DETECTION OF HYPOTHALAMIC HORMONES IN THE MID-TERM HUMAN FETAL CEREBROSP1NAL FLUID

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Abstract

Fetuses were obtained immediately after their removal from the uterus by hysterotomy and CSF was aspirated by lumbar puncture and frozen in liquid nitrogen. The presence of hypothalamic hormones was detected by infusing CSF samples into the carotid artery of suitably primed ovariectomized rats and measuring changes in circulating levels of the different trophic hormones. Significant rises in circulating levels of serum, prolactin and LH were obtained, demonstrating the presence of prolactin releasing and LHRH activity in the mid-term fetal CSF (JPMA 35 :337, 1985).

INTRODUCTION

Recent studies[1,2] have indicated that the anterior pituitary secretes biologically active substance into the cerebrospinal fluid (CSF). Changes in the concentrations of biogenic amines and neuropeptide hormones in the CSF may reflect physiological and pathophysiological alterations in central nervous system activity. Various ways in which the pituitary hormones might reach the CSF has been postulated from the results of experimental studies on animals[3]. Pituitary CSF relationships in man have been also reported.[4] Because there is a close relationship between the median eminence and the third ventricle, an upward flow of blood from the anterior pituitary[1,2] could carry hormones to the median eminence. The blood brain barrier is weak in the circumventricular region[5], at least for the substances with small molecular size and there is therefore the possibility that these could pass into the CSF in this area. In addition, the structure of tanycytes around the third ventricle favours the transport of hormones into the CSF[3,5] Furthermore, the pituitary brain transport of some hypothalamic hormones has been also demonstrated[6,7]

The presence of anterior pituitary hormones, hypothalamic hormones and biogenic amines in the human CSF has been a subject of interest for many investigators[8-13]. Evidence is accumulating that CSF may be involved in the transmission of chemical information from various regions of the brain to the hypothalamus[14,15]. Hormones and biogenic arnines may be released into the CSF and carried through the ventricles to be tracted by the brain at a site distal to the release, or concentrated by the neural tissue and later released into the vascular system[16-

Considering these reports, experiments were planned to examine further the presence and activity of hypothalamic hormones in the mid-term human fetal CSF and to elucidate their possible mode of action on pituitary hormone release.

MATERIAL AND METHODS

Human fetuses of mid-term gestational age were collected immediately after their remval from the uterus by hysterotomy (performed for gynaecosocial reasons under general anaesthesia). They were packed in ice and brought to the Institute of Physiology where dissection was carried out. The time on average between hysterotomy termination and freezing of the tissue in liquid nitrogen was less than 45 minutes. Fetal sex was initially determined by examination of the external genetalia and subsequently confirmed by histology of the gonads. Crown rump length (CRL) was measured and the fetuses were weighed to assess their age[17]. CSF was aspirated by lumbar puncture, frozen in liquid nitrogen and stored at 20°C.

A total of 39 one ml CSF samples from fetuses of 10.5 22.5 weeks gestational age were infused into the carotid artery of ovariectomized, oestrogen and progesterone primed rats to determine their action on the control of pituitary hormone release following the procedure of Gilmore et. al.[18] Prolactin and LH concentrations in the rat plasma were measured by radioimmunoassay.

RESULTS

Due to a large variation in individual absolute concentrations, the percentage change in prolactin concentration from the pre-infusion level was determined for both 15 and 30 minutes post infusion collections. Percentage changes in prolactin concentrations following infusion of 19 human fetal CSF samples from male and female fetuses (10.5 22.5 weeks gestational age) are presented in Fig. 1.

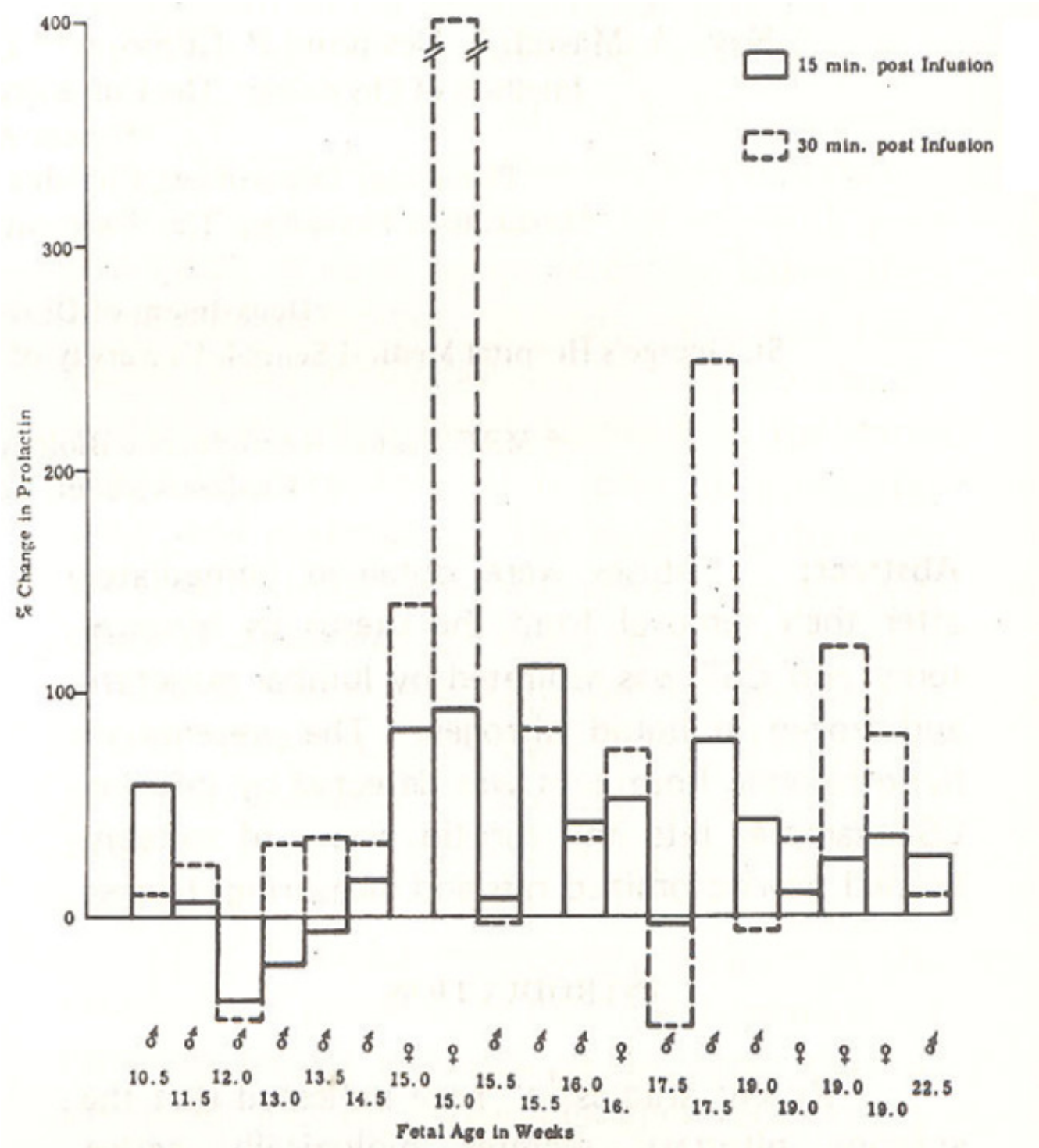

Fig.1 Post Infusion Changes in Prolactin Concentration following the Infusion of Humal Fetal CSF Samples.

Statistical analysis of these observations showed significant prolactin releasing activity in the CSF samples. The infusions of male and female fetal CSF samples both caused a significant increase in serum prolactin concentrations.

The presence of LHRH activity was also detected in human fetal CSF samples of mid-term gestational age. Twenty - CSF samples were gestational age. Twenty CSF samples were examined using the same

experimental procedure as followed for prolactin releasing activity determinations. LHRH activity was demonstrated by the rise in circulating LH brought about by the infusion of CSF. The results obtained in this study (Fig. 2

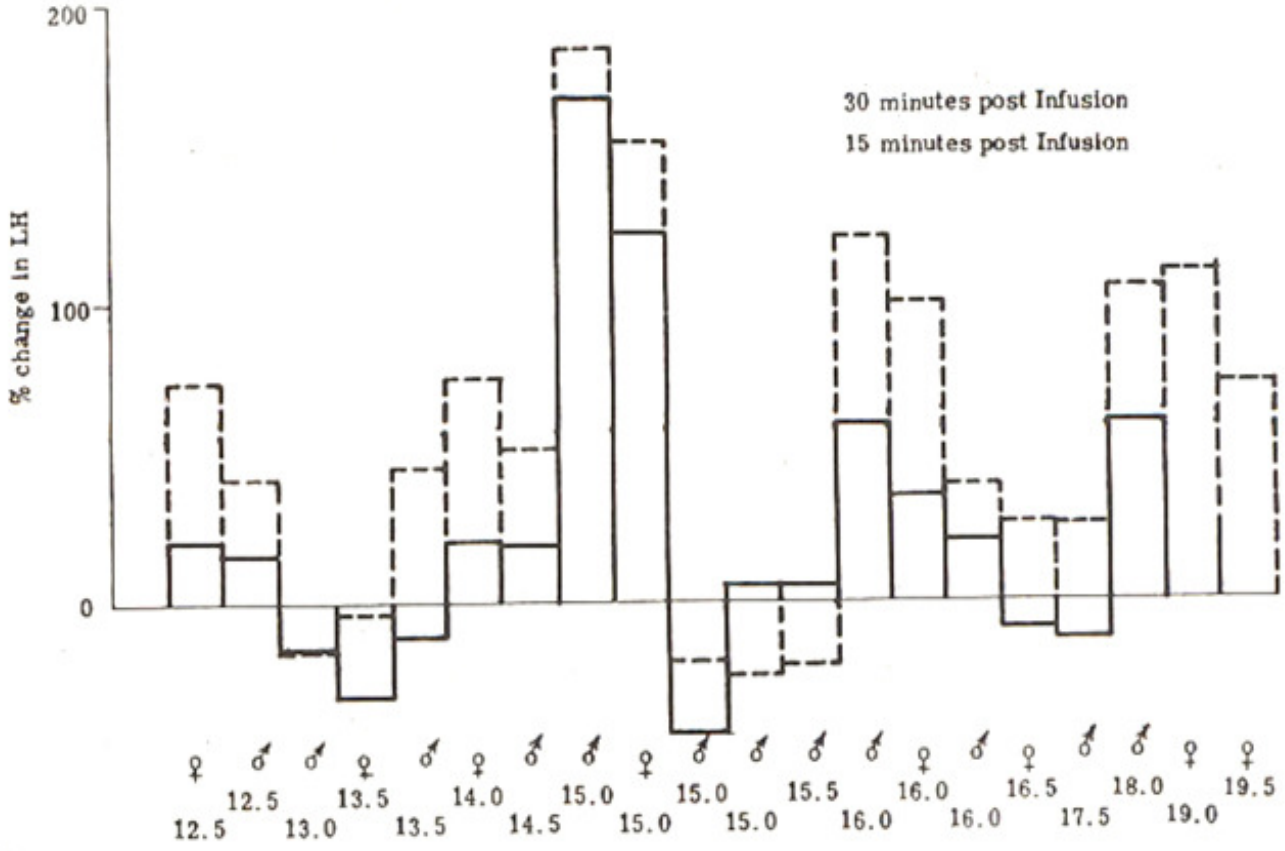

Fig. 2. Post Infusion Changes in LH Concentrations following Infusion of Human Fetal CSF Samples.

clearly confirmed the presence of LHRH activity in human fetal CSF collected from both male and female fetuses. Significantly higher ($P < 005$) serum LH concentrations were obtained in the post infusion 15 minutes blood samples in both sexes. This rise became even30 minutes after more significant ($P < 0.00\ 1$) the infusions were carried out.

DISCUSSION

It is now widely accepted amongst neuroendocrinologists that brain-pituitary relationships in the human are more complex than had previously been considered. Since hypothalamic hormones and biogenic arnines can be detected in the CSF, it is natural to speculate that the CSF has an important role to play in carrying information between the brain and pituitary[9]. Very little information is, however, available regarding the presence of hypothalamic hormones and biogenic amines in CSF collected from mid-term human fetuses.

The possible role of the CSF in carrying hypothalamic releasing and/or inhibitory hormones towards the pituitary via the third ventricle has been reported by a number of workers[13,14] A demonstration in this study of the presence of LHRH and prolactin releasing activity in human fetal CSF confirms some of the previous work carried out in the adult human CSF[12,19-24]

Intraspinal TRH injections in the human produce a significant rise in blood thyrotrophins and prolactin

levels[25]. Thus it could be assumed that the natural release of TRH and LHRH into the human fetal CSF may be having a similar effect. These hormones could diffuse into the pituitary and so affect particular pituitary cells to produce their respective trophic hormone. This view is further supported by another similar observation in rats. LHRH injected into CSF was found to significantly elevate plasma LH Levels[16,26].

It is well known that until some time between the 18th and 20th week of gestation, the hypothalamic anterior pituitary portal connections are not well established in the fetus[27,28] Therefore, the CSF may, prior to this time, have a major role in transporting LHRH from the hypothalamus to the anterior pituitary. The presence of LH in the fetal pituitary gland as early as 10 weeks gestational age and equally-early the presence of LHRH in the hypothalamus[29] imply the potential for an early hypothalamic pituitary functional relationship. The presence and activity of LHRH seen in fetal CSF in this study suggests the CSF does have a role in this functional relationship.

The results of the present study also clearly indicate that prolactin releasing activity (like that of LHRH) may be effected by either:

(a) a direct action of the hypothalamic hormones at the level of the pars tuberalis and the tuber cinereum, which are distinctly vascularized from an early stage[30], or

(b) indirectly through transport in the CSF to the infundibular recess into the pars distalis.

ACKNOWLEDGEMENTS

We thank Professor M.C. MacNaughton, Dr. Man Calder and their staff at Glasgow Royal Infirmary for enabling us to obtain the hysterotomy specimens; Miss Alison McCulloch, Miss Georgina Docherty for their excellent technical assistance and Mrs. Moira McRae for typing this manuscript.

This work was supported by grants from the British Council, London under Technical Cooperation Training Development Programme under Colombo Plan.

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