Effects of Yohimbine on CNS Structures:
Neurophysiological and Behavioral Correlations*

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Abstract. Yohimbine (by intravenous and/or intraperitoneal routes at doses between 0.5 to 3 mg/kg) produces behavioral changes (in freely moving cats and dogs) characterized by: a) an increase in alertness, extreme agitation, and nervousness; b) an increase in motor reaction to a variety of sensory stimuli; and c) an appearance of muscular shaking and tremors. These behavioral changes are associated with electrographic alterations characterized by: a) an increase in the amplitude of the local evoked potentials (LEP) recorded from the mesencephalic reticular formation, posterior hypothalamus and intralaminar thalamic system; b) a decrease in the amplitude of the LEP recorded from preoptic area, lateral hypothalamus and septal region; c) a slight diminution in the LEP amplitudes of the amygdala and hippocampus; d) an initial increase (15 to 25 min) followed by a long period of strong diminution in the amplitude of the cortical LEP; e) an increase in the percent time of fast cortical activity and in the amplitude of all frequencies; f) an appearance of subcortical and cortical epileptiform discharges in the normal animals during administration of the compound at doses of 2 to 3 mg/kg; and g) a marked activation of epileptiform discharges in the subcortical or cortical epileptic animals in association with occasional clinical seizures. These results were discussed from the point of view of neuronal excitability changes in CNS structures.

Key words: Yohimbine — Anxiety — Spontaneous and Evoked Activities — Epilepsy.

Yohimbine is an indole alkaloid (obtained from a West African tree, Yohimbéché) that has adrenergic blocking activity, but little direct effect on smooth muscle, and its central nervous system (CNS) actions are much less prominent than those of the ergot alkaloids or benzodioxans (Nickerson, 1965). In human subjects, yohimbine induces a state simulating considerable anxiety with tenseness, restlessness, and irritability (Holmberg and Gershon, 1961). This clinical observation was duplicated in experimental conscious animals in whom yohimbine in-

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jections caused behavioral changes suggestive of severe anxiety accompanied by a rise in arterial blood pressure and heart rate (Lang and Gershon, 1963; Gershon and Lang, 1962; Sanghvi et al., 1969). From these studies Gershon and collaborators concluded that the model anxiety state induced by the alkaloid yohimbine in animals and man could be useful as a tool for assessment of the therapeutic potential of antianxiety agents. It has been previously reported (Guerrero-Figueroa et al., 1969) that anxiety-relieving drugs; e.g., chlordiazepoxide, diazepam, and meprobamate produce inhibition of neuronal excitability in the mesencephalic reticular formation, intralaminar thalamic system of the thalamus, and periventricular areas, accompanied by simultaneous facilitation of neuronal excitability in the septal region, preoptic area and lateral hypothalamus. The present investigation was designed to study the effects of yohimbine on spontaneous and evoked electrical activity recorded from central nervous system (CNS) structure which are responsible for the expression of emotion and feeling in conscious normal and epileptic cats and dogs.

Material and Methods

Experiments were performed in twenty-two adult cats and six adult mongrel dogs of both sexes. Chronic implantation of cortical and subcortical electrodes was performed under pentobarbital sodium anesthesia. The physical dimensions of the stereotaxic apparatus imposed a restriction on dog size; all of these animals weighed approximately 10 kg with very little variation in either direction. Electrodes were implanted stereotaxically according to maps of Jasper and Ajmone-Marsan (1954) for the cat brain and according to maps of Lim et al. (1960) for the dog brain. Electrodes were made with six stainless steel wires insulated with enamel or Teflon except for tips of 100 μ. The distance between the tips of the multipolar electrodes varied from 100 to 200 μ. Multipolar depth electrodes were unilaterally or bilaterally implanted into the septal region, preoptic area, hypothalamus ventromedialis, median forebrain bundle (MFB), basolateral part of the amygdaloid complex, olfactory bulb, hippocampal formation, posterior hypothalamus, intralaminar system of the thalamus, in different levels of the mesencephalic reticular formation (MRF), and on the sensory-motor cortical areas. In addition, two intramuscular hook stainless steel bipolar electrodes were implanted bilaterally into the neck muscles for recording muscular action potentials (EMG). Each electrode was soldered to a 50 prong male plug (Cannon 50 PLI) and permanently fixed to the skull over the frontal sinus by means of dental cement. In a second operation, a subcortical or cortical epileptogenic focus was made in 10 cats by using a technique (Guerrero-Figueroa et al., 1964a) for creating discrete irritative lesions with alu-