Control of glycine receptor activation by a glycine transporter co-expressed in *Xenopus* oocytes

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Inhibitory glycinergic neurotransmission in the dorsal horn of the spinal cord is essential in regulation of nociceptive signalling, through reduction of neuronal excitability. Failure of glycinergic transmission in the dorsal horn causes normally innocuous stimuli to become painful (allodynia) and increases sensitivity to noxious stimuli (hyperalgesia). The development of chronic, pathological pain is thought to be attributed to the loss of inhibitory signalling. Management of neuropathic pain with current therapeutics is challenging and there is a great need for more effective treatments. In studies assessing compounds which increase glycinergic signalling by potentiating glycine receptor activity or inhibiting transporter activity, this system has shown potential for therapeutic targeting. The spatially restricted expression of glycine receptors and transporters is an advantage for targeting specific pathologies such as pain.

In this study, we demonstrate that the membrane transporter, glycine transporter 2 (GlyT2) can control the glycine membrane receptor α1's (GlyRα1) agonist activation in restricted extracellular space of a biological model. The model consists of co-expression of the GlyT2 and GlyRα1 in *Xenopus* oocytes. We show that glycine uptake by GlyT2 can dramatically alter the GlyRα1 currents in extracellular spaces in which diffusion is restricted. Lipid compounds which have shown possible therapeutic benefits in either GlyT2 or GlyRα1 are assessed in the system described.