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THE FIXATION OF TETANUS TOXIN BY GANGLIOSIDE

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TETANUS toxin, which contains about 40 million mouse LD_{50}/mg, has been shown by Eccles[1] to act by suppressing synaptic inhibition. In this respect its mode of action appears to be the same as that of strychnine.

In order to identify the toxin receptor substance at the inhibitory synapses the Wassermann–Takaki phenomenon of 1898 was reinvestigated. This is the fixation of tetanus toxin by the grey matter of nervous tissue. It was shown that this fixation is highly specific for tetanus toxin and the receptor was identified as a water-soluble ganglioside, which exists in nervous tissue in water-insoluble complexes with cerebrosides, sphingomyelin and doubtless other substances.[2–7]

Gangliosides form high-particle-weight micelles in water. This provides the basis for an analytical ultracentrifugal assay of toxin fixation.[5] The fixation is highly specific, and very avid, some gangliosides fixing up to twenty times their own weight of toxin.[8] The fixation is not electrostatic as with certain basic proteins.

There are a number of different gangliosides differing in hexosamine content and ramification of residues[9] and in sialic acid content.[5, 10] Toxin fixation is dependent on sialic acid (within limits) and hexosamine contents, and on other factors. Gangliosides having the same sialic content may vary in toxin fixing capacity from 2·6 to 19 mg toxin fixed/mg ganglioside.[8, 10] Hexosamine-free ganglioside from normal brain does not fix toxin.[8, 9] Hexosamine-containing ganglioside from Tay–Sachs brains does not fix toxin.[8]

Ganglioside also fixes the convulsant drugs, strychnine, brucine and thebaine, which have the same action as tetanus toxin in suppressing synaptic inhibition.[1, 8] γ-Aminobutyric acid, β-hydroxy-γ-aminobutyric acid, histamine, adrenaline, noradrenaline and dopamine are not fixed by ganglioside, but serotonin is fixed, as well as tryptamine, lysergic acid diethylamide and ergometrine. Reserpine is not fixed.[8]

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