Protein that regulates hormones critical to women's health found in pituitary

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University of Wisconsin-Madison researchers have solved the mystery surrounding a "rogue protein" that plays a role in the release of neurotransmitters and hormones in the brain.

The scientists found abundant amounts of the puzzling protein — whose main location and function were unknown until now — in a specific area of the pituitary gland. Like someone at a control knob, the protein may adjust the release of the two hormones that come almost exclusively from the posterior pituitary: oxytocin, which controls many reproductive functions, and vasopressin, which controls fluid balance.

"The findings raise very interesting possibilities for women's health, in which rising and falling hormone levels play a key role in many biological processes," says senior author Meyer Jackson, a professor of physiology at the UW-Madison School of Medicine and Public Health (SMPH). More studies will be needed to better understand the protein, he adds.

The study appears in the Jan. 11 *Nature Neuroscience*.

The research focused on Syt IV, a maverick member of the synaptotagmin family of 17 proteins, which are present in both mice and humans. Synaptotagmins are usually embedded in the membranes of small sacs, or vesicles, filled with neurotransmitters and hormones within nerve terminals. When an electrical impulse from one cell reaches a nerve terminal, it triggers the release of calcium, which in turn triggers

the spilling out of the vesicle's contents — neurotransmitters and hormones — so they can act on other cells.

"Most synaptotagmins are triggering molecules that drive a vesicle's membrane into the membrane that surrounds a neighboring cell so that chemicals inside the vesicle can come out," says Jackson.

But Syt IV is an odd member of the family because it doesn't bind to calcium, said Jackson. In addition, Syt IV is found only sparsely in most parts of the brain. But Jackson and his colleagues were surprised a few years ago when they discovered large amounts of it in the posterior pituitary, one of the three primary parts of the gland.

He teamed with Edwin Chapman, a Howard Hughes Medical Institute investigator, fellow SMPH physiology professor and synaptotagmin expert. The UW-Madison researchers conducted high-powered biophysical measurements to understand exactly what Syt IV does in the pituitary. They made a thorough comparison of the pituitaries from normal mice and mice in which Syt IV had been knocked out.

The work showed conclusively that, like other members of the synaptotagmin family, Syt IV resides on vesicles. But unlike the others, Syt IV doesn't trigger neurotransmitter or hormone release.

"It does not simply translate a calcium signal into a command for hormone release," says Jackson. "Unlike other synaptotagmins, Syt IV tunes the triggering command and determines whether the same electrical impulse will let a large or small amount of hormone out of the nerve terminal."

This ability to modulate hormone release may have important implications for pregnancy, birth, lactation and the menstrual cycle, all of which are linked to fluctuations in oxytocin levels.

"Any change in the body that entails releasing more or less of this hormone into the bloodstream could well be a result of the brain's making more or less of this protein," says Jackson, who for two decades has studied the powerful pea-sized pituitary located at the base of the brain.

For example, early release of oxytocin can lead to premature birth, a phenomenon that has intrigued Jackson for a long time.

"It's quite possible that Syt IV levels change during pregnancy, birth and even post partum," he conjectures.

Confirming the possibility will be the next order of business for the Wisconsin researchers and others.

Jackson's interest in the effects of oxytocin, also known as the "love hormone," is not restricted to the female reproductive system. Last year, his team showed that Viagra acts in the posterior pituitary by enabling electrical impulses to release more oxytocin.

Source: University of Wisconsin-Madison