LETTERS TO THE EDITORS

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Synaptic Transmission in the Spinal Cord

THE preparation used in this investigation has been either the spinal cord of the decerebrated or anæsthetized cat or the isolated oxygenated spinal cord of the frog, and it has been activated by electrical stimulation of a dorsal root (the 7th lumbar or 1st sacral in the cat, the 9th or 10th in the frog).

As Barron and Matthews[1] have shown, a single dorsal root volley normally sets up a large and prolonged negative potential of adjacent ipselateral motoneurones on which are superimposed spike potentials of discharged impulses (cf. ref. 2). The prolonged negative potential differs from the spike potentials in being decrementally transmitted by electrotonus along the axons of the motoneurones, and in the present experiments it has been recorded from the ventral root as it emerges from the spinal cord. This potential has been found to be diminished and shortened by nembutal anæsthesia, and ultimately with deep anæsthesia (about 100 mgm. per kgm. intravenously in the cat or prolonged soaking in 1 in 5,000 in the isolated frog's cord). A dorsal root volley sets up no spikes, but only a simple brief negative potential with a quick rise and a slower, approximately exponential, decay. It spreads electrotonically along the ventral root. The durations of latent period, time to summit, and time of half-decay are about 0·8, 3 and 7 msec. in the cat and 1·5, 5 and 25 msec. in the frog. When the potential is sufficiently large, owing either to a lower depth of anæsthesia or to summation of two or more successive responses, the motoneurones discharge impulses. The potential is thus analogous to the local catelectrotonic potentials set up by trans-synaptic stimulation of curarized ganglia[3] or neuro-muscular junctions[4,5], and may be termed a synaptic potential. Similarly, too, it appears to be set up by a brief active depolarizing agent, its decay being passive and governed by the electric time constant of the membrane.

The brief synaptic potential recorded in deep anæsthesia must be set up in the motoneurones by impulses in those dorsal root fibres which end in direct synaptic contact. By making the anæsthesia deep enough to block all synaptic transmission of impulses, the setting up of internuncial impulses has been prevented, and the spinal cord has been reduced to a single synaptic preparation (the two-neurone reflex arc). The complex and prolonged synaptic potential normally set up in motoneurones by a dorsal root volley results from summation of the synaptic potentials set up by bombardment of the motoneurones by the initial direct volley and later internuncial discharges.

With rapid repetitive stimulation (up to 200 per sec. in frog, 400 per sec. in cat) synaptic potentials in the anæsthetized cord sum to a plateau which decays abruptly on cessation of stimulation. There appears to be no building up of a persistent actively depolarizing agent such as gives the initial slowed decay with synaptic potentials of ganglia[3].

Eserine (intravenous doses up to 1 mgm. per kgm. in cats, prolonged soaking in 1 in 100,000 to 1 in 10,000 in isolated frog's cord) has no appreciable action on the time course of the synaptic potential of the anæsthetized motoneurones (single, double or repetitive stimulation). There is no trace of the prolonged junctional potential which was observed after repetitive trans-synaptic stimulation of the eserinized and curarized muscle or ganglion, and attributed to the accumulation and persistence of acetylcholine[6,7] Dale and co-workers have provided convincing evidence that acetylcholine acts as a synaptic transmitter at such junctions. With synapses in the central nervous system, however, there is no unequivocal evidence of synaptic transmission by acetylcholine, so the present negative results with eserine make it unlikely that acetylcholine plays any part in the synaptic transmission of simple spinal reflexes. On the other hand, the time course of the active depolarizing agent is so brief that it could be due to direct electrical stimulation of the motoneurones by the action currents of impulses in the terminals of the dorsal root fibres. Similarly, it was suggested[7] that the analogous brief transmitter action observed in sympathetic ganglia was possibly due to a direct electrical action, but with ganglia it is superimposed on the more prolonged depolarization due to acetylcholine transmission.

Synaptic transmission in the spinal cord is also different from that in muscle and ganglia in that it is not paralysed by curarine. In fact, curarine has the reverse effect, having a mild strychnine-like action in concentrations so low as 12 μmol. per litre.

JOHN C. ECCLES.

Physiology Department,
Medical School, King Street,
Dunedin, N.Z. Feb. 1.

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Induction of Sleep by Simultaneous Administration of Posterior Pituitary Extracts and Water

THE following investigation arose from considerations based upon well-known observations on the state of normal sleep. These are: (*a*) that during sleep the urine volume output is decreased and the blood diluted; (*b*) that many drugs (caffeine, etc.) which cause wakefulness are diuretics; and (*c*) that severe muscular work which, it is recognized, often facilitates the onset of sleep, has an antidiuretic action. It was thought, therefore, that the antidiuretic principle of the posterior pituitary, if given together with water, might possibly bring about an internal milieu so similar in many ways to that of normal sleep (for example, antidiuresis, dilution of the blood) that this state might eventually cause, deepen or prolong natural sleep.

Experiments were made on a number of subjects, many of whom were unaware of the object of the procedure, and were carried out after the average time had been recorded for which each subject would sleep spontaneously after lunch when good and repeatable conditions were given. Through the kind permission of Prof. P. C. Cloake and other clinicians, a number of these experiments were made on suitable hospital patients. Other experiments were made on students where, though the element of suggestion