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Title : TYPE OF STIMULUS AND REVERSAL OF NM BLOCK IN VIVO

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Introduction. In mammals voluntary muscle movements are initiated by short trains of tetanic stimuli of 16 to 60 Hz.[1] Despite this in the past in most neuromuscular (NM) studies either single stimuli of 0.1 to 2 Hz or relatively long 50 to 500 Hz tetani have been employed. It has been observed that in rats the type of stimulus significantly influenced the reversal of the d-tubocurarine (d-Tc) induced NM block by neostigmine and 4-aminopyridine (4-APYR).[2] In these studies, however, in any animal only one type of stimulation was employed. The present study was undertaken to eliminate the influence of individual variation and to extend our observations to other NM blocking agents and antagonists.

Methods. Twenty-eight male Sprague-Dawley rats were anesthetized with i.p. pentobarbital and urethane, tracheostomized and mechanically ventilated with O_2. Drugs were administered through cannulated jugular veins and i.a. blood pressure and heart rate were continuously monitored from a carotid artery. The tendons of both tibialis anterior muscles were attached to FT03 transducers and a pretension of 25 g was applied to both muscles. Muscles were indirectly stimulated with platinum electrodes applied to the distal part of the severed sciatic nerves in the gluteal region. One nerve was stimulated with supramaximal single impulses of 0.2 msec duration at 0.1 Hz; the other with 0.1 sec trains of 50 Hz supramaximal impulses of 0.2 msec duration every 10 sec. The tension outputs were recorded on a Grass polygraph. The preparations remained stable for at least 3 hours. Greater than 90% steady state block was produced in the muscles stimulated by short trains of tetani ("tetanus" side) by the continuous i.v. infusion of d-Tc in 12, pancuronium in 12 and succinylcholine (SCh) in 4 animals. During the continuous infusion of NM blocking agents, 4 animals each in the d-Tc and pancuronium groups received i.v. neostigmine, pyridostigmine or 4-APYR in fractional doses until the last dose caused no further improvement of the tension output of the muscle stimulated by single impulses. The ED50 values of the antagonists were calculated from the log dose - response regression lines.

Results. The results summarized in table 1 indicate that the intensity of the steady state NM block produced by the 3 relaxants was significantly greater ($p < 0.01$, paired t test) on the "tetanus", than on the "twitch" side. Both d-Tc and pancuronium were antagonized by neostigmine, pyridostigmine and 4-APYR but their calculated ED50 was higher on the "tetanus" than on the "twitch" side. The maximal reversal of the d-Tc block by the optimal doses of the antagonists was also significantly greater ($p < 0.001$, paired t test) on the "twitch" than on the "tetanus" side. The antagonism of the SCh block by neostigmine and pyridostigmine (1 experiment with each) was insignificant. 4-APYR, however, caused a 40% to 48% reversal on both the "tetanus" and "twitch" side (2 experiments).

Conclusions. The findings of this study indicate that testing with single impulses may not give reliable information on the status of NM transmission. Apparent recovery of NM transmission during stimulation with single impulses does not mean that NM apparatus can respond equally well to short trains of tetanic stimuli associated with voluntary muscle movements. For this reason stimulation with short trains of tetani may be preferable to stimulation with single impulses for testing for residual NM block at the termination of surgery.

References.

1. Zierler KL: Mechanism of muscle contraction and its energetics, Medical Physiology. Edited by Mountcastle VB. St. Louis, The Mosby Company, 1974, Vol. 1, pp 84.
2. Foldes FF, Rao DBS, Deery A, et al: Stimulation parameters and reversal of d-Tc block in vivo. Anesthesiology 51:S286, 1979

Table 1. Stimulation Parameters, and the Intensity and Reversibility of the Neuromuscular Block In Vivo

Relaxant	Stimulation	NM Block (%)	ED50 (µg/kg) Neostig.	Pyrid. stig.	4-Ami. pyr.
d-Tc	Twitch[2]	87.4[4]	4.8	42.3	290
	Tetanus[3]	92.3**	9.4***	61.0*	650*
Pancur.	Twitch	89.5	5.1	40.2	170
	Tetanus	92.3**	6.1 n.s.	45.4 n.s.	290**
SCh	Twitch	82.8	Reversal <50%		
	Tetanus	89.7**	(see text)		

[1]Dose of antagonist that returned tension output to 50% of control. [2]Single impulses [3]Short trains of 50 Hz tetani. [4]Means of 4 experiments, SEM omitted for lack of space. *,** and *** indicate significance (paired t test) between the "twitch" and "tetanus" sides at the p <0.05, 0.01 and 0.001 levels respectively.