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Glutamate and Gamma Amino Butyric Acid Levels after Intracerebral Injection of Follicle Stimulating Hormone in Pubertal and Post-Pubertal Rat Brain

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ABSTRACT
Intracerebral injection of follicle stimulating hormone (FSH) at a dose of 10 µg produced a significant increase in glutamate levels of the cerebral cortex, cerebellum, and brain stem in pubertal rat brain and only cerebral cortex of post-pubertal rat brain. However, intracerebral FSH brought about a significant increase in gamma amino butyric acid (GABA) levels of brain stem of pubertal rat brain and cerebral cortex GABA levels of post-pubertal rat brain. The results are discussed in relation to the probable interaction between these neuroactive amino acids and FSH in the rat brain.

Key words: *Glutamate, Gamma amino butyric acid, Follicle stimulating hormone, Puberty, Rat brain.*

1. INTRODUCTION

In the brain, it is well established that a greater proportion of synaptic function is mediated by neuroactive aminoacids such as glutamic acid and gamma amino butyric acid (GABA). While glutamic acid is neuroexcitatory, and GABA is generally found to be neuroinhibitory. Besides these functions, these aminoacids are also involved in general metabolic reactions by the brain [1-4]. GABA is also known to be involved in the release of anterior pituitary hormones [5-8]. Most of the anterior pituitary hormones and a variety of neuropeptides including oxytocin and vasopressin were shown to be present in cerebrospinal fluid [9,10]. Intraventricular administration of glutathione has been found to release selectively more of follicle stimulating hormone (FSH). Hypothalamic glutathione levels were found to be very high at puberty [11-14]. These results indicate a possible interaction between glutathione and FSH. Although the extrapituitary localization of FSH in the brain is not known, it is possible that FSH secreted from pituitary may have effects on the behavior apart from its role in gonadal function. Furthermore, as the major proportion of synaptic function is mediated by GABA and glutamate, the levels of these two amino acids have been studied to know whether FSH would affect the synaptic function besides the metabolism in brain.

2. MATERIALS AND METHODS

Female rats of Wistar strain maintained under controlled conditions of light (12 h light:12 h dark) with free access to drinking water were used in the study. All animal experiments were performed in accordance with rules and Regulations of Animal Ethics and the International Guidelines for Handling of Laboratory Animals. Rats attain puberty around 42 days in our animal facility. Female pubertal rats (42 days old) and immediate post-pubertal rats (45 days old) were given intracerebral injection of FSH at a dose of 10 µg in a volume of 10 µl. Controls received an equal volume of saline. The animals were sacrificed by decapitation after 30 min of injection. Brains were quickly removed and cerebral cortex, cerebellum, and brain stem were dissected out as per the procedure of Sadasivudu and Lajtha [15]. Hypothalami were dissected out as a single block as described by Vijayan [16]. Glutamate and GABA contents were estimated as per the procedure of Chandrakala as described by Vali Pasha and Vijayan [17,18].

2.1. Statistical Analysis

Experimental data was analyzed by Student's t-test.

3. RESULTS

FSH, given intracerebrally at a dose of 10 µg produced a significant increase in glutamate levels of cerebral cortex, cerebellum, and brain stem in pubertal rat brain. However, in the case of immediate post-pubertal rats, only cerebral cortex glutamate levels were increased significantly. Intracerebral FSH brought about a significant increase in GABA levels of brain stem of pubertal rat brain and cerebral cortex GABA levels of post-pubertal rat brain (Tables 1 and 2).

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Table 1: Effect of intracerebral FSH on glutamate and GABA levels in 42 days old female rat brain at 30 min after injection.

Brain Region	Glutamate		GABA	
	Saline	FSH	Saline	FSH
Cerebral cortex	4.00±0.24 (5)	5.28±0.67 (6)*	1.08±0.07 (5)	1.28±0.20 (6)
Cerebellum	6.66±0.34 (5)	7.89±0.57 (6)*	1.58±0.06 (5)	1.59±0.09 (6)
Brain stem	4.05±0.47 (5)	5.75±0.73 (6)*	1.34±0.06 (5)	1.55±0.05 (6)**

Values are µmol/g. wet wt. of tissue, values are mean±SD of number of experiments given in parentheses. *These values at a $p<0.01$ and **This value at a $p<0.02$ are significantly different from those of control groups. SD=Standard deviation, FSH=Follicle stimulating hormone, GABA=Gamma amino butyric acid

Table 2: Effect of intracerebral FSH on glutamate and GABA levels in 45 days old female rat brain at 30 min after injection.

Brain Region	Glutamate		GABA	
	Saline	FSH	Saline	FSH
Cerebral cortex	4.42±0.47 (5)	5.57±0.40 (6)*	1.09±0.20 (5)	1.68±0.12 (6)*
Cerebellum	7.43±0.33 (5)	7.98±1.24 (6)	1.67±0.08 (5)	1.60±0.29 (6)
Brain stem	5.48±0.74 (5)	5.31±0.77 (6)	1.42±0.06 (5)	1.38±0.21 (6)

Values are µmol/g. wet wt. of tissue, Values are mean±SD of number of experiments given in parentheses, *These values at a $p<0.01$ are significantly different from those of control groups. SD=Standard deviation, FSH=Follicle stimulating hormone, GABA=Gamma amino butyric acid

4. DISCUSSION

The role of GABA as a modulator of anterior pituitary hormone secretion by hypothalamic and pituitary action is clearly established. Besides its role in pituitary hormone release the role of GABA in the central nervous system as a neuroinhibitory transmitter and the role of glutamate as a neuroexcitatory transmitter is very clear. The universal rise in the glutamate in the cerebral cortex, cerebellum, and brain stem along with a lone increase in GABA in brain stem would suggest that FSH administration through intracerebral route brought about generalized changes in the metabolism of brain promoting either increased formation of glutamate or decreased utilization of glutamate. Since both glutamate and GABA showed an increase in brain stem under these experimental conditions, the effects of both glutamate and GABA on a reticular activating system located in brain stem get neutralized. However, the increased content of glutamate in cerebral cortex and cerebellum would facilitate a state of neuronal excitation in these regions with effects on the subcortical brain regions including hypothalamus. During the onset of puberty, a number of stimuli from different parts of the brain impinge on hypothalamic neurons causing the release of hypothalamic peptides [19,20]. It was also shown that the significant decrease in the content of glutathione in hypothalamus at puberty without any change in the same in the immediate post-pubertal period following intracerebral injection of FSH indicate that the action of FSH in this regard on the glutathione content in hypothalamus is not direct but probably mediated by other mechanisms such as involvement of neurotransmitters [21]. It is tempting to speculate that the specific decrease in glutathione in hypothalamus might have been through the glutamatergic pathway. However, the mechanisms involved in the changes in the content of glutamate and GABA by intracerebral FSH are not well understood.

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***Bibliographical Sketch**

Dr. K. Vali Pasha has done his M.Sc and Ph.D from University of Hyderabad, Hyderabad in the years of 1982 and 1988, respectively. His major areas of research are neurobiochemistry, clinical biochemistry, herbal drugs, antioxidants. He was a NIH post-doctoral fellow at University of Connecticut, USA. He was a faculty member at Jamia Hamdard University, New Delhi and later moved to Nizam Institute of Medical Science, Hyderabad where he worked as Asst. Professor and Associate Professor. At present he is a Professor of Biochemistry and Dean of Faculty of Science in Yogi Vemana University, Kadapa, Andhra Pradesh, India.