Think fast! Scientists unlock nerve speed secret

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In the second it takes you to read these words, tens of thousands of vesicles in your optic nerves are released in sequence, opening tiny surface pores to pass chemical signals to the next cell down the line, telling your brain what you're seeing and your eyes where to move.

Thanks to two new studies – including one spearheaded by an undergraduate biochemistry student at Rice University and published online today by *Nature Structural and Molecular Biology* – scientists have defined the function of a key protein that nerve cells use to pass information quickly.

Like all cells in our bodies, nerve cells are encased in a membrane, a thin layer of fatty tissue that walls off the outside world from the cell's interior. And like other cells, nerve cells use a complex system of proteins as sensors, switches and activators to scan the outside world and decide when to open membrane doorways to take in food, expel waste and export chemical products to the rest of the body.

Many studies suggest that a group of proteins called SNAREs act like the cell's loading dock managers, deciding when to open the door to release shipments of chemical freight. SNAREs form a docking bay for cartons of chemicals encased in their own fatty membranes.

"Nerve cells are one of the few cells in our bodies in which vesicles are prepositioned at the cell membrane, because they have to be ready to release neurotransmitter to the next nerve cell at a moment's notice," said

principal researcher James McNew, assistant professor of biochemistry and cell biology.

SNAREs are a key player in membrane fusion. They oversee the merger of the cell's outer membrane with the membrane encasing the chemical freight, and they do it in such a way that the freight can be exported, but no outside cargo can enter.

"With nerve cells, we've known that SNAREs provide the mechanical energy for membrane fusion, and another protein called synaptotagmin is the actuator," McNew said. "We also knew there was a chemical brake in the system, something that held the pre-positioned vesicle in check, but poised for release. These new studies clearly show that the brake is a protein called complexin."

Rice's study, which was conducted in McNew's lab, largely by undergraduate Johanna Schaub, involved in vitro experiments on a synthetic and highly controlled complex of membranes and proteins. Via these experiments, Schaub was able to show that SNARE-driven membrane fusion – the act that opens the door for neurotransmitter to leave the neuronal cell – was inhibited by complexin.

"By halting fusion partway, complexin essentially shortens the response time for signal transmission," said Schaub, who will begin graduate school at Stanford University in the fall. "The nerve cell can almost instantaneously pass on its information."

McNew said the finding is independently confirmed by work published online June 22 by Science magazine. In that study, Columbia University's James Rothman and colleagues created mutant cells with SNAREs on the outside rather than the inside, and they used the cells to show that complexin could inhibit fusion that would otherwise be expected to proceed.

"Complexin is the brake," McNew said. "It says, 'Stop. Don't go any further until you get the signal from synaptotagmin.'"

Source: Rice University