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SHORT COMMUNICATION

Effect of Tubocurarine on the Central Generator of Embryonic Spontaneous Motility

J. SEDLÁČEK

Institute of Physiology, Faculty of Medicine, Charles University, Prague

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Summary

The continuous administration of d-tubocurarine (6.5 ± 0.4 mg/kg e.w./24 h) to chick embryos from the 4th to the 12th day of incubation had a positive effect on defects produced in the development of spontaneous motility either by decentralization of the spinal cord or by chemical phenobarbital depression, or by a combination of both experimental factors. In normal embryos, d-tubocurarine had no effect on the development of spontaneous motility.

Key words

Chick embryo – Spontaneous motility – d-tubocurarine – Phenobarbital – Spinal cord

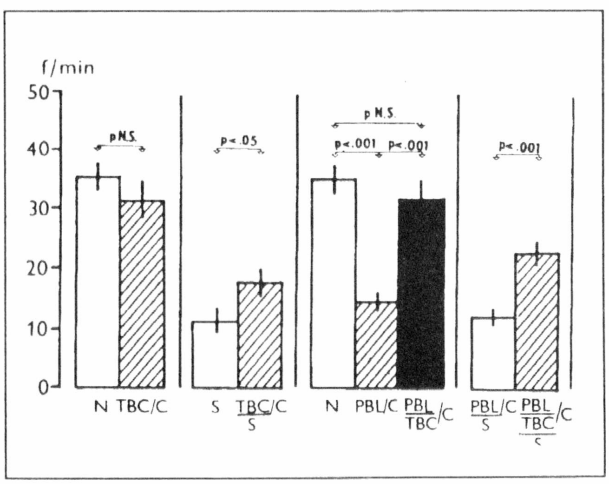

Fig. 1

The effect of chronic administration of d-tubocurarine on the spontaneous motility of 17-day-old embryos. Abscissa: the experimental group (n = 10): N – normal embryos; TBC/C – d-tubocurarine 6.5 ± 0.4 mg/kg e.w./24 h on day 4 to 12 of incubation; S – spinal embryos; PBL/C – phenobarbital 10.8 ± 0.8 mg/kg e.w./24 h on day 4 to 12 of incubation. Ordinate: spontaneous movement frequency per min (M ± S.E.M.).

Pittman and Oppenheim (1979) showed that a neuromuscular block of transmission reduced the natural death of motoneurones in the ventral horns of the chick spinal cord. When administered between 4 1/2 and 9 days of incubation, d-tubocurarine, α-bungarotoxin and botulotoxin were equally effective. The positive effect ended on the 11th day of incubation. This remarkable finding prompted us to test d-tubocurarine in chick embryos in which developmental reduction of spontaneous motility had been induced in various ways.

In these experiments, d-tubocurarine (TBC) (TUBARINE Miscible, Wellcome Found.) was administered in a mean dose of 6.5 ± 0.4 mg/kg e.w./24 h from the 4th to the 12th day of incubation, drawing it off continuously by suction across the egg paper membrane (Sedláček 1988). The indicator of the resultant effect was the resting frequency of the embryo's spontaneous movements on the 17th day of incubation.Motility was recorded by a modification of the vibration method in intact incubated eggs. The frequency of spontaneous movements was evaluated on a laboratory computer. The results were expressed as the mean minute frequency value of a 60 min continuous recording period (Sedláček 1977). The drug was administered chronically to four groups of chick embryos (of at least 10 embryos each): 1.normal control embryos, 2. spinal embryos decapitated on the 2nd day of incubation at stage 11-13 (Sedláček and Doskočil 1978), 3. embryos in which spontaneous

motility was suppressed from the 4th to the 12th day of incubation by the continuous administration of phenobarbital in a dose of 10.76 ± 0.78 mg/kg e.w. /24 h and 4. spinal embryos with chronic phenobarbital inhibition of motility from the 4th to the 12th day of incubation (Sedláček 1988).

The results in the above four groups have been summed up in Fig. 1. No significant effect on the development of spontaneous motility was found in normal embryos. In the second group, however (i.e. in the control spinal embryos), resting spontaneous motility increased by an average of 56 % compared with the respective controls. In embryos in which spontaneous motility developed under the depressive influence of phenobarbital (group 3), the chronic presence of tubocurarine in the administered cocktail had a significantly positive effect on the development of motility, which, on the 17th day of incubation, attained the same value as in normal embryos. In group 4 (spinal embryos developing under the permanent influence of phenobarbital), it had a similar positive effect, with motility attaining double the value found in the control spinal embryos.

The above results show that, when administered chronically from the 4th to the 12th day of incubation, tubocurarine had a positive effect on the functional development of the generator of embryonic spontaneous motility, but only in cases in which its development had been in some way morphologically or pharmacologically impaired, since in normal embryos the effect of chronicaly administered TBC was nil. A positive effect was found in the development of activity of the chronically decentralized spinal cord – when the development of motility is usually arrested at the level reached by the 13th day of incubation (Sedláček and Doskočil 1978) – and in the development, under the chronic depressive influence of phenobarbital, in both normal and spinal embryos (Sedláček 1988). If the positive effects of TBC were based on a block of neuromuscular transmission – and hence on a positive effect on the process of the natural death of motoneurones between the 4th and 12th day of incubation – it would have had to be manifested primarily in completely normal embryos. It is thus evident that the positive effect of TBC on the development of spontaneous motility is more complex, chiefly as regards its interference with functional maturation of the neuronal apparatus of the central generator of embryonic motility-all the more as the positive effect of TBC recorded in all spinal embryos takes place in a situation in which early decentralization itself causes a quantitative increase in motoneurone death above the natural level and prolongs this process to at least the 16th day of incubation.In 16-day-old chick embryos with a normal spinal cord, the ratio of living to dying motoneurones is 6-7:1, whereas in the decentralized spinal cord it falls to 1-2:1 (Sedláček et al. 1978). TBC thus either limits death of the motoneurones at the output of the spinal generator of embryonic motility, or enables the smaller number of neurones in this generator to develop embryonic spontaneous motor activity with a significantly higher rhythm. Since the elimination of small neurones by short-term N_2 hypoxia likewise leads to marked reduction of embryonic motility (Sedláček 1980), the TBC phenomenon described above should not only be considered as an effect of TBC on the spinal motoneurone population, but also to be due to the role of activity of spinal interneurones (Kostyuk and Vasilenko 1979).

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Reprint Requests
Prof. dr. J. Sedláček, Institute of Physiology, 1st Faculty of Medicine, Charles University, CS-128 00 Prague 2, Albertov 5.