IN THE NEWS

A riddle wrapped in a mystery

Most women believe that men simply don't understand them. A lot of men would agree that the mind of a woman is a mystery. But at the Society for Neuroscience meeting in New Orleans, some of the most newsworthy stories tried to unravel the workings of the female brain.

For example, what is going on in the brain of a woman in love? Helen Fisher from Rutgers University found that "women showed more activity in the caudate, septum and posterior parietal cortex, which are linked to reward, emotion and attention." By contrast, "men showed more activity in visual processing areas, including one associated with sexual arousal." (*BBC Online*, 12 November 2003).

***STL Today* (11 November 2003) described a study from a Dutch team who used functional imaging to look inside the brains of women as they experienced orgasm. According to the authors, "the workings of the female brain during sex have been a mystery and something of a taboo until now."**

The brains of new mothers also came under scrutiny (*The Atlanta Journal-Constitution*, 14 November 2003). Tracey Shors, also from Rutgers University, found that "female rats in the postpartum period are less anxious and more resistant to stress than females without babies."

And finally, what happens during the menopause? As described in the *Sofia Morning News* (14 November 2003), monkeys eat more and gain weight after ovariectomies, and they also show higher levels of leptin.

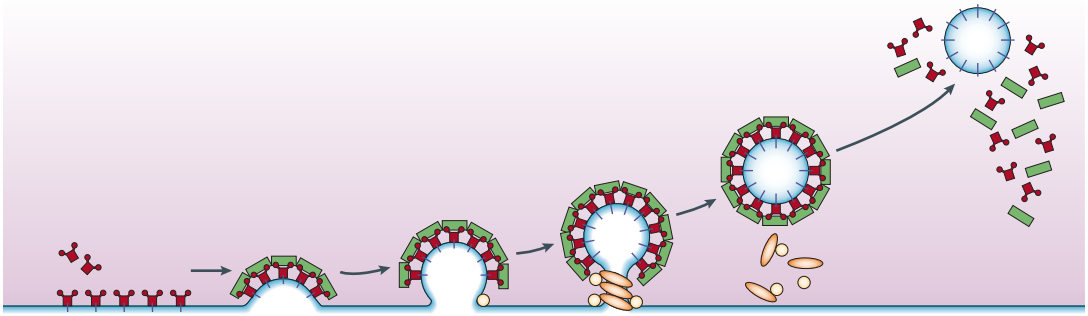
Rachel Jones

CELL BIOLOGY OF THE NEURON

Endocytic partnership

Many accessory proteins have been linked to clathrin-mediated endocytosis, but their exact roles and functional interactions are not always clear, as the cases of endophilin and synaptojanin exemplify. Genetic studies have associated these molecules with endocytosis at the synaptic terminal, and the enzymatic activities of both proteins have been characterized. However, the details of their involvement in endocytosis had remained obscure. Now, two complementary articles in *Neuron* shed some light on the function of these proteins *in vivo* and highlight the importance of a direct interaction between them for endocytosis to occur.

Synaptojanin is a phosphoinositide phosphatase that can hydrolyse phosphatidylinositol-4,5-biphosphate ($PtdIns(4,5)P_2$), a key regulator of the assembly of the clathrin coat. Endophilin, a protein with several binding partners including synaptojanin, has been thought of as an adaptor molecule that recruits synaptojanin to its site of action. But endophilin also has an enzymatic activity — it is an acyl transferase that can synthesize phosphatidic acid. So, owing to its ability to alter the lipid composition of the membrane, endophilin could affect endocytosis in ways other than as an adaptor. The two new studies come from opposite angles to converge on the idea that the direct interaction between synaptojanin and endophilin is crucial for



NEUROLOGICAL DISORDERS

Fragile X functions

A study published in *Proceedings of the National Academy of Sciences of the USA* provides evidence that the fragile X mental retardation protein (FMRP) might be involved in the translational regulation of synaptic proteins. Mutations in *FMR1*, which encodes FMRP, cause fragile X syndrome, one of the most common causes of mental retardation.

Although FMRP has been implicated in translational regulation, and is known to bind to many messenger RNAs that are found in the brain (including its own), its functions are far from clear. The new study, by Todd and colleagues, shows that levels of FMRP are increased in primary cortical neurons that are treated with a metabotropic glutamate receptor (mGluR) agonist. This rise is accompanied by an increase in the translation of PSD95, a scaffolding protein that is important for synaptic assembly. Both of these effects can be prevented by treatment with an mGluR antagonist, and the rise in PSD95 is not seen in cultures derived from mice that lack FMRP.

The mRNA for PSD95 contains a so-called 'G-quartet' sequence, which is found in other mRNAs that are bound by FMRP. The evidence indicates that activation of mGluRs causes translation of FMRP to be increased, and that this acts on the mRNA of PSD95 to increase its translation. Surprisingly, neither treatment of the neurons with glutamate nor depolarization with KCl leads to upregulation of FMRP or PSD95. This indicates that the context in which mGluR receptors are activated is important for these effects.

Although FMRP is known to bind to many other mRNAs, and therefore is likely to influence translation of a wide range of proteins, these results raise the possibility that some of the neuropathology of fragile X syndrome might result from abnormal regulation of PSD95 expression, which could alter mGluR-dependent synaptic plasticity. Further work will need to define how mGluR activation upregulates FMRP translation, and which other proteins are regulated in this way.

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References and links

ORIGINAL RESEARCH PAPER Todd, P. K. *et al.* The fragile X mental retardation protein is required for type-1 metabotropic glutamate receptor-dependent translation of PSD-95. *Proc. Natl Acad. Sci. USA* **100**, 14374–14378 (2003)

FURTHER READING Chelly, J. & Mandel, J.-L. Monogenic causes of X-linked mental retardation. *Nature Rev. Genet.* **2**, 669–680 (2001)