

**SHORT COMMUNICATION**

**EFFECT OF APPLICATION OF GAMMA AMINO BUTYRIC ACID AT THE MEDIAL PREOPTIC AREA ON SLEEP-WAKEFULNESS<sup>+</sup>**

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**Abstract:** Intracerebral microinjections of gamma amino butyric acid were given bilaterally at the medial preoptic area (mPOA) to determine the possible role of this neurotransmitter in the genesis and regulation of sleep-wakefulness. GABA (50 µg/0.2 µl) when administered through chronically implanted cannulae in free moving rats, did not produce any significant alterations in sleep-wakefulness. This may be attributed either to the non-involvement of GABA at the level of mPOA in the regulation of sleep, or to other factors like the low dose and rapid breakdown of the injected drug.

**Key words:** medial preoptic area                      gamma amino butyric acid  
sleep wakefulness    EEG    rats

**INTRODUCTION**

The medial preoptic area (mPOA) plays an important role in the genesis and regulation of sleep-wakefulness (1, 2, 3). This area has been shown to contain high levels of the inhibitory neurotransmitter GABA as well as its synthesizing enzyme, glutamic acid decarboxylase (4, 5, 6). However, there are no reports available on the role of GABA, at the mPOA, in the regulation of sleep-wakefulness. Mendelson and Martin demonstrated in 1992 that microinjection of benzodiazepines at the mPOA enhances sleep (7). The benzodiazepines are thought to exert their pharmacological effects via a mechanism of enhancing GABA mediated inhibition (8). On the other hand, injection of the GABA agonist, muscimol at the POA produced arousal (9). In view of these contradictory findings, this study was undertaken to find out the effect of direct application of GABA at the mPOA on sleep-wakefulness.

**METHODS**

Experiments were conducted on five male Wistar rats (200-250 gms body wt). These rats had free access to food and water and were maintained on a 14 h light (5.00h to 19.00h), 10h dark cycle. They were operated stereotaxically with aseptic precaution under pentobarbitone anaesthesia (40 mg/kg body wt.). Bilateral cannulae, for microinjection of drugs were chronically implanted at the mPOA (A 7.8, L 0.6, H -1.5) as per DeGroot's atlas (10). EEG, EOG and EMG electrodes were implanted for electrophysiological assessment of sleep (11). Four to five days after recovery from operative trauma, polygraphic recordings were carried out during the dark period (21.00 h-03.00 h). Animals were kept in the recording room and cage for at least half an hour before the experiment. The experimental procedure consisted of uninterrupted recordings of EEG, EOG and EMG for 90 min before and 180 min after local injections of GABA (Sigma Chemical

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Co., USA). Bilateral microinjections of GABA (50  $\mu\text{g}/0.2 \mu\text{l}$ ) were given at the mPOA at the rate of 0.1  $\mu\text{l}/\text{min}$ . At the end of the experiment, the animals were anaesthetized and 0.2  $\mu\text{l}$  of 3% ferric chloride was administered bilaterally at the mPOA. Subsequently, they were perfused intracardially with a solution of 3% potassium ferrocyanide in 30% formalin to stain the injection site for histological studies (12). Polygraphic data obtained was split into 30s epochs and analyzed to quantify sleep-wakefulness (13). Data was then grouped into 10 min bins for statistical analysis. Pre-injection data was subjected to Friedman's test to determine if there was any significant difference in the data obtained prior to the injection. Thereafter, preinjection and postinjection data were compared by applying Friedman's multiple range test.

## RESULTS

The preinjection data showed that the rats slept, on an average, for 43.6% of the recording time. Though there were differences in the preinjection data recorded during different time bins, on statistical analysis these variations were not found to be significantly different from animal to animal during the entire period of control recording. When the preinjection data, was compared with postinjection data it was found that GABA had not produced any significant alterations in sleep-wakefulness. The initial increase in wakefulness seen in the postinjection record can be attributed to the handling of the animals for injection of the drug (Fig. 1). Histology revealed the injection site to be at the mPOA.

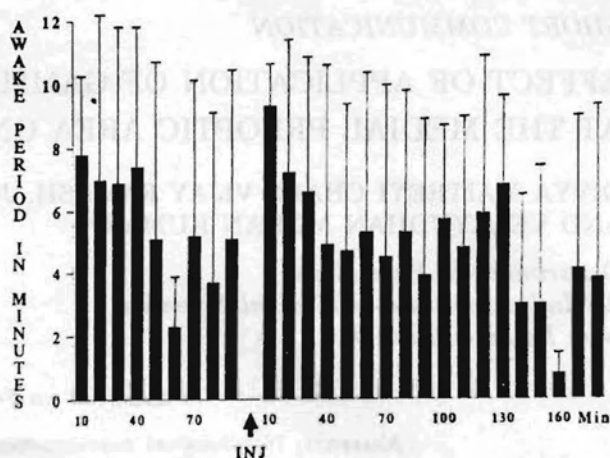


Fig 1 : Shows the effect of injection of GABA in the mPOA on the awake period of free moving rats during the night. Injection time is indicated by the arrow. Each bar represents the awake period in a time bin of 10 min.

## DISCUSSION

The findings from this study indicate that GABA may have no physiological role to play in the regulation of sleep-wakefulness at the mPOA. The other possibility is that the concentration of GABA administered in the present study may be inadequate to produce alterations in sleep-wakefulness. A dose response relationship study would be useful in this regard. However, it should be kept in mind that the amino acid neurotransmitters have a short duration of action as they are broken down rapidly in the central nervous system (14). This rapid breakdown may be responsible for the absence of observable effects of GABA on sleep-wakefulness. Further studies using GABA agonists and antagonists, as well as long acting forms of GABA, will help in the elucidation of the role of this transmitter at the mPOA.

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