NEUROENDOCRINOLOGY AND ENDOCRINE SYSTEM.
(CPY605)
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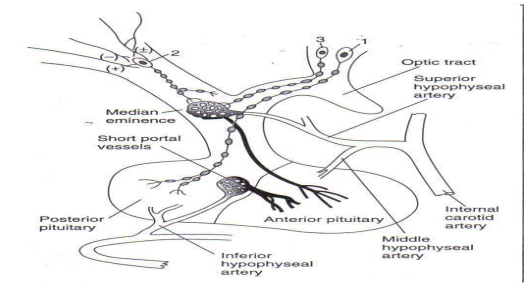
Neuroendocrinology

- It is the study of the interactions between the nervous system and the endocrine system to link aspects of cognitive and non-cognitive neural activity with metabolic and hormonal homeostatic activity.(1)
- Neurosecretory cells serve as the final common pathway linking the brain with the endocrine system.

- The neurohypophysial neurones originate from the paraventricular and supraoptic nuclei,traverse the hypothalamic- pituitary stalk and release vasopressin and oxytoxin from nerve endings in the posterior pituitary.
- Hormones of the anterior pituitary gland(adenohypophysis) are secreted from endocrine cells that, in mammals are not innervated.
- Secretion of these hormones are under the control of the brain by ''releasing factors''and ''releasing inhibitors''released by the hypothalamic neurones into blood vessels at the base of the brain, at the median eminence.

•The neuroendocrine system operates through a series of feedback loops.

- Target hormones can feedback at both the hypothalamic and pituitary levels to complete the loops.The factors may be stimulatory or inhibitory.



HYPOPHYSIOTROPIC HORMONES .

- The hypophysiotropic neurones,localized in specific hypothalamic nuclei,project their axons to the median eminence to secrete their peptide and bioamine releasing and inhibiting hormones into the proximal end of the hypothalamic-pituitary vessels.

- The first of the hypothalamic factors to be identified were the thyriotropin releasing hormone(TRH) and gonadotropin releasing hormone(GnRH) from sheep and pigs.(2,3)
- TRH functions stimulating the synthesis ad release of thyroid- stimulating hormone (TSH) and prolactin although its role as a physiologic prolactin releasing factor remains questionable.

•TRH can also stimulate growth hormone (GH) secretion in patients with acromegaly

- TRH can also stimulate follicle-stimulating hormone (FSH) secretion in some patients with gonadotroph adenomas, but not in normal individuals.

GONATROPIN-RELEASING HORMONE(GnRH).

- GnRH is a 10 amino acid peptide.
- Its secretion is also stimulated by dopamine and norepinephrine but inhibited by serotonin .
- Its primary function is to stimulate the secretion of luteinizing hormone(LH) and FSH which can feedback both positively and negatively on GnRH.

•GnRH pulsatile secretion also directly up-regulates its own receptors.

- At puberty,negative feedback of steroid hormones decrease leading to increase levels of GnRH.
- At menopause,levels are also elevated due to lack of production of the ovarian oestrogen.(4,5)

SOMATOSTATIN(Somatotropin releasing-inhibitory factor).

- It is a 28 amino acid which has GH inhibitory activity which blocks the rise in GH that occurs with all stimuli in a dose-dependent fashion as oppose to GHRH.
- Somatostatin also inhibits basal and stimulated TSH secretions.
- It is also present in the D cells of the pancreatic islets and the gut mucosa, where it suppresses the secretion of insulin,glucagon,gastrin etc through the endocrine and paracrine actions.

•Its analogues have been developed for the treatment of acromegaly,islets cell tumours,TSH-secretory tumours etc

CORTICOTROPIN-RELEASING HORMONE (CRH)

- CRH releases adrenocorticotropic hormone(ACTH), beta endophin,beta lipotrophin,melanocyte –stimulating hormone (MSH) and other peptides.These hormones are synthesized from a large peptide pre-opiomelanocortin(POMC).
- Beta lipotrophin is inactive and is rapidly converted tom endophin(neurotransmitter)

•CRH mediates 75 percent of the ACTH response and 25 percent is due to vasopressin.

- CRH and vasopressin have synergistic effects on ACTH release.These hormones coexist in about half of the CRH-containing paraventricular neurones and even in the same neurosecretory granules.
- Acetylcholine,dopamine,norepinephrine and epinephrine stimulate and gamma-aminobutyricinhibites CRH secretion .

•Cytokines (IL-1,IL-6,TNGF-alpha) stimulate CRH and ACTH secretion

- Biosynthetic human CRH has recently been used in the differential diagnosis of Cushing's disease.

GROWTH HORMONE RELEASING HORMONE(GHRH)

- It stimulates GH secretion in some individuals, it is capable of eliciting a small increase in prolactin.
- Alpha-2 adrenergic receptors and serotonin activate GHRH and GH secretion ,but gamma-aminobutyric acid is inhibitory to GHRH secretion.

PROLACTIN INHIBITORY FACTOR(PIF)

- This inhibitory component of the hypothalamic regulation of prolactin secretion predominates over the stimulatory component.
- Dopamine is the predominant physiologic prolactin inhibitory factor.

PROLACTIN RELEASING FACTOR(PRF)

- Vasoactive inhibitory polypeptide(VIP) stimulates the synthesis and release of prolactin at concentrations found in hypothalamic –pituitary portal blood.
- VIP is also synthesized by the anterior pituitary tissue.
- The peptide histidine methionine also has PRH activity.

CNS RHYTHMS AND NEUROENDOCRINE FUNCTION

- Pituitary hormones are secreted in a pulsatile fashion with a number of rhythms superimposed and this pulse amplitude reflects the amount of releasing hormone.i.e.hormones are released in termittently.
- The amplitude is altered by the presence of inhibitory factors and feedback effects of target hormones.

•Ultradian rhythms which are shorter than a day.

- Circadian rhythm with approximately 24-hour periodicity.
- Infradian rhythm with a periodicity longer than 24 hours.
- Some hormones e.g. TSH ,also exist with diurnal rhythm with slightly higher values at night for a normal sleep pattern.

NEUROENDOCRINE DISEASE. DISEASE OF THE HYPOTHALAMUS

- They can be localized to the hypothalamus, by being part of more generalized CNS disease such as neurosarcoidosis or by indirect means. This affects the hormonal level.
- Symptoms depend on the area involved, size of the lesion and rapidity of the increase in lesion size.
- These diseases include tumours especially pituitary adenomas,craniopharyngiomas etc.

•Other disease are trauma, inflammatory disorders and vascular disease,tuberculosis,meningitits etc

- Irradiation.whole brain irradiation for intracranial neoplasms frequently results in hypothalamic dysfunction.
- The most common being hyperprolactinaemia ,but hypopituitarism can also occur especially when the radiotherapy is targeted to the hypothalamic area ,in patients suffering from tumours such as nasopharyngeal carcinomas.

EFFECTS OF THE HYPOTHALAMIC DISEASE ON PITUITRAY FUNCTION.

- These disease can cause either hyperfunction or hypofunction in varying degrees of severity.

GROWTH HORMONE

- Loss of normal GH secretion is the most common defect with structural hypothalamic diseases.

- One autosomal dominant form of complete GH deficiency has been found to be associated with deletion of the gene for GH.
- GH deficiency has also been found to be caused by a mutation in GHRH receptors.

GONADOTROPINS(HYPOTHALAMIC HYPOGONADISM)

- It is the second most common defect after GH deficiency due to GnRH deficiency.
- GnRH deficiency has also been found to be caused by mutation in GnRH receptors.
- Depending on the time of onset ,they are manifested as either delayed puberty,interruption of pubertal progression ,or loss of adult gonadal function.
- GnRH deficiency can also be due to hyperprolactonaemia.

HYPOTHALAMIC HYPERGONADISM(Precocious puberty)

- Precocious puberty is defined as the onset of puberty before the ages of 8 in girls and 9 in boys."Pseudo"-precocious puberty is that resulting from peripheral causes.

PROLACTIN (Hypothalamic hyperprolactinaemia)

- Most structural or infiltrative lesions of the hypothalamus decrease the amount of dopamine reaching the lactotrophs leading to modest hyperprolactinaemia.

THYROID STIMULATING HORMONE

- Hypothalamic hypopituitarism due to a central lesion that impairs the secretion of TRH ,usually along with the loss of other hormones .
- Defects in the gene have not been detected, but can be caused by TRH receptor mutation.

ADRENOCORTICOTROPHIC HORMONE

- Hypothalamic ACTH deficiency caused by lesion is uncommon. It may occur with the loss of other hormones.
- Isolated ACTH deficiency appear to be as a result of pituitary autoimmune disorder.

Vasopressin; deficiency results from lesions in the supraoptic and paraventricular nuclei containing vasopressin.This leads to diabetes insipidus.

EFFECTS OF HYPOTHALAMIC DISEASE ON OTHER NEUROMATABOLIC FUNCTIONS

- A number of functions that affect the internal milieu , in addition to anterior and posterior pituitary functions are regulated by the hypothalamus.
- This includes; carbohydrate metabolism, temperature control,memory,sleep and food intake(regularly by leptin and ghrelin)
- Leptin is secreted from the adipocytes and ghrelin from stomach,both of which bind to hypothalamic leptin and ghrelin receptors and feed back negatively on food intake and energy expenditure.

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THANK YOU FOR YOUR KIND ATTENTION!!!!!!!!!!