

## ● Cellular/Molecular

**Glycine Receptor Activation: When Three Out of Five Is Enough**

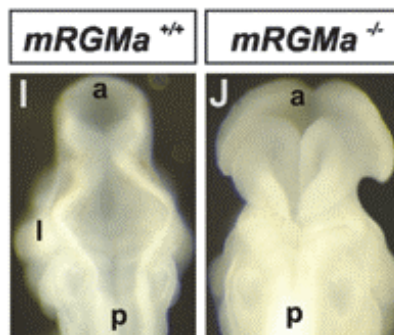
Marco Beato, Paul J. Groot-Kormelink, David Colquhoun, and Lucia G. Sivilotti

The prototypic member of the acetylcholine receptor family, the muscle nicotinic receptor, is a heteromeric complex with five subunits but only two ligand-binding sites. However, some members of this receptor superfamily are homomeric, containing five seemingly identical binding sites. Whether activation actually requires binding of five agonist molecules in this situation is unclear. Such questions cannot be answered using classical pharmacological methods. Thus Beato et al. analyzed the single-channel activity of recombinant glycine receptors containing five  $\alpha 1$  subunits, the principal juvenile form of this inhibitory synaptic receptor. The channels opened more efficaciously as the glycine concentration increased, but gating saturated when three glycine molecules were bound. They could not resolve whether the fourth and fifth bindings occur or are silent. The three out of five odds may be a general rule, because similar results have been suggested for homomeric GABA<sub>C</sub> and 5-HT<sub>3</sub> channels.

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## ▲ Development/Repair/Plasticity

Mouse RGMa (mRGMa) and mRGMb were expressed in a nonoverlapping pattern in the nervous system, whereas mRGMc was confined to skeletal muscle. Despite its expression in the superior colliculus, mRGMa is not essential for patterning of ganglion termination zones, as demonstrated by normal retinotectal mapping in mRGMa-deficient mice. Instead, one-half of the mRGMa-deficient embryos were exencephalic (they failed to close the neural tube), suggesting a more significant role in early development. The latter function appears to be a role shared with the Ephrins.



Dorsal head view of embryonic day 10.5 mice showing exencephalic phenotype in mRGMa-deficient mice (J) compared with wild-type mice (I).

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## ■ Behavioral/Systems/Cognitive

**Painful Memories**

Thomas Klein, Walter Magerl, Hanns-Christian Hopf, Jürgen Sandkühler, and Rolf-Detlef Treede

They focused on a behavioral correlate that is easy to evoke and measure in humans: pain. While both stimulation patterns led to a corresponding change in perception (hyperalgesia with LTP-like stimuli and hypoalgesia with LTD-like stimuli), the specific outcomes and mechanisms differed subtly. Although the underlying mechanisms may be complex, these results add to the idea that LTP-like plasticity contributes to hyperalgesia and chronic pain, whereas LTD-like plasticity may contribute to the analgesia associated with treatments such as transcutaneous electric nerve stimulation (TENS) and perhaps its ancient relative, acupuncture.

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## ■ Behavioral/Systems/Cognitive

**CRE, Transcription, and HD**

Karl Obrietan and Kari R. Hoyt

The neurodegeneration in Huntington's disease (HD) has been linked to polyglutamine repeats in the huntingtin protein. The consequences of this mutation, and indeed the normal function of the protein, remain a mystery. Recently, *in vitro* evidence suggested that huntingtin-related intranuclear inclusions interfere with cAMP response element (CRE)-mediated gene transcription, presumably by binding of mutant huntingtin with CRE-binding protein (CBP). However, in this issue Obrietan