NORRIS, W. (1971). Wy 4036 (Lorazepam)—A study of its use in premedication. *Br. J. Anaesth.*, in the Press.

TURNER, P. & HARRY, T. V. A. (1971). Preliminary studies on the central effects of Lorazepam, a new benzodiazepine. *J. Clin. Pharm.*, in the Press.

Action of edrophonium on acetylcholinesterase at the mammalian neuromuscular junction

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A new method has been developed for estimating the degree of inhibition of the physiologically important acetylcholinesterase at the neuromuscular junction (Ferry & Marshall, 1971). This method is based on the prolongation of the extracellularly recorded endplate potential of a curarized rat diaphragm after treatment with anticholinesterase drugs.

In this work, endplate potentials were recorded extracellularly from the fully curarized rat phrenic nerve-diaphragm preparation with an insulated wire electrode located at the endplate region. The preparation was immersed in a saline medium (Liley, 1956) at 36°C. The effect of edrophonium in concentrations ranging from $0{\cdot}5 \times 10^{-6}$ M to 10^{-4} M was investigated; the duration of the endplate potential at half amplitude was measured. After the lowest concentration of edrophonium the duration was $1{\cdot}13 \pm 0{\cdot}025$ ($n=7$), and after the highest concentration, $3{\cdot}71 \pm 0{\cdot}27$ ($n=11$) relative to the individual controls.

In curarized preparations, the mean quantal content of the endplate potential of each of a number of cells was calculated from the variance of the amplitude of a series of intracellularly recorded endplate potentials elicited at 1 Hz. Under control conditions the overall mean quantal content was 178 (thirty-one cells) and after edrophonium 5×10^{-5} M it was 167 (twenty-three cells). There is no significant difference between these values ($P=0{\cdot}05$).

The effect of edrophonium on the contraction of the partially curarized diaphragm after indirect stimulation was investigated. With edrophonium ($0{\cdot}5 \times 10^{-6}$M) some reversal of the block was evident. From the electrophysiological work it was estimated that this concentration of edrophonium produced about 15% inhibition of the physiologically important acetylcholinesterase.

It is concluded that edrophonium inhibits the physiologically important acetylcholinesterase at the neuromuscular junction and that even a small degree of inhibition of the enzyme will facilitate transmission in the curarized phrenic nerve-diaphragm preparation.

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REFERENCES

FERRY, C. B. & MARSHALL, A. R. (1971). Electrophysiological estimation of inhibition of acetylcholinesterase with normal transmitter release. *Proc. Physiol. Soc.* in the Press.

LILEY, A. W. (1956). An investigation of spontaneous activity at the neuromuscular junction of the rat. *J. Physiol., Lond.*, **132**, 650–666.