that we can examine and analyze whole pieces of tissue and give information about the effect of the mutation on the native structure of the myelin as well as on its stability," said Kirschner.

The researchers have been focusing on genetically modified mice for approximately four years as part of research into the role of myelin degeneration in a range of diseases of the central and peripheral nervous systems. Kirschner says his team is also exploring use of the technique in animal models of spinal cord injury and repair.

Source: Boston College (news : web)