merely reduces the potassium conductance at activated inhibitory synapses[9], these amino-acids may not necessarily interact with the same receptor as the transmitter. The failure of strychnine to reduce the hyperpolarizing postsynaptic inhibition of certain supra-spinal neurones[10], which presumably also involves an increased permeability to potassium ions, however, suggests that the interfering effect on spinal inhibition is most probably at the transmitter receptor site.

Glycine is rapidly metabolized in the spinal cord[11] and the distribution of incorporated glycine is remarkably similar to that of glycine as extracted by 5 per cent trichloracetic acid[12]. Observations on the lack of action of a variety of enzyme inhibitors, including amino-oxyacetic acid, hydroxylamine, 2-hydroxy-ethyl-hydrazine, *p*-aminohippuric acid and aminopterin on the glycine-induced depression of interneurones and Renshaw cells may indicate that glycine is effectively removed from the extraneuronal environment by rapid intracellular transfer, rather than by enzyme inactivation. This mechanism may be similar to the active accumulation of amino-acids by tumour cells[13] and brain slices[14]. It is perhaps significant that different membrane sites have been proposed for the transfer of "glycine-like" and "GABA-like" amino-acids into brain slices[14]. It is possible that the actual hyperpolarizing action of glycine is produced by intracellular transfer and the consequent re-distribution of potassium and chloride ions: such a mechanism is not incompatible with a function of glycine as a spinal inhibitory transmitter. If this glycine-induced ionic transfer was not solely restricted to inhibitory synapses which are sensitive to strychnine, this proposal provides an explanation of the finding that glycine depresses the firing of cortical neurones in the apparent absence of a postsynaptic inhibitory process affected by strychnine[3].

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Acetylcholine, Strychnine and Spinal Inhibition

It was recently proposed[1] that the action of strychnine at spinal inhibitory synapses may be explained by an antagonism between strychnine and acetylcholine, an interaction between acetylcholine and presynaptically located receptors which are sensitive to strychnine being an essential requirement for the release of the inhibitory transmitter. This proposal, which would "eliminate blockade by strychnine as an essential qualification for the identification of a putative inhibitory transmitter" in the mammalian spinal cord, is based on the finding that strychnine, in concentrations of the order of $3–300 \times 10^{-6}$ molar, reduces the release of acetylcholine by impulses in the preganglionic terminals of the perfused feline superior cervical ganglion.

An opportunity has been taken to test this hypothesis on spinal neurones for which there is very good evidence that acetylcholine is an excitatory transmitter. The pharmacology of the excitation of Renshaw cells by impulses in motor axon collaterals bears some resemblance to that of cholinergic excitation in sympathetic ganglia[2–4]. Furthermore, Renshaw cells can be inhibited by appropriate spinal volleys[5,6], and this inhibition is reduced by strychnine administered micro-electrophoretically[7].

It has invariably been found that concentrations of strychnine, adequate to suppress the inhibition of lumbar Renshaw cells evoked by hind limb afferent volleys, enhance rather than reduce the excitation of these neurones by sub-maximal ventral root volleys. This facilitation might be explained as a blockade of a simultaneously occurring inhibition but, in view of the associated increase in the sensitivity of Renshaw cells to both acetylcholine and excitant amino-acids, a direct excitation of these cells by strychnine is a more likely explanation. Under conditions of comparatively high strychnine concentrations there is a reduction in the number of synaptically evoked spikes. This is, however, presumably indicative of a postsynaptic, rather than presynaptic, depressant action because it is accompanied by changes in the shape and size of action potentials recorded outside the cells and a diminution in the sensitivity of Renshaw cells to electrophoretically administered excitants[7].

Thus no evidence has been obtained which would indicate that concentrations of strychnine sufficient to block the inhibition of Renshaw cells diminish the amount of acetylcholine released from axon collateral terminals. Unless it can be shown that there are differences in the susceptibility to strychnine of the acetylcholine-releasing mechanisms at the terminals of motor axon collaterals, the postsynaptic acetylcholine receptors on Renshaw cells and the proposed acetylcholine receptors on the terminals of inhibitory nerve fibres, the postulate that acetylcholine interaction with these latter receptors is necessary to initiate the release of inhibitory transmitter appears unnecessary. Furthermore, the recent demonstration that glycine hyperpolarizes spinal neurones, and that this effect is blocked by strychnine[8], provides a more satisfactory explanation of the action of strychnine in terms of postsynaptic antagonism at inhibitory synapses.

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Pharmacological Characteristics and Ionic Bases of a Two Component Postsynaptic Inhibition

Several types of postsynaptic inhibition have been observed in molluscan neurones; in *Aplysia*, the most common is a rapidly decaying inhibitory postsynaptic potential (IPSP) with pharmacological characteristics which have been described by Tauc and Gerschenfeld[1].