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NEURON–GLIA INTERACTIONS

Glia make waves

CORBIS

The 'slow waves' in slow-wave sleep represent cortical activity that is synchronized at a low frequency. Several mechanisms probably control these slow oscillations, and Fellin *et al.* now show that 'gliotransmitters' released by astrocytes play an important part in this process.

The authors used transgenic mice in which astrocytes expressed a dominant-negative (dn) form of a SNARE protein, preventing vesicle release from these cells. Electroencephalogram recordings showed that sleep deprivation (which increases homeostatic sleep pressure) enhanced slow oscillations during subsequent sleep more in control than in dnSNARE mice.

The authors next examined the mechanisms underlying this effect in anaesthetized animals. As previous studies have shown, urethane-anaesthetized mice also displayed cortical slow oscillations. The power of these oscillations was lower in dnSNARE mice than in wild-type mice and *in vivo* patch-clamp recordings revealed that pyramidal neurons in the somatosensory cortex of dnSNARE mice had shorter periods of depolarization and prolonged periods of hyperpolarization.

The authors showed that cortical neurons of dnSNARE mice had a reduced surface expression of the NMDAR (*N*-methyl-D-aspartate receptor) subunits NR2A and NR2B, resulting in decreased NMDAR activity and an increased AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid)/NMDA current ratio (which is known to affect the generation of slow oscillations). In agreement with this finding, applying an NMDAR antagonist to the brain decreased slow oscillations more in wild-type than in dnSNARE mice. By contrast, applying the gliotransmitter D-serine, a co-agonist of NMDARs, to the brains of dnSNARE mice increased cortical slow oscillations more than it did in control mice.

Another gliotransmitter, ATP, is hydrolysed to produce adenosine, which activates neuronal A1 receptors (A1Rs). The authors showed that applying an A1R antagonist to the brain increased slow oscillations in control but not in dnSNARE animals; these results are in agreement with earlier findings supporting the view that astrocytic activation of neuronal A1Rs inhibits cortical synapses.

This study highlights an important role for glial cells in the regulation of neuronal network activity. The ability of astrocytic gliotransmitters to activate neuronal NMDARs and A1Rs and increase or decrease, respectively, slow oscillations suggests that the coordinated action of gliotransmitters, perhaps released in different amounts depending on sleep pressure, regulates synchronized cortical activity during slow-wave sleep.

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ORIGINAL RESEARCH PAPER Fellin, T. *et al.* Endogenous nonneuronal modulators of synaptic transmission control cortical slow oscillations in vivo. *Proc. Natl Acad. Sci. USA* **106**, 15037–15042 (2009)