

## **M<sub>2</sub> muscarinic receptors possibly facilitate oxytocin synthesis in the mouse supraoptic nuclei**

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In the paraventricular (PVN) and supraoptic nuclei (SON) of the hypothalamus, oxytocin and arginine-vasopressin (AVP) are synthesized to cause the lactation and reabsorption of water in the kidney, respectively. We have previously reported that M<sub>2</sub> muscarinic receptors in the SON, but not PVN, promote AVP synthesis. The present study was carried out to examine whether M<sub>2</sub> muscarinic receptors also regulate oxytocin synthesis in the hypothalamus. M<sub>2</sub> receptor knockout (M<sub>2</sub>KO) mice and wild-type (WT) mice (3-4 months old) were used in the following experiments. The oxytocin neuron, AVP neuron and M<sub>2</sub> muscarinic receptor were identified by immunohistochemistry. c-Fos immunoreactivity was used as a marker for neuronal activity in the hypothalamus. In M<sub>2</sub>KO mice, the number of oxytocin neurons was significantly decreased in the SON, but not in the PVN, compared with WT mice. The muscarinic agonist pilocarpine increased the number of c-fos positive cells in SON of WT mice. However, the increase of c-fos positive cells was significantly decreased in SON of M<sub>2</sub>KO mice. Immunoreactivity of M<sub>2</sub> receptor was detected in the SON region, although it seemed to be not expressed in the cell body of oxytocin or AVP neurons. These results suggest that M<sub>2</sub> receptors may stimulate oxytocin synthesis in SON neurons as is the case of AVP, possibly through an unidentified, indirect pathway.