EVALUATION OF THE HYPOTHALAMIC-PITUITARY-GONADAL AXIS IN MALE INFERTILITY

Thesis for the Partial Fulfilment of Master degree in Dermatology and Venereology

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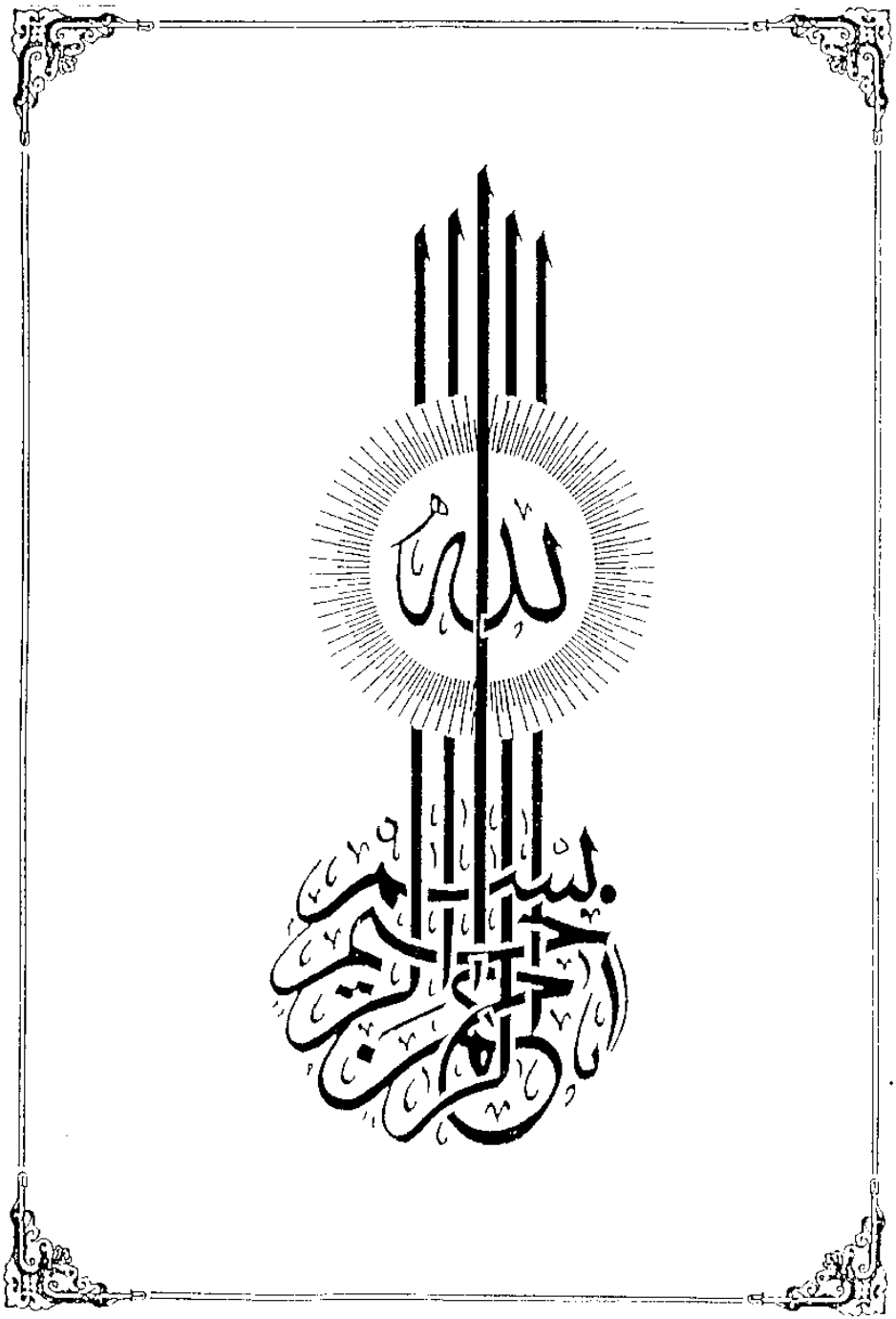

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Introduction

INTRODUCTION

Testes are regulated by two gonadotropins, luteinizing hormone (LH) and follicle stimulating hormone (FSH). These hormones which are glucopeptides, are synthesized and stored in the anterior pituitary and their release is regulated by centres in the hypothalamus. LH acts on the Leydig cells to stimulate the secretion of testosterone. FSH acts on the regulation of spermatogenesis. The role of gonadotropins in regulation of spermatogenesis lies between the initiation and maintenance. The initiation of spermatogenesis usually requires follicle stimulating hormone and testosterone, while its maintenance usually requires testosterone **(Walsh and Amelar, 1977).**

Central nervous system regulation of hormonal secretion by the pituitary gland has been a subject of research for several decades. Much evidence indicated afferent neural pathway on the hypothalamus which influences the pituitary hormone secretion via neurotransmittors activity. All secretions by the pituitary gland are controlled by either hormonal or nervous signals from the hypothalamus. Indeed, when the pituitary gland is removed from its normal position beneath the hypothalamus and transplanted to some other part of the body, its rate of secretion of the different hormones (except for prolactin) fall to low levels **(Guyton, 1981).**

Secretion from the posterior pituitary is controlled by nerve fibers originating in the hypothalamus and terminating in the posterior pituitary. In contrast, secretion by anterior pituitary is controlled by hormones called hypothalamic releasing and inhibitory hormones (or factors) secreted within the hypothalamus itself and then conducted to the anterior pituitary through minute blood vessels called hypothalamic-hypophysial portal vessels. In the anterior pituitary these releasing and inhibitory hormones act on the glandular cells to control their secretion **(Guyton, 1981).**

Hypothalamic-pituitary-gonadal axis consists of a closed loop. Hormones produced by the testes have inhibitory effects on the secretions of LH & FSH, so castration results in an elevation of both leuteinizing hormone and follicle stimulating hormone **(Walsh and Amelar, 1977).**

The aim of this thesis is to elucidate the physiology of the hypothalamus, pituitary and gonads and to discuss some abnormalities of this axis and their implication on male infertility.

Review
Of Literature

REVIEW OF LITERATURE

The two major functions of the testis, steroid hormone secretion and gametogenesis, are segregated anatomically, with androgen biosynthesis occuring in Leydig cells and spermatogenesis in seminiferous tubules.

The anterior pituitary participates in the control of both of these functions through its secretion of the gonadotropins, LH and FSH. The anterior pituitary is in turn regulated by multiple parts of the central nervous system which are coordinated via the hypothalamic secretion of gonadotropin-releasing hormone (GnRH) **(Bardin and Paulsen, 1981).**

When GnRH is administered intravenously to human, it results in a prompt increase in serum LH and to much lesser extent FSH levels in blood.

The response of the pituitary to GnRH is modulated by steroidal hormones. Estradiol inhibits the effect of GnRH on LH and FSH secretions **(Walsh and Amelar, 1977).**

PHYSIOLOGY OF HYPOTHALAMUS

The hypothalamus lies in the very middle of the limbic system (Fig.1). It also has communicating pathway with all levels of this system. in turn, it and its closely allied structures, the septum and mammillary bodies, send output signals in two directions: (1) downward, through the brain stem mainly into the reticular formation of the mesencephalon, pons and medulla, and (2) upward to many areas of the cerebrum especially the anterior thalamus and the limbic cortex. In addition, the hypothalamus indirectly affects cerebral cortical function very dramatically through activation or inhibition of the reticular activating system that originates in the brain system **(Morgane and Panksepp, 1979).**

The hypothalamus, one of the major areas of recent advances in medicine, is the elucidation of the regulation of anterior pituitary function by the central nervous system. It has been known that the anterior pituitary gland, although housed within the cranium, is not a neural structure **(Schally, 1978).**

Pituitary function is regulated by releasing inhibitory factors secreted by certain hypothalamic neurons. The hypothalamic cells are secretory structures, producing small polypeptides that are released directly into the hypophyseal portal system (Fig.2) for delivery via a secondary capillary plexus to the cells of the anterior pituitary **(Federman, 1981).**

Several anatomic features of the hypothalamus contribute to the functioning of the hypothalamic-pituitary unit.

First there is no blood-brain barrier at the hypothalamus; therefore, circulating messages such as the serum sodium or cortisol level have a direct access to regulatory sites.

Second, the hypothalamus contains centers for other crucial functions including thirst, hunger, osmoregulation, blood pressure, and pulse rate.

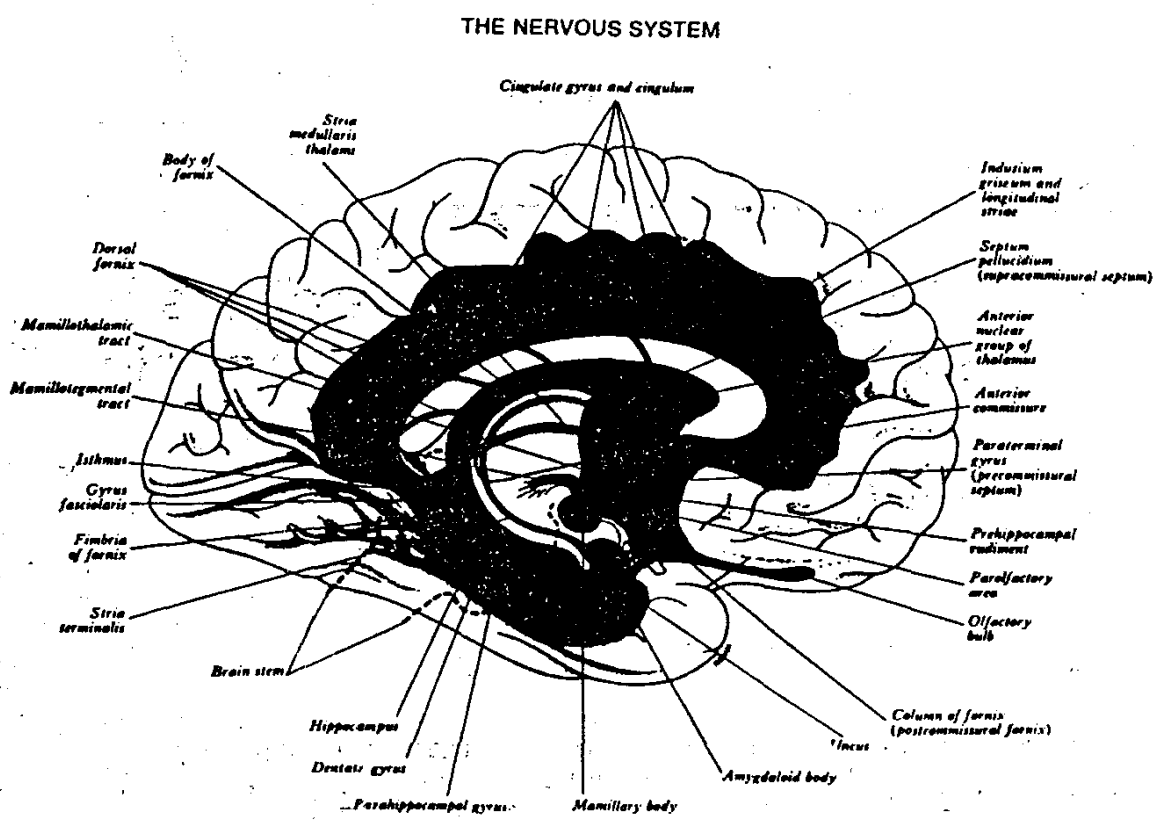

Figure 1: anatomy of the limbic system illustrated by the shaded areas of the figure. **(From : Warwick and Williams: Gray's Anatomy. 35th Brit. ed. London, Longman group Ltd., 1973, P.700).**

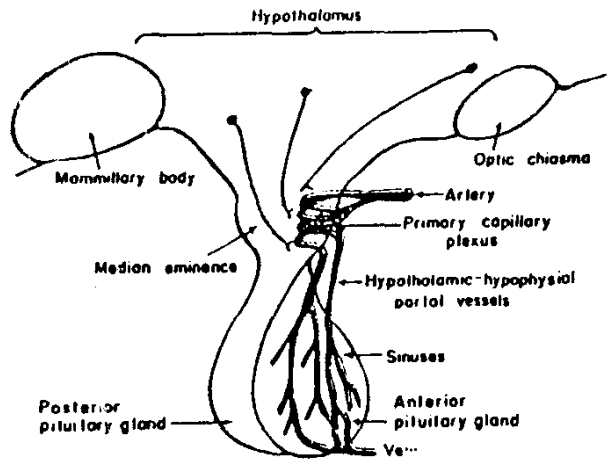

Figure 2: The hypothalamic-hypophysial portal system. **(From Text-Book of Medical Physiology, edited by A.C. Guyton, 1981, P. 921).**

Third, the portal circulation allows substances of hypothalamic origin to reach the pituitary gland in concentrations that cannot be duplicated elsewhere in the body.

Finally, investigation has revealed the linkage of pituitary secretion to sleep onset and depth as well as to vision, smell and body mass **(Federman, 1981).**

Special neurons in the hypothalamus synthesize and secrete hormones called hypothalamic releasing and inhibitory hormones that control the secretion of the anterior pituitary hormones. These hormones are immediately absorbed into the capillaries of the hypothalamic-hypophysial portal system and carried directly to the sinuses of the anterior pituitary gland **(Besser, 1977).**

For each type of anterior pituitary hormone there is corresponding hypothalamic releasing hormone. Some of the anterior pituitary hormones also have a corresponding hypothalamic inhibitory factor **(Arimura, 1977).**

For most of the anterior pituitary hormones it is the releasing hormone that is important; but for prolactin, an inhibitory hormone probably exerts most of the control.

All or most of the hypothalamic hormones are secreted at nerve endings in the median eminence before being transported to the anterior pituitary gland.

The neuronal cell bodies that give rise to these median eminence nerve endings are located in other discrete areas of the hypothalamus or in closely related areas of the basal brain.

Electrical stimulation of this region excites these nerve endings and therefore causes release of essentially all the hypothalamic factors.

Unfortunately, the specific loci of the neurons that secrete the different hypothalamic hormones are incompletely known that it would be misleading to attempt a delineation here **(Guyton , 1981).**