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The influence of mescaline on the flexor reflex of the hind limb of the spinal rat

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We have stated previously that serotoninergic agents like L-5-hydroxytryptophan, L-tryptophan, LSD and fenfluramine stimulate the flexor reflex of the spinal rat which is antagonized by the 5-hydroxytryptamine (5-HT) receptor blockers, cyproheptadine, Danitracen (WA-335) and methergoline (Maj, Palider & Baran, 1976b). Mescaline possesses a strong depleting action on the 5-HT of blood platelets, which are regarded as a model of 5-HT neurons (May, Menkens & Westermann, 1969). Also, electrophysiological and biochemical findings show evidence of the influence of mescaline on 5-HT neurons (Tonge & Leonard, 1968; Aghajanian, Foot & Sheard, 1970; Bradshaw, Roberts & Szabadi, 1971; Haigler & Aghajanian, 1972; Tilson & Sparber, 1972; Bevan, Bradshaw & others, 1974). We now report the action of mescaline on the flexor reflex of the spinal rat, and the influence on this action of cyproheptadine and WA-335 (Stone, Wenger & others, 1961; van Riezen, 1972; Engelhardt, 1975; Maj, Baran & others, 1976a). Experiments were on Wistar male rats, 180–270 g, according to the method described previously in which an animal paw is stimulated electrically and contractions of the musculus tibialis anterior recorded (Maj & others, 1976b). Drugs: clomipramine, desipramine, imipramine—all as hydrochlorides and mescaline sulphate were injected into the femoral vein as solution in 0·9% NaCl. Cyproheptadine and WA-335 were used intraperitoneally as suspensions in a 1% aqueous solution of Tween 80.

Mescaline 1·5–10 mg kg^{-1}, stimulated the flexor reflex of the spinal rat (Fig. 1). The effect appeared immediately after injection and lasted 30–90 min. As

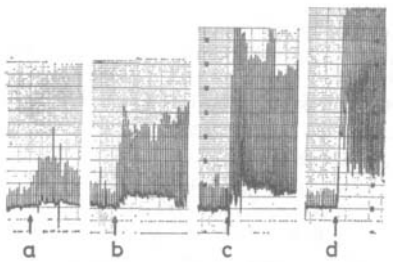

FIG. 1. Showing the effect of mescaline in 0·9% NaCl solution given into the femoral vein a—1·5, b—2, c—3, d—5 mg kg^{-1} on the flexor reflex (m. tibialis anterior) of the hind limb of the spinal rat.

* Correspondence.

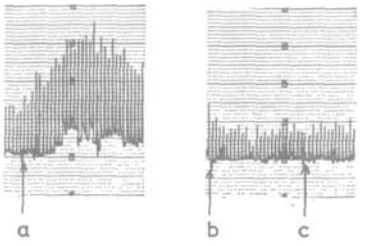

FIG. 2. Showing the effect of c-second dose of mescaline (3 mg kg^{-1}, i.v.) on the flexor reflex (m. tibialis anterior) of the hind limb of the spinal rat pretreated with b—cyproheptadine (1 mg kg^{-1}, i.p.) given as a suspension in 1% aqueous solution of Tween 80 30 min before the second dose of mescaline. a—first dose of mescaline (3 mg kg^{-1}, i.v.).

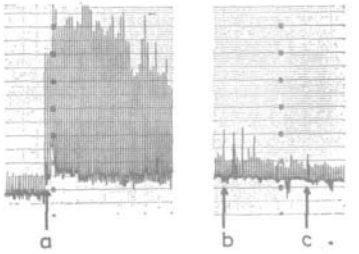

FIG. 3. The effect of c—second dose of mescaline (2 mg kg^{-1}, i.v.) on the flexor reflex (m. tibialis anterior) of the hind limb of the spinal rat pretreated with b—WA-335 (3 mg kg^{-1}, i.p.) given as a suspension in 1% aqueous solution of Tween 80 30 min before the second dose of mescaline. a—first dose of mescaline (2 mg kg^{-1}, i.v.).

shown in Fig. 2, cyproheptadine (1 mg kg^{-1}, given 30 min earlier prevented the stimulation caused by mescaline. WA-335 (3 mg kg^{-1}, given 30 min earlier) displayed similar antagonism. Cyproheptadine or WA-335 had no influence on the flexor reflex. Doses of mescaline active in this test are much lower than those used in behavioural tests.

Fenfluramine stimulates the flexor reflex which is antagonized by cyproheptadine and WA-335 (Maj & others, 1976b). Also, imipramine and clomipramine, but not desipramine, prevented the action of fenfluramine, which indicates that both tertiary amines inhibit the transport of fenfluramine into 5-HT neurons (Maj, Rawłów & Palider, 1976c). The similar mechanism of antagonism of imipramine or clomipramine towards fenfluoramine had been suggested in other experiments (Ghezzi, Samanin & others, 1973; Samanin, Bernasconi & Garattini, 1975; Maj & others, 1976a). The tricyclic antidepressant drugs (imipramine, clomipramine, desipramine) in doses 5–10 mg kg^{-1}, given 60 min earlier, did not modify the stimulating properties of mescaline (2–4 mg kg^{-1}). On the assumption that the action of mescaline is through presynaptic mechanisms, the results obtained suggest that the transport of mescaline into 5-HT neurons is realized by a mechanism different from that influenced by tricyclic drugs. Such a conclusion was derived from the finding of the lack of influence of desipramine on the uptake of mescaline by Bevan (1975). From the results of the present experiments, the possibility of a direct stimulating action of mescaline on 5-HT neurons cannot be ruled out. The results obtained indicate that mescaline induces central or at least spinal serotoninergic stimulation. Whether this action is related to the hallucinogenic properties of mescaline may be asked since LSD in very low doses also causes a stimulation of the flexor reflex that is antagonized by 5-HT blockers.

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