α-Chloralose and the central dopaminergic system

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In a previous investigation the eeg and behavioural effects of three gabaergic drugs: baclofen, muscimol and γ-hydroxybutyrate (GHBNa) have been studied (Scotti de Carolis & Massotti, 1978). These drugs induce comparable modifications in brain electrical activity of rabbits and rats, consisting of continuous hypersynchronous large amplitude waves intermingled with spikes. Behaviourally, they induce a biphasic effect, consisting of motor stimulation, jerks, hyperreflexia, followed by depression and a sleep-like state. These changes strongly resemble those described for α-chloralose (Balis & Monroe, 1964; Winters & Spooner, 1966) and led us to classify these drugs as "convulsant anaesthetics".

The biochemical data reported in the literature by various authors (cf. for references Da Prada & Keller, 1976; Biggio, Casu & others, 1977; Massotti, 1977a) indicate that baclofen, muscimol and GHBNa increase the content of dopamine and its acid metabolites, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA), in whole brain as well as in the corpus striatum (CS). Baclofen and GHBNa, but not muscimol, also increase dopamine content in the brain and CS. The question arises whether the state of "convulsive anaesthesia" can be related to an alteration of the dopaminergic system. We have therefore considered the effect of α-chloralose on dopamine, DOPAC and HVA brain content in the rat.

180 rats of Wistar strain (Morini, Reggio Emilia), 120–160 g, were kept in a thermoregulated room (22 ± 2°) with free access to water and food. Groups of at least 5 animals were injected intraperitoneally with doses of 3·12, 6·25, 12·5, 25, 50 and 100 mg kg^{-1} of α-chloralose. The drug was dissolved in hot (70°) distilled water and the injection was made when the solution reached a temperature of 40°. Freshly made solutions were used for each experiment. Control groups were injected with water at the same temperature The animals were decapitated 30 and 60 min after drug administration. Measurement of dopamine, DOPAC and HVA was carried out in the total brain and in the CS by spectrophotofluorimetry according to a method reported by Massotti (1977b).

The control values, expressed in $\mu g\ g^{-1}$, found in CS were: dopamine, 8·676 ± 0·653; DOPAC, 0·919 ± 0·089; HVA, 0·560 ± 0·060; in the whole brain were: dopamine, 1·297 ± 0·201; DOPAC, 0·197 ± 0·008; HVA, 0·157 ± 0·030. No modifications of these values were found in the CS, 30 and 60 min after administration of α-chloralose at all the doses tested. In the whole brain no modifications were observed 60 min after the administration of the drug at all dose ranges.

Behaviourally, the dose of 12·5 and 25 mg kg^{-1} induced sedation; the dose of 50 mg kg^{-1} induced a biphasic effect consisting of jerks and tremors, followed by hemiballism, ataxia, miorelaxation and loss of righting reflex. These symptoms resemble those reported for baclofen, muscimol and GHBNa (Scotti diCarolis & Massotti, 1978). The dose of 100 mg kg^{-1} induces the same behavioural effects observed at 50 mg kg^{-1}, but with more intensity. One hour after administration of the highest dose, 10 out of the 30 animals treated died and were excluded from the biochemical analysis.

The data obtained in the present experiments indicate that α-chloralose does not alter dopamine content and metabolism in the brain. Therefore the electroencephalographic and biochemical similarities between this drug and baclofen, muscimol and GHBNa cannot be ascribed to a common effect on the dopaminergic system.

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