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Comparison of the action of types A and F botulinum toxin at the rat neuromuscular junction.

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Blockade of neuromuscular transmission was produced in the lower hind limb of the rat by local injection of either type A or type F botulinum toxin (BoTx). At 1, 3, 7, and 10 days after injection, the extensor digitorum longus (edl) nerve-muscle preparation was excised and analyzed for alterations in muscle mechanical properties or spontaneous and nerve stimulus-evoked quantal transmitter release. Muscles receiving type A toxin were paralyzed up to and including 7 days after injection. Muscles treated with type F toxin, although completely paralyzed at 1 and 3 days after injection, twitched in response to nerve stimulation by 7 days. Both toxins induced a marked decrease in the frequency of miniature end-plate potentials, but type A did so to a greater extent. Between 1 and 3 days after toxin injection nerve impulse-evoked transmitter release was reduced in both type A- and type F-treated muscles. Evoked release was temperature sensitive in type A-treated muscles but not in those treated with type F. 3,4-Diaminopyridine (3,4-DAP), a compound which increases nerve-evoked transmitter release by increasing Ca²⁺ influx, was more effective in reversing the paralysis in type A than in type F-treated muscles. 3,4-DAP induced asynchronous end-plate potentials in response to nerve stimulation in type F-paralyzed muscles, but not in muscles treated with type A. Amidination of the amino groups (presumably lysine) on the toxin by treatment with ethylacetimidate increased the potency and efficacy of only type F BoTx. The results show that type F BoTx differs from type A, mainly by its lower potency, efficacy, shorter duration of action, and by being less effectively antagonized by 3,4-DAP.

Major Subject Heading(s)	Minor Subject Heading(s)	CAS Registry / EC Numbers
<ul style="list-style-type: none"> • 4-Aminopyridine [analogs & derivatives] • Botulinum Toxins [toxicity] • Neuromuscular Junction [drug effects] 	<ul style="list-style-type: none"> • Aminopyridines [pharmacology] • Animals • Botulinum Toxins [antagonists & inhibitors] • Evoked Potentials [drug effects] • Imidooesters [pharmacology] • Injections, Subcutaneous • Lethal Dose 50 • Mice • Motor Endplate [drug effects] • Muscle, Smooth [drug effects] • Rats, Inbred Strains • Rats • Synaptic Transmission [drug effects] 	<ul style="list-style-type: none"> • 0 (Aminopyridines) • 0 (Botulinum Toxins) • 0 (Imidooesters) • 1000-84-8 (ethyl acetimidate) • 504-24-5 (4-Aminopyridine) • 54-98-6 (3,4-diaminopyridine)

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*NB Diller
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