The Effect of Vincamine, Hydergine and Piracetam on the Firing Rate of Locus Coeruleus Neurons

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Summary

Vincamine, hydergine and piracetam are used for the treatment of memory disturbances as well as for the treatment of various other brain dysfunctions seen in the elderly patient.

The action of these three psychogeriatric compounds on the activity of noradrenergic neurons in the rat locus coeruleus was investigated. All three compounds, when administered intraperitoneally, increased the firing rate of noradrenergic neurons in the chloral hydrate anaesthetised animals. Vincamine and hydergine had a similar potency producing a maximal mean increase of about 70% at a dose of 1mg/kg. Likewise, piracetam was significantly less potent eliciting a 30 to 40% increase in firing at doses of 300 and 1000 mg/kg, respectively.

A role for the locus coeruleus in processes related to attention, cortical and behavioral arousal, learning and memory has been proposed on the basis of behavioral and electrophysiological experiments. In the awake rat, the firing rate of noradrenergic neurons in this brain nucleus has previously been shown to relate directly to the level of vigilance. The activating action of vincamine, hydergine and piracetam on these neurons may be linked with some of the drugs’ beneficial therapeutic effects.

Key words: Vincamine, piracetam, hydergine, locus coeruleus, memory disturbances, aging.

Introduction

Vincamine, hydergine and piracetam are among the most often prescribed psychotropic agents used for the psychogeriatric treat-
ment of various disorders in elderly patients. All three compounds have been claimed to improve cognitive functions and mood (Ban, 1980). Their sites of action are not known in detail and appear to be different. Vincamine is thought to improve cerebral metabolism through increase of glucose and oxygen utilization (Tesseris et al., 1975). Piracetam was found to activate brain adenylate cyclase (Nicholson and Wolthius, 1976) and to increase glucose consumption (Burnott et al., 1973). Hydergine appears to affect brain metabolism thus leading to an improvement in brain blood flow (Ban, 1978; Hollister, 1976; Iwangoff et al., 1976). A causal link between these physiological effects and their therapeutic action may be assumed but remains speculative.

In the present investigation, we have studied the action of the three above-mentioned drugs on the discharge rate of the spontaneously active, noradrenergic neurons of the locus coeruleus. It has been suggested that this brain nucleus plays a role in memory (Amaral and Foss, 1975), learning (Crow and Arbuthnott, 1972; Anlezark et al., 1973; Koob et al., 1978) and attention (Mason and Iversen, 1978). An other function of the locus coeruleus might also be to regulate brain metabolism through its action on brain vessels (Raichle et al., 1973; Bates et al., 1977). Furthermore, recent electrophysiological observations are consistent with the hypothesis that the noradrenergic system may facilitate the transfer of afferent information to the cerebral cortex (Waterhouse and Woodward, 1980).

In the awake rat the tonic discharge of neurons in the locus coeruleus covaries with stages of the sleep-waking cycle. Highest cell activities are found during waking (Aston-Jones and Bloom, 1981). Bursts of impulses accompany orienting responses to spontaneous or sensory-evoked interruptions of such ongoing behavior. Most tonic EEG-periods are anticipated by locus coeruleus neuronal discharge (Aston-Jones and Bloom, 1981). Furthermore, conditioning stimulation of the locus coeruleus enhances the responsiveness of cortical somatosensory neurons to the activation of afferent, somatosensory pathways (Waterhouse and Woodward, 1980; Waterhouse et al., 1980).

**Materials and Methods**

The experiments were performed on 103 male rats (RAIF) (SPF) weighing 280–320 g. The animals were anaesthetized with chloral hydrate (400 mg/kg, i.p.) and mounted in a stereotaxic apparatus. Body temperature was maintained between 36.5 and 37°C. A 3 mm burr hole was drilled in the skull over the approximate coordinates of the LC. Extracellular single unit recording was carried out by means of single barrel electrodes (tip size