8996 P

Decurarizing Effect of Repetitive Stimulation of a Motor Nerve.

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One of us[1] described a temporary return of indirect excitability in the tongue of the curarized cat, following tetanization of the hypoglossal nerve. We have made some additional observations on the phenomenon, using the cat's peroneal nerve and tibialis anticus muscle. The experimental conditions were as described in our accompanying paper,[2] except that crude curare (1% solution) was administered instead of $MgSO_4$.

Curarization was carried to the stage at which single stimuli, applied to the otherwise resting nerve, failed to elicit a muscular twitch. The nerve was then tetanized, for periods varying from 1 second to one minute, the frequency also being varied from 14 to 120 per second.

Comparing the results with those obtained on animals "curarized" to the same stage with Mg[2], certain similarities appear. In both conditions, (a) tetanization of the nerve is followed by a return of the response to single stimuli; (b) the degree of this recovery varies with the frequency of tetanic stimuli employed; (c) the duration of the recovery is about the same, following a given period of stimulation.

Under curare, however, the first twitches obtained during the recovery are relatively weak. The curve described by the successive twitches shows first a rising and then a longer falling phase. Following 5 seconds of stimulation of the nerve, at 120 per second, the maximum recovery is seen in 6 to 10 seconds. If the period of tetanization is lengthened to 20 seconds the entire recovery curve is stretched out, so that the rising phase lasts for half a minute or more.

It seems to have been proven earlier[1] that this recovery is produced through the motor innervation of the muscle, and not through other fibers in the mixed nerve. If we attribute it to a chemical decurarizing agent, released at the nerve endings, the curve described seems to indicate that the concentration of the agent increases for a time after activity of the nerve has ceased. Acetyl

[1] Boyd, T. E., *Am. J. Physiol.*, 1932, **100**, 569.

[2] Brosnan, J. J., and Boyd, T. E., Proc. Soc. Exp. Biol. and Med., 1936, **35**, 405.

choline, accumulating in excess, might have a depressing effect, although this action of acetyl choline is said to be reversed under curare.[3, 4] The delayed recovery here is evidently not so caused, for acetyl choline (1 mg. in 1 cc.) injected intra-arterially during the rising phase of the recovery curve, has an immediate potentiating, not a depressing, effect.

Nevertheless repetitive stimulation of the nerve, under curare, does appear to leave some kind of after-depression which is not found with Mg. No muscular response was ever obtained *during* tetanization of the nerve, even with frequencies as low as 14 per second (*Cf.* Bremer and Titeca[5]). The recovery curve may be determined by 2 factors, the changing concentration of a decurarizing chemical and gradual recovery from a depression which varies in depth and duration according to the previous activity of the nerve. Unless the latter factor is assumed to exist, the decurarizing agent appears to be too slowly mobilized to be concerned in the normal excitation of muscle.

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Chemical Transmission from Nerve to Muscle, in Animals "Curarized" with Magnesium Sulphate.

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Lubinska[1] has described a type of peripheral summation or facilitation in cats. Following the administration of sufficient $MgSO_4$ intraperitoneally, the muscular response to single stimuli applied to a motor nerve is lost. Repetitive stimuli, however, evoke a tetanus, and temporarily thereafter single stimuli are again effective.

It seems to us that such effects might be due to local accumulation of some decurarizing chemical agent released at the nerve endings. Acetyl choline[2] and potassium[3] are temporarily effective antagonists

[3] Rosenblueth, A., Lindsley, D. B., and Morison, R. S., *Am. J. Physiol.*, 1936, **115**, 53.

[4] Briscoe, Grace, *J. Physiol.*, 1936, **87**, 425.

[5] Bremer, F., and Titeca, J., *Arch. Int. Physiol.*, 1935, **42**, 223.

[1] Lubinska, L., *Arch. Int. de Physiol.*, 1935, **41**, 456.

[2] Rosenblueth, A., Lindsley, D. B., and Morison, R. S., *Am. J. Physiol.*, 1936, **115**, 53.

[3] Wilson, A. T., and Wright, S., *Quart. J. Exp. Physiol.*, 1936, **26**, 127.