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# 魚類下視丘對腦下垂體促性腺激素分泌之管制作用

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## 摘　要

魚類腦下腺雖各羣魚種有演化上差異，不過腦下腺激素種類之分泌相仿，相似於哺乳類之所有。以鰻魚爲例，魚之腦下腺藉其腦垂體柄之神經組織及門脈血管系（hypothalamo-hypophysial system）與腦及下視丘等腦組織溝通。整個腦下腺構造包括腺性腦下腺（adenohypophysis）及神經性腦下腺（neurohypophysis）兩大部份，前者由許多腺細胞組成，共區分爲吻部（RPD）、基部（PPD）及間部（PI）。RPD 通常分泌 ACTH 及催乳素(PRL) 及 TSH；PPD 則包括有 GH 以及 GtH (s)激素的產生細胞。至於 PI，共有兩種細胞，其中 PbH＋ve 分泌 MSH，而 PAS＋ve 細胞則有些魚類表現與生殖和滲透壓之調節有關，尙待深入研究。

下視丘的視前核（PON）及其分佈於腦下腺之軸突纖維末梢，組成魚腦下腺之神經內分泌管制系統，可分泌 arginine vasotocin 及 isotocin 等激素，具有影響生殖系統之平滑肌收縮，影響產卵（精）之作用。

魚腦下腺含有血管系統，分別供應 腺性腦下腺之 PD 及 PI。「下視丘一腦下腺門脈系」是携帶神經激素及下視丘釋放因子或激素釋放之抑制因子至腦下腺的重要管道。分佈於腦下腺的神經纖維至少包括 type A 和 B 兩種，渠等或直接連會於激素分泌細胞之膜或隔基膜擴散分泌物以調節腦下腺激素之分泌和釋放。

硬骨魚之促性腺激素分泌的神經激素調節已被檢討。促性腺激素(GtH) 之釋放調節，受釋放素（GnRH）及抑制素之調節。此外，GtH 的分泌也受松果腺、攝護腺素和兒茶酚胺類（catecholamine）等之調節，再者 GtH 也受性腺類固醇激素之負廻饋調節。腎上腺皮質促進素（ACTH）的分泌，受其釋放因子（CRF）的調節，CRF 來自 NLT 及視前核。ACTH 所支配之皮質素（corticoids）在於平衡體內細胞之有機代謝及抗緊張的作用，這些也間接或直接地影響了魚類的生殖作用。

對於 GtH 之分泌調節，除下視丘之 GnRH 外，還有 GnIF。多巴命

(DA) 已被證實是一種具 GnIF 作用的物質。此外，乙醯膽鹼 (acetylcholine) 有抑制 GtH 分泌，而正腎上腺素及腎上腺素則有促進 ( 適當季節) GtH 分泌之作用。因此：應用(1)各種 GnRH 類似物 (analogues) 和(2)適當之抗多巴命製劑，(3)找出最適時期選用正腎上腺素及其增强劑 (agonists) (4)促進神經葉之神經激素分泌以及(5)利用類固醇之廻饋作用等，將有助於魚類生殖作用之調節。

## 內容

## 一、前言

魚是地球上出現最早的水生脊椎動物，爲數多分布廣，其體制構造頗具演化上的歧異。有關魚類之「下視丘——腦下腺的研究」，在現生魚類中較具代表性的有：(1)無頜類 (Agnatha; jawless fishes)——是最原始型之現生脊椎動物，如盲鰻 (hagfish) 和八目鰻 (lamprey) 等。(2)軟骨魚類 (Chondrichthyes)——包括板鰓類 (Elasmobranches)，如鮫 (Selachii) 和鱝類 (Bathoidae) 等。(3)原始條鰭魚類 (primitive actinopterygian fishes)——如鱘類 (Acipenseriformes) 和全骨下綱 (Holostei) 魚類等。(4)硬骨魚類 (Teleosts)——如鰻 (the eel) 和花鱂魚 (the molly, *Poecilia latipinna*) 等。(5)總鰭魚類 (Crossopterygians)——也就是指「內鼻魚綱」的魚類，例如：肺魚類 (Dipnoi)、腔棘魚類 (Coelacanthiforms) 等。有關上述各魚種之腦下腺構造和功能，Holmes and Ball 兩氏 (1974)，曾就其演化上之重要特性，加以系統化之描述和比較，這些資料詳實，可做爲更進一步探究內分泌及其應用的參考。

衆所周知，腦下腺 (the pituitary; hypophysis cerebri) 在於分泌各種促進激素 (trophic hormones)，用以調節和控制動物之周邊內分泌腺的發育、合成和分泌激素，用以調節動物體細胞的生長、代謝和體色變化等等。內分泌組織分泌之激素(hormones) 的作用，要而言之，包括四大項如下：(1)形態發生的 (morphogenic) 功能；(2)動力發生的 (kinetic) 功能；(3)代謝的 (metabolic) 以及(4)行爲發生的 (behavioural) 功能等的管制和調節作用。唯這些激素 ( 荷爾蒙 ) 的合成分泌，却直接或間接地由腦下腺激素來控制或調節。因此，脊椎動物的腦下腺便被稱爲是動物內分泌的主腺 (master gland)，它負有維持動物體「內部恒定」(homeostasis)、控制生長和發育與生殖的作用。至於腦下腺之分泌，主要由神經內分泌所調節。

神經內分泌之調節——即激素之合成和釋放(分泌)以發生功能——是屬於一種長程的影響作用 (long-term influence)；單純之神經傳遞物質 (neurotransmitter)，如運動神經原(motoneuron)分泌則屬較短程之影響作用(short-term influence)。不過有些神經傳遞物質也具有神經激素之功能，例如多巴命 (dopamine) 有調節哺乳類泌乳素 (proloctin)分泌之作用(MacLeod, 1976; Vale *et al.*, 1977)。本文所强調探討的是分佈於腦之神經原的分泌及其調節作用，尤其是有關下視丘 (hypothalamus) 神經原的分泌等。

下視丘的內分泌調節，包括視前核處 (preoptic region) 之神經激素，依其基本功能可分之爲二類：第一類爲經由循環作用送到非內分泌腺之受器而發生作用者，如條鰭魚類，分別於視前核和垂體神經葉合成與釋放的 arginine vasopressin 和 isotocin (Perks, 1969)；第二類爲具有調節腺性腦下腺之內分泌活動的神經激素。這些將於以下各節再加介紹討論。

## 二、脊椎動物之腦下垂體及其分泌之激素

八目鰻 (lamprey) 以至鳥類、哺乳類之腦下腺的構成，雖有其胚胎來源的一致性：包含「神經性腦下垂體」(neurohypophysis) 及「腺性腦下垂體」(adenohypophysis) 兩部份（表一）。但是其組成比例、構造之形態、位置等顯然有其演化上的差異（Fig. 1, 2，表一）。因此，腦下垂體構造也隨着動物種類有其不同的名稱。現將各級動物之腦下垂體構造名稱，列表比較如下：

表一　脊椎動物腦下垂體構造名稱表

| 腦下腺構造<br>動物種類 | 腦下腺（腦下垂體；腦垂腺）pituitary gland; hypophysis cerebri | | | | | 中央隆突 median eminence |
|---|---|---|---|---|---|---|
| | 腺性腦下腺（腺葉）adenohypophysis | | | | 神經性腦下腺（神經葉）neurohypophysis | 中央隆突 |
| 哺乳類<br>爬蟲類<br>兩生類 | 端部（前葉）pars distalis pars anterior | | 中間部（中葉）pars intermedia middle lobe intermediate lobe | 結節部 pars tuberalis (PT) | 神經葉（後葉）pars nervosa, neural lobe, posterior lobe (NH)（延伸至腺葉外圍或內部） | 中央隆突 |
| 鳥類 | 頭部 cephalic part | | 尾部 caudal part | | | |
| 板鰓類 | 吻部 rostral pars distalis (RPD) | 主（基）部 proximal pars distalis (PPD) | 中間部 pars intermedia (PI) | 腹葉 ventral lobe | | |
| 硬骨魚類 | | | | | | |
| 八目鰻 | | | | | | ? |
| 盲鰻 | 腺性腦下腺 | | | | | |

由圖一示無頜類之盲鰻 (hagfish) 以上至爬蟲類、哺乳類動物之腦下垂體的演化情形：在構造上，神經葉 (pars nervosa, PN)、中間部 (pars intermedia, PI) 及端部（pars distalis；前葉）的位置、比例具有相當程度的差異（圖一）。就是在魚類，種類

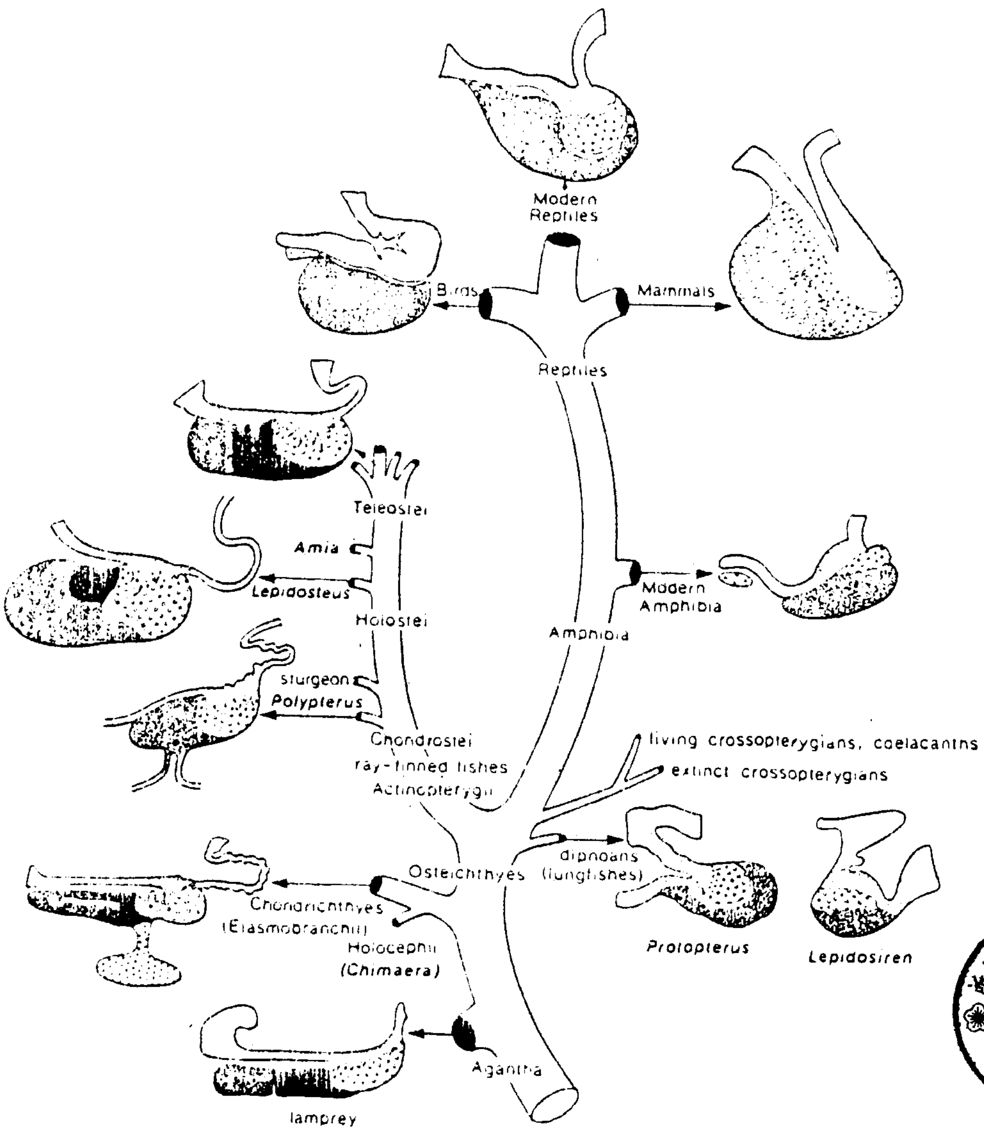

Fig. 1. Schematic representation of evolutionary relationships of the vertebrate groups and the structure of the pituitary gland in each group, as seen in sagittal section, anterior to the left. Sparse stippling, neural lobe; small circles, pars intermedia; small crosses, pars tuberalis; medium stippling, pars distalis (dipnoans, *Polypterus*, tetrapods) or rostral pars distalis (fishes); dense stippling, proximal pars distalis, which differentiated in fishes; coarse dots, ventral lobe of elasmobranchs. (From Gorbman and Bern (1962). A textbook of comparative endocrinology. New York: John Wiley and Sons.)

之間也有相當不同程度的變化（圖二）。

在現生魚類中，硬骨魚類（teleost fishes）爲數超過 20,000 種，其分佈幾佔所有可能之地球生態水域。這羣魚類的腦下腺具有幾個基本上的特化現象：其一、中央隆突（median eminence, ME）缺如或僅具痕跡程度。其次，下視丘—腦下腺門脈血管系統（hypothalano-hypophysial portal system）延伸進入腦下腺，而且更爲特殊的是自下視丘有神經原軸纖維直通腦下腺端部（pars distalis），並與之激素分泌細胞癒會，如此，

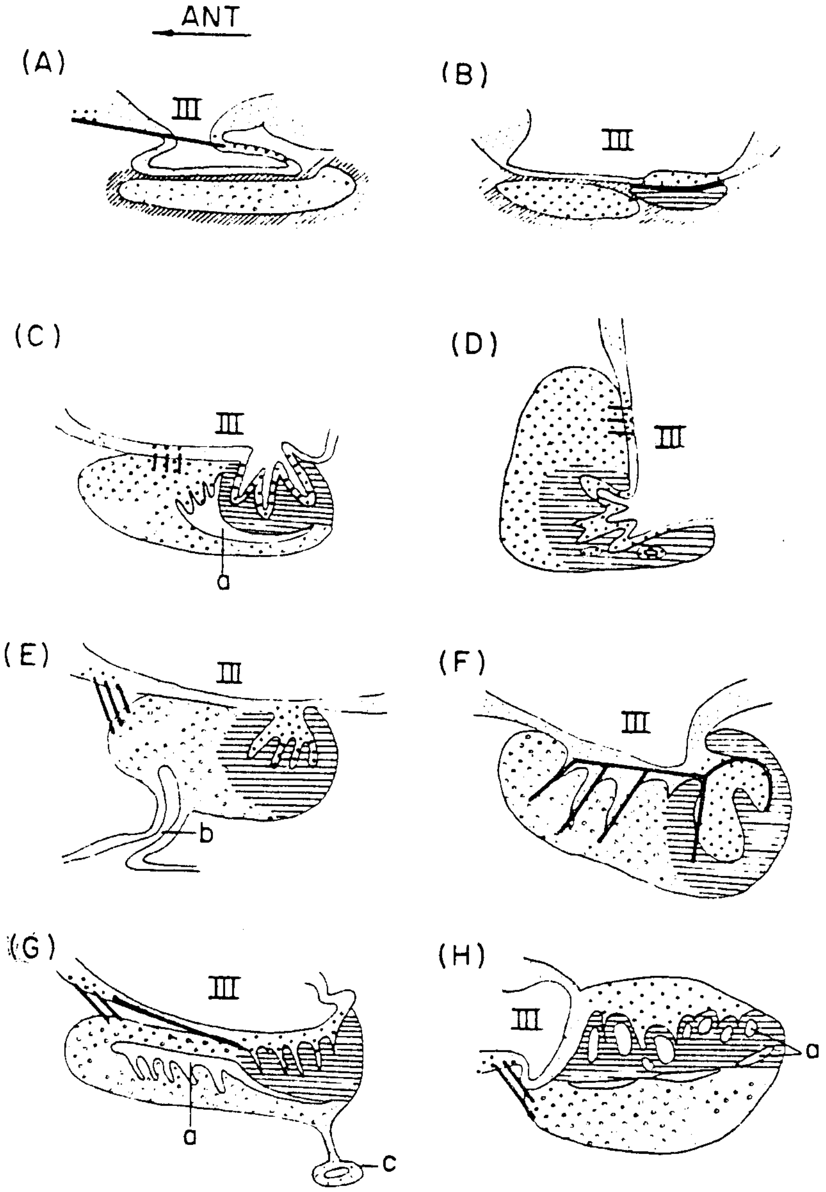

Fig. 2. Diagrammatic midsagittal sections to illustrate the main features of pituitary structure in the different fish groups. In all cases, anterior is to the left. (A) myxinoid, (B) lamprey, (C) *Acipenser*, (D) *Amia*, (E) *Polypterus*, (F) teleost, (G) elasmobranch, and (H) dipnoan. Small dots, nervous tissue; large solid dots, stainable neurosecretory material; large open dots, pars distalis; horizontal lines, pars intermedia; thick black lines, blood vessels which appear to convey neurosecretory products to the adenohypophysis or (myxinoid) to the neurohypophysis; oblique hatching, connective tissue; a, hypophysial cavity; b, hypophysial duct; c, ventral lobe of elasmobranchs; and III, third ventricle. (From Ball and Baker, 1969)

使腦及下視丘與神經葉和腺葉縱的聯繫關係更密切。現爲說明方便起見，選硬骨魚類之鰻腦下垂體爲例（圖三、四a、四b）說明其各種促進激素的分佈與分泌。

鰻之腦下垂體，包括：腺葉 (adenohypophysis, AD) 和神經葉 (neurohypophysis,

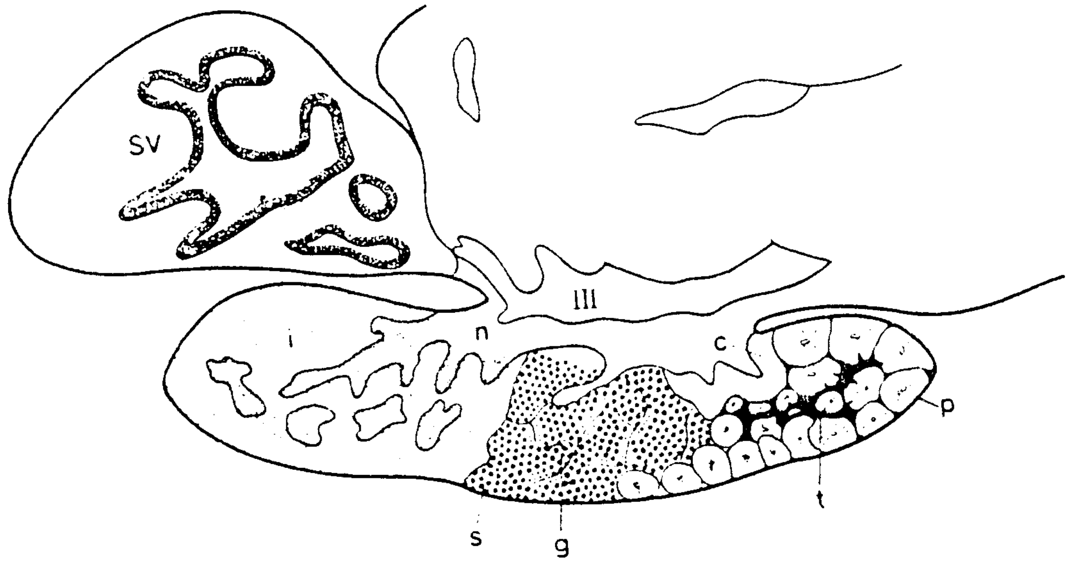

Fig. 3. *Anguilla anguilla.* Diagram of midsagittal section through the eel pituitary, anterior to the right. Follicles of lactotropes (p), mixed with TSH cells (t), and bordered posteriorly by ACTH cells (c), form the rostral pars distalis. The proximal pars distalis comprises cords of cells below the neurohypophysis (n), mainly composed of somatotropes (s) in the sexually immature fish, with scattered immature gonadotropes (g). Posteriorly is the pars intermedia (i), deeply invaded by processes of the neurohypophysis which in this region displays masses of AF+neurosecretory material (fine stipple). The saccus vasculosus (SV) projects behind the pituitary. III, third ventricle. (From Olivereau, 1967).

NH)。兩者之間由基膜 (basement membrane) 分界。腺葉又依組織學及細胞學的分野劃分爲吻部 (rostral pars distalis, RPD)、基部 (proxinal pars distalis, PPD) 和中間部 (pars intermedia, PI) 等三部份。在鰻魚，其吻部含三類激素分泌細胞：其中 η (eta) cells 佔最多數，分泌催乳素 (leuteotropic hormone, prolaction, PRL)。如同其他較原始性魚類，η cells 在 RPD 亦排列成濾泡狀分布，其分泌之 PRL 具有滲透壓調節作用 (osmoregulation)。另外一種 δ (delta) 細胞分散於 η 細胞間，在於分泌促甲狀腺激素 (thyrotropin, TSH) 具有促進甲狀腺發育，調節甲狀腺激素之合成與分泌的作用。甲狀腺激素 (thyroid hormones) 與促進幼魚發育、變態與生長有關，它也是體細胞能量產生的重要主宰者，甲狀腺分泌之激素，也具有負廻饋調節 THS 分泌的作用；促腎上腺皮質素產生細胞爲 ε (epsilon) 細胞（即 ACTH 細胞），分佈腦下腺吻部之背方邊緣接近神經葉處，所分泌之促腎上腺皮質素 (corticotropin; ACTH) 具有調節腎上腺皮質激素 (corticosteroids) 之合成與分泌的作用。腎上腺皮質素肩負維持個體之醣類、肪脂以及蛋白質等有機代謝的平衡。皮質素也是魚類對付各種緊張 (stress) 刺激的激素。Sundararaj and Goswami (1969)，甚至認爲「下視丘——腦下垂體——間腎」成爲一影響鯰魚 (*Heteropneustes fossilis*) 排卵的模式。腦下垂體的基部至少含有兩類激素分泌細胞；這些細胞常成索狀排列。其中 α (alpha) 細胞，可染以 Orange G 呈現金黃色，是分泌生長激素 (growth hormone, GH；或 somatotropin, STH) 的細

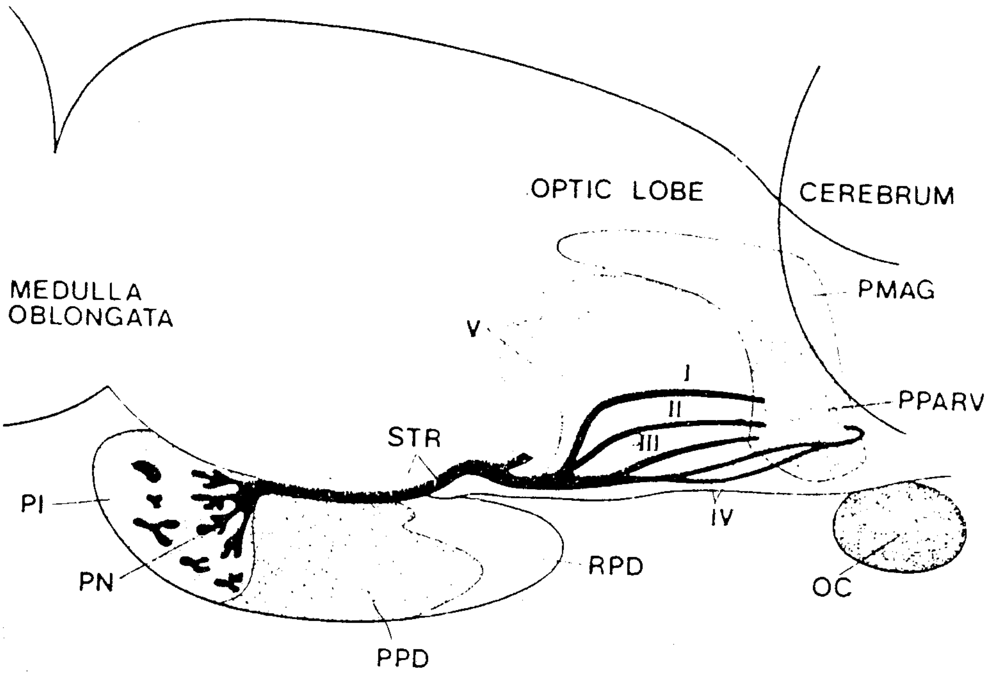

Fig. 4a. *Anguilla anguilla.* Diagram of midsagittal section of brain and pituitary (anterior to the right), to show the PON-neurohypophysial system. PMAG, preoptic nucleus, pars magnocellularis; PPARV, preoptic nucleus, pars parvocellularis; I-V, component preoptico-neurohypophysial tracts; STR, sub-terminal region of the common preoptico-neurohypophysial tract; OC, optic chiasma; RPD, rostral pars distalis; PPD, proximal pars distalis; PI, pars intermedia; PN, posterior neurohypophysis. The nucleus lateralis tuberis, not shown in this diagram, lies in the floor of the hypothalamus, above the pituitary gland. (From Leatherland, J. F., Budtz, P. E. and Dodd, J. M, (1966). *Gen. Comp. Endocr.*, **7**, 234-244.)

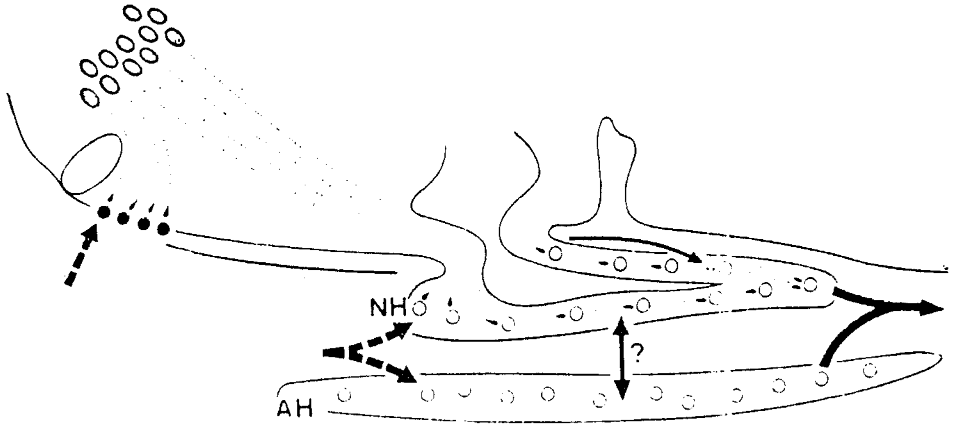

Fig. 4b. Myxinoid pituitary, diagrammatic sagittal section, to show hypothalamohypophysial vascular and neurosecretory links. Question mark indicates unsettled direction of blood in the vertical vessels between neurohypophysis (NH) and adenohypophysis (AH). Dotted circles, neurosecretory cells of the preoptic nucleus; dotted lines, neurosecretory axons, with axon terminals marked at their endings; filled circles, prehypophysial plexus; empty circles, intrahypophysial capillaries; interrupted arrows, arteries; solid arrows, veins; thin arrows, possible portal veins. (From Jasinski, 1969. *Gen. Comp. Endocrinol. Suppl.* **2**, 510-521)

胞，STH細胞在生長迅速或斷食(饑餓)之魚的腦下腺相當活動，表示與個體之生長與血中葡萄糖量有關。另一類與 STH 細胞雜混一起之好鹽基性細胞，爲促性腺激素細胞(gonadotropes; GtH cells)。產生GtH之細胞質所含的肝糖蛋白性顆粒，具有强PAS+, Alcian blue (AB), AF+ 和 Aniline blue 正反應的特性。雖然魚類之 GtH 並無哺乳類 FSH 的相像特性（GtH 較近似 LH 作用），但由實驗觀察知道，GtH 細胞中其顆粒數量之多寡，與生殖腺之成熟或萎縮的周期變化，呈正相關關係。很多硬骨魚類之 GtH 細胞及其分泌，已可區分爲二個種類（或類型），卽：（i）此類細胞，其所含顆粒爲 PAS+, AB, AF 及 PbH 染色都呈正反應，當魚在產卵（精）時，細胞中的顆粒減少，並有出現空泡現象；(ii) 另一類 GtH 細胞，其顆粒雖也呈 PAS 正反應，但却對 AB−, AF− 及PbH 呈負反應。這兩類細胞在下列魚種中被發現，例如鰻 (*A. anguilla*)，鯔 (*Mugil auretus*; *M. cephalus*)；金魚 (*Carassius auretus*)，鮭 (*Oncorhynchus spec*)，鰕虎 (*Pomatoschistus microps*) 等 (Shih, 1980; Van Oord and Peute, 1983)。

腦下腺中間部 (pars intermediate, PI) 含兩種細胞，其中 PbH+Ve 細胞被認爲是分泌促色素胞激素 (melanocyte stimulating hormone; MSH) (Olivereau, 1971; Baker and Ball, 1970)，而另一種 PAS+Ve 細胞則特別在魚生活於黑色背景下最爲活動。

神經性腦下腺又稱神經葉(pars nervosa)（圖四 b)其神經纖維多來自下視丘，並分泌 arginine vasotocin 和 isotocin。實際此兩種神經激素被發現來自視前核區 (nucleus preoptic area) (Leatherland and Dodd, 1967, 1969; Vigh-Teichman *et al.*, 1976)。Arginine vasopressin 有如 ADH，具有增加腎絲球體過濾作用 (Maetz and Lahlou, 1974; Pang, 1977)。Isotocin 尙有對刺激卵巢、子宮肌之平滑肌纖維收縮的作用 (La Pointe, 1977)，這種作用當然也影響魚之生殖產卵的作用。

## 三、腦下垂體促性腺激素之分泌調節

腦下垂體之促性腺激素（GtH）的性質、分泌變化，隨動物之種類有別。哺乳類分泌之促性腺激素 (GtH) 包括：濾泡生成激素 (follicular stimulating hormone, FSH) 及黃體生成激素 (luteinizing hormone; LH)。但在魚類其 GtH 並無相等於 FSH 之激素。因此，在魚類常以促性腺激素 (GtH) 總稱之。腦下垂體之 GtH 分泌的管制，主要受下視丘之神經內分泌，促性腺素釋放激素 (gonadotropin-releasing hormone, GnRH or luteinizing hormone-releasing hormone, LHRH) 之調節。除此之外，可能尙有促性腺激素之抑制因子 (gonadotropin release-inhibitory factor; GnIF) (Peter *et al.*, 1986) 的存在。現在將 GnRH 之性質、分泌來源及其生理功能加以討論如下。

### ㈠促性腺激素釋放素之性質

在哺乳類，自猪、羊之下視丘所分離出之促性腺激素釋放素(GnRH; LHRH)，屬十胜類 (decapeptide) (Matsuo *et al.*, 1971; Burgus *et al.*, 1972; Krey and silverman, 1983)，具有調節腦下垂體之濾泡生成激素 (follicular stimulating hormone, FSH) 及黃體生成激素 (luteinizing hormone, LH) 分泌之生理功能 (Jackson and Mueller,

1982)。在老鼠，兼具生物性及免疫性反應之 LHRH，發現主要來自下視丘之弓狀核 (arcuate nucleus, ARC) 及視前核 (preoptic nucleus, PON)，此兩中心分別在於控制非周期性的與周期性的 LH 分泌。這與 Pohl and Knobil (1982) 發現靈長類調節 LH 之潮湧分泌 (surge) 乃因 LHRH 受間動性 (pulsatic) 所支配不同，而靈長類之 LHRH 可能來自下視丘之中基部 (medial basal hypothalamus, MBH)。Hsueh and Jones (1981) 發現 LHRH 之受器在生殖腺，而 LHRH 也有刺激 (*in vitro*) 胎盤絨毛膜促性腺素 (chorionic gonadotropin, CG) 分泌功能。哺乳類之 LHRH 對鳥類、兩生類及魚類等動物之生殖腺都有促進之功能，而鳥類所具有者包括 bGnRH-I 及 bGnRH-II 兩種，顯然與鮭魚 (salmon) 所具者不同，因後者僅有軸鏈上第 7 和 8 位置之胺基酸不同(圖五) (Millar and King, 1983; Jackson, 1986)。

| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammalian : | pGlu | - | His | - | Trp | - | Ser | - | Tyr | - | Gly | - | Leu | - | Arg | - | Pro | - | $GlyNH_2$ |
| Chicken I : | pGlu | - | His | - | Trp | - | Ser | - | Tyr | - | Gly | - | Leu | - | Gln | - | Pro | - | $GlyNH_2$ |
| Chicken II : | pGlu | - | His | - | Trp | - | Ser | - | His | - | Gly | - | Trp | - | Tyr | - | Pro | - | $GlyNH_2$ |
| Salmon : | pGlu | - | His | - | Trp | - | Ser | - | Tyr | - | Gly | - | Trp | - | Leu | - | Pro | - | $GlyNH_2$ |
| α-YMF : | Trp | - | His | - | Trp | - | Leu | - | Gln | - | Leu | - | Lys | - | Pro | - | Gly | - | Gln-Pro-Met-Tyr |

Fig. 5. Structure of the various vetebrate LH-RH decapeptides. The variability is located at positions 5, 7 and 8 and changes from the mammalian form are boxed. α-YMF. yeast α-mating factor.

LHRH之作用，除負腦下垂體GtH細胞之分泌管制外，Moss and McCaunn (1973) 證實，其具有增强去卵巢雌鼠之「接受交配」行爲 (lordosis) 的作用。LHRH 促進雌鼠接受交配行爲的分子構造，相信在 LHRH 軸鏈後半 5 個胺基酸 (Ac-LHRH $^{5-10}$) 之 6～9 的位置，而非在前 6 個胺基酸羣中 (Dudley *et al.*, 1983)。LHRH 之軸鏈第 2、3位置，相信是與 GtH 之分泌的調節有關 (Coy and Schally, 1978)。爬蟲類、鳥類及魚之 LHRH 的免疫性和色層分析結果頗相似，唯不同於哺乳類之所有。至於酵母之 α-配對因子 (α-mating factor)，與動物之 LHRH 分子構造相似(圖五)，推想 α-YMF 也許就是代表古老原始性之 LHRH 生殖功能及分子演化之型式。

綜而言之，產自腦中之促性腺激素釋放素 (GnRH)，主要在控制生殖作用。可確定分爲四種GnRH代表分子：包括哺乳類，鳥類 I 和 II，及鮭之 GnRH 等四種(圖五)。在 GnRH 構造中 $His^2$-$Trp^3$ 乃代表了它釋放 GtH 的重要特性。置換 GnRH 軸鏈之第 5、7、8 位置，將分別代表了不同動物之 GnRH 之受器結合 (binding) 的型式。鮭魚，*Oncorhynchus keta* 之 GtH 釋放素爲 [$trp^7$, $Leu^8$]-LHRH (Sherwood *et al.*, 1983)，在家禽則兩種 GnRH 分別爲：[$Gln^8$]-LHRH，和 [$His^5$, $Trp^7$, $Tyr^8$]-LHRH (Miyamoto *et al.*, 1983)。至於人工合成之 GnRH 相似物 (GnRH analagues) 及鯉魚之 GnRH 更是多樣化(表二) (Peter, *et al.*, 1987)。其他類似 GnRH 之分子構造物，將於下節討論。

Table 2. Primary structure of mGnRH and several other peptides used in the study

| Peptide designation | Peptide primary structure | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| mGnRH | *p*Glu | His | Trp | Ser | Tyr | Gly | Leu | Arg | Pro | Gly - NH$_2$ |
| cGnRH-1 | | | | | | | | Gln | | |
| [His]-GnRH | | | | | | | | His | | |
| [Ser]-GnRH | | | | | | | | Ser | | |
| [Glu]-GnRH | | | | | | | | Glu | | |
| [Asn]-GnRH | | | | | | | | Asn | | |
| [Ile]-GnRH | | | | | | | | Ile | | |
| [Phe]-GnRH | | | | | | | | Phe | | |
| [Met]-GnRH | | | | | | | | Met | | |
| [Leu]-GnRH | | | | | | | | Leu | | |
| cGnRH-II | | | | | His | | Trp | Tyr | | |
| cGnRH-IIA | | | | | His | D - Arg | Trp | Tyr | | |
| IGnRH | | | Tyr | | Leu | Glu | Trp | Lys | | |

## ㈠魚類之促性腺激素釋放素

硬骨魚類之腦中促性腺激素釋放素 (LHRH) 之血清免疫的早期資料，可由 Ball (1981), Peter (1983a, b) 的評論獲得。由觀察比目魚及金魚瞭解 LHRH 分佈於視前核之前及腹側部、終腦以及 the nucleus lateralis tuberis (NLT)。此外，中腦背部、嗅球部 (Olfactory bulbs) 也有此種激素出現 (Stell *et al.*, 1984)。由 Schreibman, *et al.*, (1979) 和 Stell, *et al.*, (1984) 實驗證實：具 LHRH 之免疫反應，自視前葉細胞傳至中腹面終達下視丘之前端和腦下腺柄部。較近報告，更明顯地發現到由嗅球發出之神經系以及經由視網膜通達視神經都有 LHRH 之正血清免疫反應 (Stell *et al.*, 1984)。

利用成熟早期及成熟後期之比目魚爲材料，Halpern-Sebold and Schreibman (1983) 發現 LHRH 之免疫反應次序爲：先經腦前部之嗅球，次爲視前核區，再次爲 nucleus laterallis tuberis。若剔除魚之腦下腺 (hypophysectomy) 則染色降低的次序爲：視前核和下視丘之腹基部，但在嗅球及終腦前部的反應却增强，這表示視前核及下視丘腹基部與腺性腦下腺有神經的直接連繫。

在無頜類之太平洋八目鰻(*Entosphenus tridentata*)及對其他兩種八目鰻的研究(Crim *et al.*, 1979a, b, Nozaki and Kobayashi, 1979)，發現呈現 LHRH 正反應之神經纖維，由視前葉傳到神經性腦下腺。因此，認爲自然之 GnRH 的釋放系統乃是屬於一般性循環系統。

前已述及控制動物生殖作用之 GnRH，依其主要分子構造，可歸納爲四種，即哺乳類，鳥類 I 及 II，還有鮭魚之 GnRH 等（圖五）。另依色層分析及免疫特性，間接地也發現了三種在不同魚種的「似 GnRH 分子」(GnRH-like molecules)。這三種包括了來自軟骨魚類的 GnRH，尙無法與鮭魚 GnRH II 號區分。八目鰻之「類-GnRH」分子，可能就是演化樹上較高等動物之 GnRH 的始祖分子構造 (Sherwood, 1986)（圖六、七），因在盲鰻則一直未被發現含有 GnRH 分子。

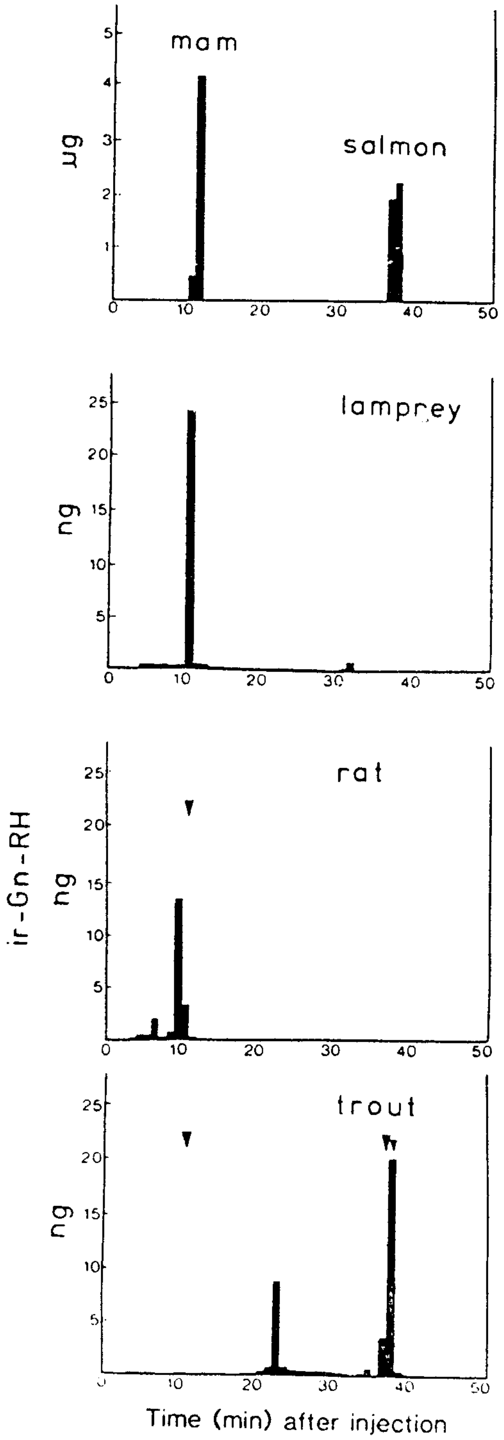

Fig. 6. Reverse-phase HPLC of lamprey brain extract containing immunoreactive gonadotropin-releasing hormone (ir-GnRH)is shown in the second figure from the top. The elution pattern of synthetic of synthetic mammalian (mam.) and synthetic salmon GnRH are shown in the top figure. The arrows in the lower figure mark the elution of the standards run with rat and trout brain extracts.

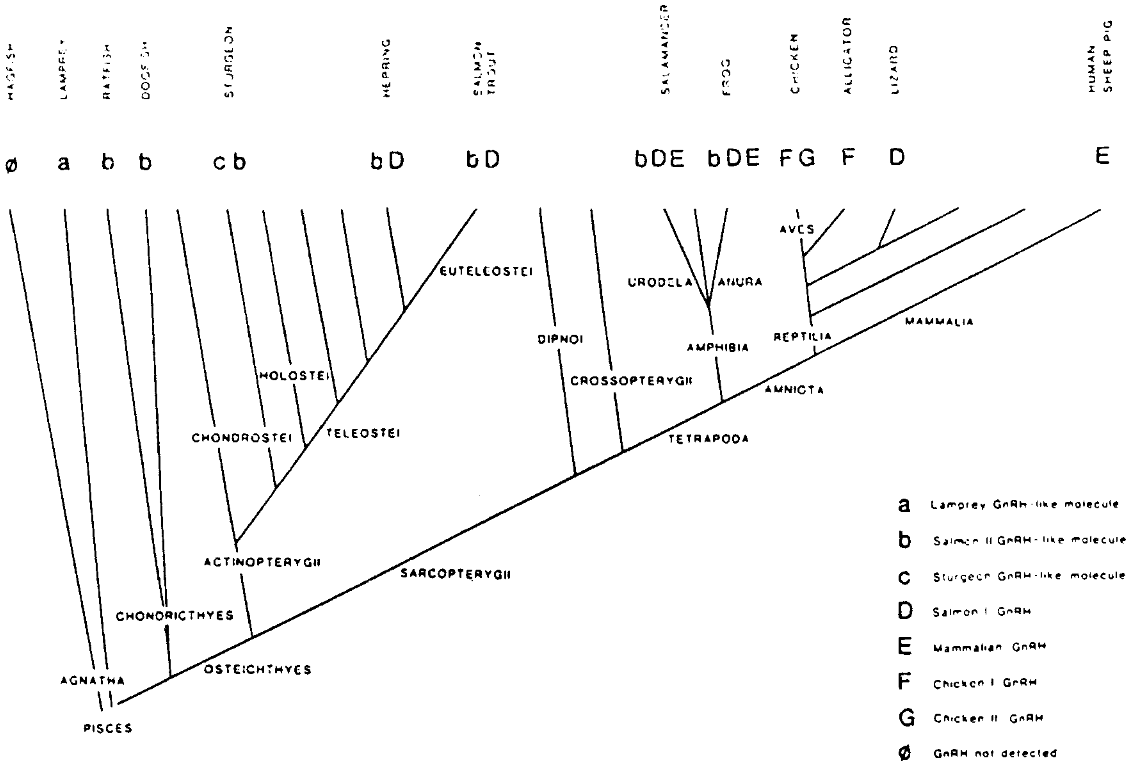

Fig. 7. A phylogenetic diagram showing the presence of GnRH-like peptides. The lower case letters (a, b, c) represent GnRH molecules which have been identified by indirect methods such as chromatography and immunoassay. The upper case letters (D, E, F, G) are for GnRH molecules with known primary structure. The animals listed at the top of the diagram are the representatives of the various subdivisions in which the peptide was studied. The presence of salmon II GnRH-like molecule in several groups is based on the fact that the peptides have not yet been differentiated by chromatographic or immunological methods. (Fig. 6 and 7. Sherwood, 1986)

### ㈢促性腺激素之分泌調節作用

NLT 的功能：從腦下腺之移植實驗，發現魚類促性腺激素（GtH）分泌細胞，在移植後發生細胞學上的退化現象，而且，這種移植的結果也使得生殖腺的作用無法持續進行（Ball *et al.*, 1972; Holmes and Ball, 1974）。這表示 GtH 細胞的活動承受腦之刺激和影響，也就是說 GTH 的分泌可能是經由 GnRH（或 LHRH）的調節作用。

從一種破壞金魚腦的研究，證明了 NLT 前與後部近腦下垂體柄部對調節 GtH 分泌使卵巢復熟（recrudescence）有關（Peter and Crim, 1978），若破壞大部分 NLT 便產生了抑制卵巢復熟並加速影響卵巢退縮，卵巢復熟卵黃成熟過程中的金魚，其 GtH 的分泌原呈日週期變化（Hontela and Peter, 1977），但一旦破壞 NLT 則影響 GnRH 分泌，遂改變了 GTH 分泌之日週期的模式（Peter and Crim, 1978）。

排卵作用：魚的排卵作用（ovulation）常伴隨促性腺激素之潮湧分泌（surge）現象（*C. auratus*, Breton *et al.*, 1972a; *Salmonides*, Crim *et al.*, 1975）。GtH 分泌之潮湧型式不一：鮭魚 *Oncorhynchus nerka* 隨着產卵（spawning）持續分泌；金魚則分泌高

峯只出現在排卵當日，但若腦破壞的是已完成卵黃形成階段或幾近完成卵黃形成者，則魚腦下垂體 GtH 分泌，會有連續數日大量潮湧式的分泌並有異常之排卵 (Peter *et al*., 1978)。上述這種排卵反應，縱然水溫降到 12～14°C 亦能產生（按此溫度，平常並不排卵）。由此，可見幾近完成卵黃形成時之魚的 GtH 分泌受有強烈的抑制作用。這種抑制反應也可能是魚為着等待適切之產卵環境的出現和 GtH 之潮湧分泌所需。唯其機制尚未全知，或許可將它視之為是腦中另有一種 GtH釋放之抑制因子存在的關係。至少今日已知多巴命 (dopamine, DA) 可能就是扮演此重要角色之一，因使用「抗一多巴命」物質於金魚等，確實收到增加此魚腦下腺 GtH 分泌以及加速其產卵的宏效。(Peter *et al*., 1986; Peter *et al*., 1987; Omeljaniuk, *et al*., 1987; Shih, 未發表資料) (圖八 a, b)。

通常金魚之產卵僅發生在每次排卵之後一次（或極少次）排空其成熟的卵，此後得一直等到下個卵巢復熟週期到來，然而雄魚則可能有較長期的延續其成熟的睪丸，並且能分別排精和釋放精子。破壞雄金魚NLT（精巢已成熟者）的結果，猶如破壞雌性者會促使大量潮湧式 GtH 分泌。對正在排精之金魚（Kyle, A. L. Stacey N. E and Peter, R. E.，未發表資料）和 *S. gairdneri* (Breton, *et al*., 1975a) 及其他鮭魚類 (Crim *et al*., 1975)，則反應出血清中促性腺激素濃度增加，且會出現大幅潮湧分泌的現象——這是在雌魚未曾發生過的。

有關下視丘具神經纖維直接影響及腦下垂體 GtH 細胞之分泌，曾發現於許多魚種，在 *Gobius mirobilis* 發現神經末梢具有 type "B" 纖維 (Knowles, 1965) 直接與 GtH cells 構成突觸構造 (synaptoid contacts) (Zambrano, 1970b)，而這些神經末梢囊又極似其 NLT 中的一些細胞所有 (Zambrano, 1970a)。對於雌魚，去腦下腺二天後，NLT 的前部與吻部細胞引起壞死，但稍後十四天則有跡象顯示恢復，更進一步將 *Gillichthy* 去勢，結果致活了 NLT 側面之神經元，而另以雄性素 (androgens) 處理者，則上述這些變化的發生便被阻斷，充分證明 NLT 和雄魚 GtH 分泌有關。Kaul and Vollrath (1974b) 發現金魚腦下腺之 type A 纖維來自視前核 (PON) 而 type B 纖維末梢則源自外側核 (NLT)。金魚在產卵期和產卵後神經末梢囊中顆粒減少，不過經雌二醇處理後 type B 及纖維之顆粒又再見增加。對於此，Peter and Nagahama (1976) 發現在金魚 NLT 具有 3 種細胞，它們仍直接分佈於腦下垂體，而其中 type III 細胞實際與調節卵巢活動的功能密切相關 (Peter, 1970; Peter and Crim, 1978)。而 PON 之 type A 末梢纖維則相信與調節細胞的活動有關。

下視丘萃取液證明有 GnRH 活動，首先由 Breton *et al*., (1971) 在鯉魚腦下腺離體細胞實驗發現。此後並證明其具有刺激羊之 LH (luteinizing hormone) 分泌的功能，相似地羊下視丘萃取物也可刺激鯉魚之腦下腺細胞分泌 GtH (Breton, *et al*., 1972b)。更進一步對鯰魚之 in vivo 實驗，顯示出 GnRH 活動之眞確性 (Weil *et al*., 1975)。其它激素，例如 epinephrine, norepinephrine, serotonin 和 dopamine，對鯉魚均無 GnRH 的功效 (Breton *et al*., 1975b)。

鯉魚之 GnRH 分子量小於 5,000。相似於此的人工合成 LH-RH (*p*Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-$NH_2$) (Vale *et al*., 1977)，經實驗證實它對許多硬骨魚類都有 GnRH 作用的效果，尤其對排卵季節之鯉魚，合成之 LHRH 和下視丘萃取物更

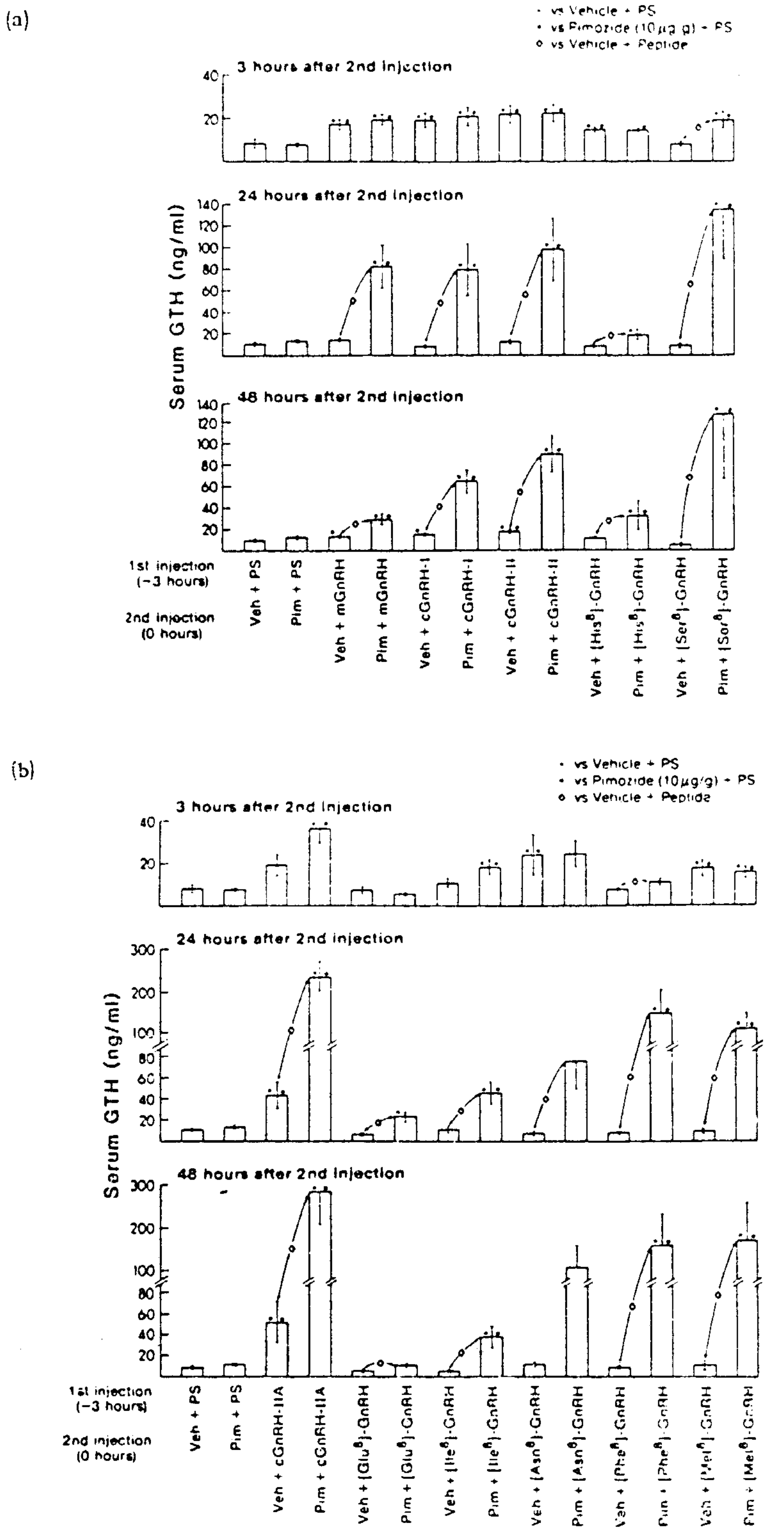

Fig. 8a, b. The effects on serum GtH levels in goldfish of mGnRH, cGnRH-I, cGnRH-II, cGnRH-IIA, and a number of analogs of mGnRH with substitutions in position 8, administered alone or in combination with pimozide (Pim). Values are means±SE ($N$=8–10). Significance level $p<0.05$ by Mann-Whitney $U$ test. (From: Peter, *et al.*, 1987)

具有高度效用。對雄性之 *Salmo trutta* 而言，除非性未成熟，否則 LHRH 確具有促使雄魚 GtH 分泌的效應(Crim and Cluett, 1974)。對於金魚，經由第三腦室注入 LHRH 也證明其促進血中 GtH 分的效果 (Crim *et al.*, 1976)。

對於誘導魚之排卵作用，注射 LHRH 於 ayu, *Plecoglossus altivelis* (Hirose and Ishida, 1974)，金魚 (Lam *et al.*, 1975, 1976)；或者使用 LH-RH 相似物 (LHRH analogues LHRH-A), des-Gly$^{10}$, [D-Ala$^{6}$] LHRH ethylamide 都證明有其良好之劑量反應，同時實驗也證明其對 *O. latipes* (Chan, K. K.-S., 1977) 有促進卵巢復熟的作用。不過特別要提出的是，使用過高劑量之 LH-RH (或 LHRH-A) 或過多次數，會造成混擾前述的正面結果。

LHRH 在腦之分佈，Goos and Murathanoglu (1977) 發現在 *S. gairdneri* 是起自終腦之中央部背方 (dorsalis pars medialis) 然後通至腦下腺柄部，然後經神經葉伸入腦下腺基部 (PPD) 之 GtH 細胞等 (Dubois *et al.*, 1978)。

有些攝護腺素(prosterglandins)，如 $PGF_{2\alpha}$ 和 $E_2$ (非 $E_1$) 經注入於性成熟之金魚的第三腦室後，降低了金魚血中 GtH 濃度 (Peter and Billard, 1976)，唯其劑量需大而且若由腹腔注射，則此種效果並不發生。這正與在哺乳類曾發現攝護腺素具有促進 LH分泌的結果相反。因此，某些 Prostaglandins 在魚類似乎具有類似 GRIH 的效應。

硬骨魚類具有年生殖週期 ( 圖 九 )，其產卵會在定期之一次或在每年之特定時段

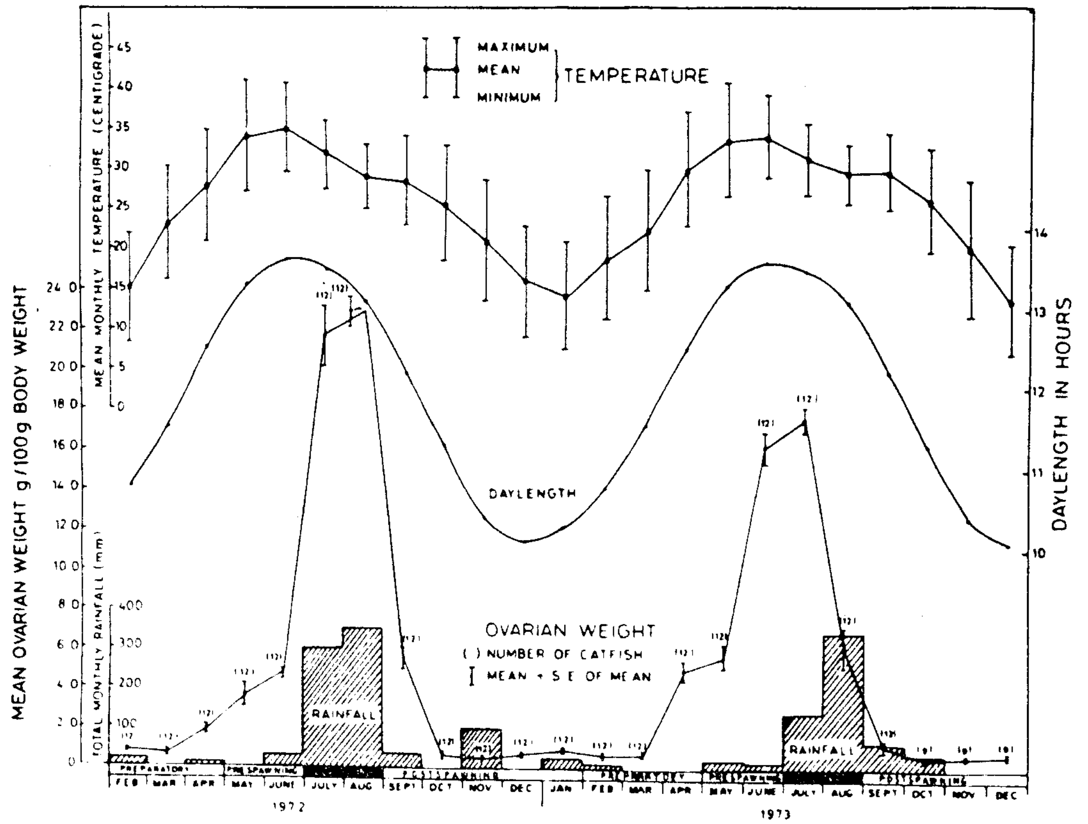

Fig. 9. Seasonal changes in ovarian weight of the catfish, *Heteropneustes fossilis*, in relation to annual fluctuations in day length, temperature, and rainfall. (From Sundararaj and Vasal, 1976)

(De Vlaming, 1974; Sundararaj and Vasal. 1976; Peter and Hontela, 1978; Shih, 1980, 1981)。環境因子包括光週期、水溫、下雨和營養等等 (De Vlaming, 1974, Peter and Hontela, 1978, Shih, 1981)。魚之松果腺可能具有光接受器和內分泌之分泌 amine, melatonin，以調節生殖的功能(De Vlaming and Vodicnik, 1977)，但以去松果腺研究發現，通常並不影響魚類的生殖腺活動 (Pang, 1967)。唯 Fenwick (1970) 則發現切除松果腺之金魚，在晚冬及初春魚在長日照下會有加强生殖腺快速復熟的作用 (recrudescence)。但此時如魚處於短日照下則出現「生殖腺」增加隆大現象。由此可見松果腺之對生殖腺作用的抑制或促進，決定於光照之長短和水溫。致盲之 *O. latipes* 會刺激生殖腺提早復熟的作用。春天盲的刺激會抑制生殖腺的再熟。注射 Melatonin 會阻斷了金魚在早春光照長又水溫高的環境的生殖腺成熟（通常此種環境促進生殖腺成熟）。這個結果與切除松果腺置長光週期下，會減少下視丘 GnRH 活動的報導互相吻合 (De Vlaming and Vodicnik, 1977)。

控制 GtH 之分泌也與生殖腺之類固醇激素 (steroid hormones) 的負迴饋作用 (negative feedback) 相關。在切除 *G. mirabilis* 之生殖腺（減除性腺固醇激素）Zambrano (1971) 發現在 NLT 的一羣特殊細胞和腦下腺之 GtH 細胞特別活動。Billard and Peter (1977) 也發現經種植抗動情激素之 clomiphene 和 I. C. I. 46,474 (tamoxifen) 於雌性金魚時，會大量增加血清 GtH 的濃度，至於若植在 NLT，則影響不大，但種植於 PON、下視丘背後部及視葉則分別均無反應。由此證明，類固醇之負回饋之主要場所爲腦下腺。

利用電刺激給予發自視前核的神經，會促進雄魚的放精和雌魚之產卵(*Lepomis cyanellus* 和 *C. auretus*) (Demski *et al*., 1975)。此種神經的活動，可以追查到下視丘、視丘、中腦、延腦以至於脊髓。推想其影響產卵和精子的作用，是由於神經影響到輸卵管和輸精管壁的平滑肌的緣故。圖十、十一提供控制硬骨魚之 GtH 分泌的模式。

### ㈣其他腦神經分泌胜類及神經傳遞物質之影響

1.魚之下視丘及腦等處尚可分泌許多 GnRH 外的釋放因子或抑制因子。控制ACTH 分泌之促腎上腺皮質素釋放素 (corticotropin-releasing facter, CRF)，具有依次控制 ACTH 和腎上腺皮質素以調節魚類有機代謝之平衡和抗緊張的功能。生長激素 (GH)的分泌受腦下腺及胰臟分泌之SRIF (somatostatins) 及GHRH 的管制，至於催乳素 (PRL) 則主要受催乳素抑制因子(PIF)的支配，一般相信它可能就是多巴命 (DA)，DA 也有抑制促性腺激素釋放素之作用，所以於調節 PRL 之分泌，必然也影響到魚類 GtH 的分泌。由下視丘釋放於中央隆突及神經葉的腦胜類很多 (表三) 相信有的也具間接影響 GtH 分泌或生殖的作用，尚待更多求證，表三所提資料僅供參考。

2.在硬骨魚類及較低等之魚種，起源於旁室核而達於腦下腺者有：正腎上腺素性纖維 (noradrenergic fibers)、血清素性纖維 (serotoninergic fiber) 以及多巴命性纖維 Kah and Chambolle, 1983; Ekstrom and Van Veen, 1984)。在金魚，Fryer *et al*., (1985) 毀腦實驗，發現旁室核有 catecholamine 纖維連通腦下腺。其他腦部是否有此纖維分佈，尚待證實。硬骨魚類中，如金魚 (Kah *et al*., 1984)，於視前核前腹部細胞

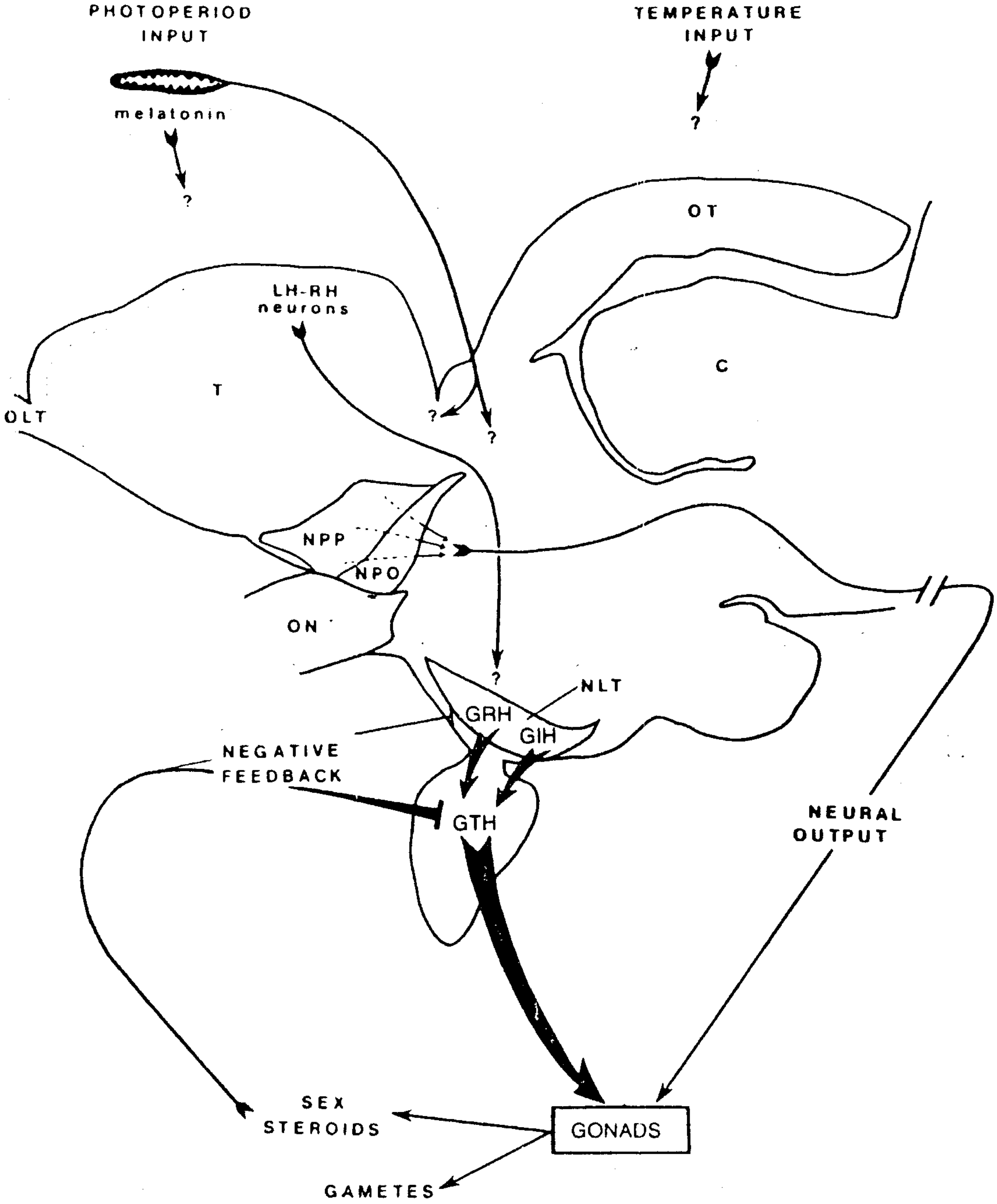

Fig. 10. A model, based on a parasagittal view of the goldfish forebrain, illustrating the neuroendocrine regulation of gonadotropin (GTH) secretion by a releasing hormone (GRH) and an inhibitory hormone (GIH). A neural pathway originating in the preoptic region stimulates gamete release. Questions indicate unknown pathways. C, cerebellum; LH-RH, luteinizing hormone-releasing hormone; NLT, nucleus lateral tuberis; NPO, nucleus preopticus; NPP, nucleus preopticus periventricularis; OLT, olfactory tract; optic nerve; OT, optic tectum; T, telencephalon. (From: Peter, 1983b)

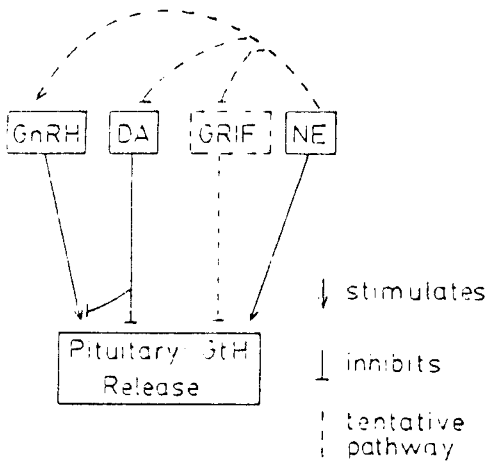

Fig. 11. Summary diagram of the influences of dopamine (DA) and norepinephrine (NE) on gonadotropin (GtH) release in goldfish. (From Peter *et al.*, 1986)

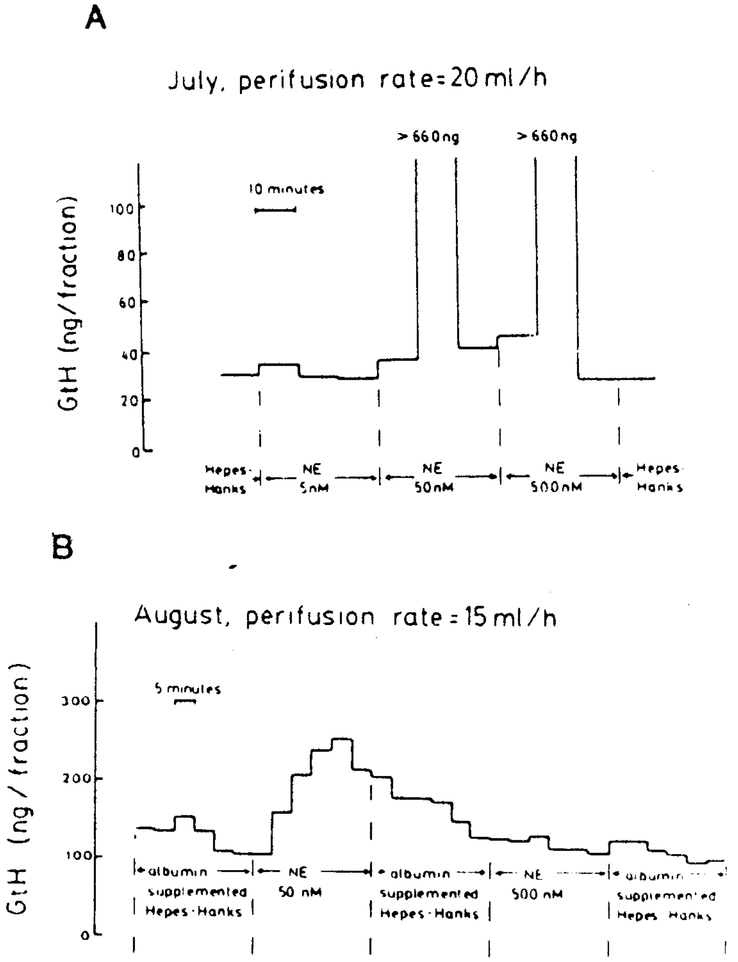

Fig. 12. Changes in gonadotropin (GtH) released from perifused (A) dispersed pituitary cells, and (B) pituitary fragments prepared from sexually regressed female goldfish during and following exposure to norepinephrine (NE). (From Peter *et al.*, 1987)

Table 3. The brain origins of some brain peptides localized by immunohistochemistry in the median eminence, posterior pituitary, or neurohypophysial tissue innervating the anterior pituitary

| Peptide | Localization suggesting neurohormonal function | Brain origin | Species or class | Reference |
|---|---|---|---|---|
| Cholecystokinin | Median eminence | Paraventricular nucleus | Mammalia | Palkovits (1984) |
| | Posterior pituitary | Supraoptic and paraventricular nuclei | Rat and bovine | Vanderhaeghen *et al.* (1981) |
| Enkephalins | Median eminence | Origin? | Japanese quail | Mikami and Yamada (1984) |
| | Posterior pituitary | Acruate, paraventricular and supraoptic nuclei | Mammalia | Follénius and Dubois (1981)<br>Goodman *et al.* (1983)<br>DiFiglia and Aronin (1984)<br>Palkovits (1984) |
| β-endorphin | Median eminence | Ventrobasal hypothalamus | Mammalia | Palkovits (1984) |
| β-endorphin (cont.) | Neurophyophysis innervating pars distalis | Ventrobasal hypothalamus | Teleostei | Follénius and Dubois (1981) |
| Neurotensin | Median eminence | Arcuate nucleus and other? | Mammalia | Arnoni *et al.* (1983a)<br>Ibata *et al.* (1984)<br>Jennes *et al.* (1984)<br>Palkovits (1984) |
| | Median eminence and posterior pituitary | Origin? | Japanese quail | Yamada and Mikami (1981) |

(From: Peter, R. E. 1983)

Table 3. Continued

| Peptide | Localization suggesting neurohormonal function | Brain origin | Species or class | Reference |
|---|---|---|---|---|
| Angiotensin II | Median eminence and posterior pituitary | Paraventricular nucleus | Mammalia | Ganong (1983)<br>Lind *et al.* (1985) |
| Substance P | Median eminence and posterior pituitary | Several hypothalamic nuclei | Mammalia | Stoeckel *et al.* (1982)<br>Aronin *et al.* (1983b)<br>Palkovits (1984) |
|  | Median eminence | Ventral hypothalamus | Japanese quail | Mikami and Yamada (1984) |
| Vasoactive intestinal peptide | Median eminence | Origin? | Mammalia | Mutt (1983)<br>Palkovits (1984) |
|  | Median eminence | Infundibular (=arcuate) nucleus | Japanese quail | Yamada and Mikami (1982)<br>Mikami and Yamada (1984) |
| FMRFamide-like | posterior pituitary | Origin? | Rat | Williams and Dockray (1983) |
| Gastrin-like | Neurohypophysis innervating pars distalis | Nucleus lateralis tuberis (ventrobasal hypothalamus) | Rainbow trout | Notenboom *et al.* (1981) |
| Glucagon-like | Neurohypophysis innervating pars distalis and pars intermedia | Nucleus lateralis tuberis | Rainbow trout | Gielen and Terlou (1983) |
|  | Media eminence | Infundibular nucleus | Japanese quail | Mikami andYamada (1984) |

中發現有多巴命正反應纖維通達腦下腺。以上這幾種神經分泌纖維的分佈與腦下腺控制生殖之激素分泌具直接或間接關係。因在金魚及其他硬骨魚類，正腎上腺素（noradrenaline, NE）及腎上腺素具有直接刺激 GtH 分泌的作用（圖十二）(Chang and Peter, 1984; Peter *et al.*, 1986)。特別對雌性金魚，在其卵巢退化（regressed）或處於初期之卵巢再熟階段的季節，in vivo 注射 NE 最能誘導出魚 GtH 之分泌。不過必須考慮 NE 之可能不通過腦障蔽（brain barrier）的情況。因此發掘在何種魚，於什麼季節（魚生殖腺處於何處狀態）才是最適應用 NE 或 NE 之增强劑（agonists）以收增加 GtH 的分泌，都是值得努力探討的。

## 四、引用文獻

Baker, B. I. and Ball, J. N. (1970). Background adaptation and the pituitary in teleosts. *J. Endocrinol.*, **48**: xxvi-xxvii.

Ball, J. N. and Baker, B. I. (1969). The pituitary gland: Anatomy and histophysiology. *In "Fish Physiology"* W. S. Hoar and D. J. Randall, (eds.), Vol. II, pp. 1-110, Academic Press, New York.

Ball, J. N., Baker, B. I., Olivereau, M. and Peter, R. E. (1972). Investigation on hypothalamic control of adenohypophysial functions in teleost fishes. *Endocrinol.*, Suppl. **3**: 11-21.

Ball, J. N. (1981). Hypothalamic control of the pars distalis in fishes, amphibians and reptiles. *Gen. Comp. Endocrinol.*, **44**: 135-170.

Billard, R. and Peter, R. E. (1977). Gonadotropin release after implantation of anti-estrogens in the pituitary and hypothalamus of goldfish, *Carassius auratus*. *Gen. Comp. Endocrinol.*, **32**: 213-220.

Breton, B., Billard, R., Jalabert, B. and Kann, G. (1972b). Dosage radioimmunologigue des gonadotropines plasmatiques chez *Carassius auratus*, au cours du nycthémère et pendant l'ovulation, *Gen. Comp. Endocrinol.*, **18**: 463-468.

Breton, B., Jalabert, B., Billard, R. and Weil, C. (1971). Stimulation *in vitro* de la libération d'hormone gonado.

Breton, B., Jalabert, B. Fostier, A. and Billard, R. (1975b). Etude sur le cycle reproducter de la truite are-en-cicl et de la tanche. *J. Physiol.* (Paris) **70**: 561-564.

Breton, B., Jalabert, B, and Weil, C. (1975a). Caracterisationpartielle d'un facteur hypothalamique de l'libération des hormones gonadotropes chez la carpe (*Cyprinus carpio* L.). Etude *in viro*. *Gen. Comp. Endocrinol.*, **25**: 405-415.

Breton, B., Weil, C. Jalabert, B. and Billard, R. (1972a). Activité réciproque des facteurs hypothalamiques de bélicr (*Ovis aries*) et de poissons téléostéens sur la sécrétion *in vitro* des hormones gonadotropes c-HG et LH respectivement par des hypophyses de carpe et de bélier, *C. R. Hebd. Seances Acad. Sci. Ser. D: Sci. Nat.* **274**: 2530-2533.

Burgus, R., Butcher, M., Amoss, M., Ling, N. Monahan, M., Rivier, J., Fellows, R., Blackwell, R., Vale, W. and Guillemin, R. (1972). Primary structure of the ovine hypothalamic luteinizing hormonereleasing factor (LRF). *Proc. Natl. Acad. Sci, U. S. A.* **69**: 278-282.

Chan, K. K.-S. (1977). Effect of synthetic luteinizing hormone-releasing hormone (LH-RH) on ovarian development in Japanese medaka, *Oryzias latipes*. *Can. J. Zool.* **55**: 155-160.

Chang, J. P., Peter, R. E., Nahoniak, C. S. and Sokolowska, M. (1984). Effects of catecholaminergic agonists and antagonists on serum gonadotropin concentrations and ovulation in goldfish: Evidence for specificity of dopamine inhibition of gonadotropin secretion. *Gen. Comp. Endocrinol.*, **55**: 351-360.

Crim, L. W. and Cluett, D. M. (1974). Elevation of plasma gonadotropin concentration in response to mammalian gonadotropin releasing hormone (GRH) treatment of the male brown trout as determined by radioimmunoassay. *Endoc. Res. Commun.*, **1**: 101-110.

Crim, L. W., Peter, R. E. and Billard, R. (1976). Stimulation of gonadotropin secretion by intraventricular injection of hypothalamic extracts in the goldfish. *Carassius auratus*. *Gen. Comp. Endocr.*, **30**: 77-82.

Crim, J. W., Urano, A. and Gorbman, A. (1979a). Immunocytochemical studies of luteinizing hormone-releasing hormone in brains of agnathan fishes. I. Comparisons of adult Pacific lamprey (*Entosphenus tridentata*) and the Pacific hagfish (*Eptatretus stouti*). *Gen. Comp. Endocrinol.*, **37**: 294-305.

________. (1979b). II. Patterns of immunoreactivity in larval and maturing western brook lamprey (*Lampetra richardsoni*). *Gen. Comp. Endocrinol.*, **38**: 290-299.

Crim, L. W., Watts, E. G. and Evans, D. M. (1975). The plasma gonadotropin profile during sexual maturation in a variety of salmonid fishes. *Gen. Comp. Endocrinol.* **27**: 62-70.

Coy, D. H. and Schally, A. V. (1978), Gonadotropin releasing hormone analogue. *Ann. Clin. Res.* **10**: 139-144.

Demski, L. S., Bauer, D. H. and Gerald, J. W. (1975). Sperm release evoked by electrical stimulation of the fish brain: A functional-anatomical study. *J. Exp. Zool.*, **191**: 215-232.

DeVlaming, V. L. (1974). Environmental and endocrine control of teleost reproduction. In "Control of Sex in Fishes" (C. B. Schreck, ed.), pp. 13-83. Virginia Polytechni Institute and State University, Blacksburg.

DeVlaming, V. L. and Vodicnik, M. J. (1977). Effects of pinealectomyon pituitary gonadotrophs, pituitary gonadotropin potenty and hypothalamic gonadotropin releasing activity in the teleost *Notemigonus crysoleucas*. *J. Fish Biol.*, **10**: 73-86.

Dubois, M. P., Billard, R. and Breton, B. (1978). Use of immunofluorescence for localization of somatostatin-like antigen in the rainbow trout (*Salmo gairdner*). Comparative distribution of LH-RF and neurophysin. *Ann. Biol. Anim. Biophys.*, **18**: 843-850.

Dudley, C. A., Vale, W., Rivier, J. and Moss, R. L. (1983). Facilitation of sexual receptivity in the female rat by a fragment of the LHRH decapeptide, Ac-LHRH$^{5-10}$. *Neuroendocrinology.*, **36**: 486-488.

Ekstrom, P. and Van Veen, T. (1984). Distribution of 5-hydroxytryptamine (serotonin) in the brain of the teleost *Gasterosteus aculeatus* L. *J. Comp. Neurol.*, **226**: 307-320.

Fenwick, J. C. (1970). Demonstration and effect of melatonim in fish. *Gen. Comp. Endocrinol.*, **14**: 86-87.

Fryer, J. N., Boudreault-Chateauvert, C. and Kirby, R. P. (1985). Hypophysiotropic neurons originating in the paraventricular organ (PVO) of the goldfish hypothalamus. *J. Comp. Neurol.*, **242**: 475-484.

Goos, H. J. Th. and Murathanoglu, O. (1977). Localisation of gonadotropin releasing hormone (GRH) in the forebrain and neurohypophsis of the trout (*Salmo gairdneri*). *Cell. Tissue. Res.*, **181**: 163-168.

Halpern-Sebold, L. R. and Schreibman, M. P. (1983). Ontogeny of centers containing luteinizing hormone-releasing hormone in the brain of platyfish (*Xiphophorus maculatus*) as determined by immunocytochemistry. *Cell. Tiss. Res.*, **229**: 75-84.

Hirose, K. and Ishida, R. (1974). Induction of ovulation in the ayu, *Plecogossus altivelis*, with LH-releasing hormone (LH-RH). *Bull.* Jpn. Soc. Sci. Fish. **40**: 1235-1240.

Holmes, R. L. and Ball, J. N. (1974). *The pituitary gland. A comparative account.* Cambridg Univ. Press, London.

Hontela, A. and Peter, R. E. (1977). Effects of tempeature and photoperiod on daily cycles of gonadotropin secretion in the goldfish. *Am. Zoo.*, **17**: 874 (abstr.)

Hsueh, A. J. W. and Jones, P. B. C. (1981). Extrapi tuitary actions of gonadotropin-releasing hormone. *Endocrine. Reviews.*, **2**: 437-461.

Jackson, I. M. D. (1986). Phylogenetic distibation and significamce of the hypothalamic releasing hormones. *Amer. Zool.*, **26**: 927-938.

Jackson, I. M. D. and Mueller, G. P. (1982). Neuroendocrine interrelationships. *In* R. F. Goldberger and Yamamoto (eds.), *Biologic regulation and development*, Vol. 3A, *Hormone action*, pp. 127-200, Plenum, N. Y.

Kah, O. and Chambolle, P. (1983). Serotonin in the brain of the goldfish, *Carassius auratus. Cell Tiss. Res.*, **234**: 319-333.

Kah, O., Chambolle, P., Thibault, J. and Geffard, M. (1984). Existence of dopaminergic neurons in the preoptic region of the goldfish. *Neurosci. Letters.*, **48**: 293-298.

Kaul, S. and Vollrath. L. (1974). The goldfish pituitary. II. Innervation. *Cell. Tissue. Res.*, **154**: 231-249.

Knowles, F. (1965). Evidence for a dual control, by neurosecretion, of hormone synthesis and hormone release in the pituitary of the dogfish, *Scylliorhinus stellaris. Philos. Trans R. Soc. Lond. B: Biol. Sci.*, **249**: 435-456.

Krey, L. C. and Silverman, A. J. (1983). Luteinizing hormone releasing hormone (LHRH). *In* "Brain peptides" (D. T. Krieger, M. J. Brownstein and J. B. Martin, eds.), pp. 680-709. John Wiley and Sons, New York.

Lam, T. J., Pandey, S. and Hoar, W. S. (1975). Induction of ovulation in goldfish by synthetic luteinizing hormone-releasing hormone (LH-RH). *Can. J. Zool.*, **53**: 1189-92.

Lam, T. J., Pandey, S. Nagahama, Y. and Hoar, W. S. (1976). Effect of synthetic luteinizing hormone-releasing homone (LH-RH) on ovulation and pituitary cytology of the goldfish *Carassius auratus. Can. J. Zool.*, **54**: 816-824.

La Pointe, J. L. (1977). Comparative physiology of neurohypophysial hormone action on the vertebrate oviductuterus. *Am. Zool.*, **17**: 763-773.

Leatherland, J. F. and Dodd, J. M. (1967). Types of secretory neurons in the preoptic nucleus of the European eel, *Anguilla anguilla* L. *Nature* (Lond.) **216**: 586-587.

_______. (1969a). Activity of the hypothalamo-neurohypophysial comalex of the European eel (*Anguilla anguilla* L.) assessed by the use of an *in situ* staining technique and by autoradiography. *Gen. Comp. Endocrinol.*, **13**: 45-59.

Leatherland, J. F., Budtz, P. E. and Dodd, J. M. (1966). In situ studies on the hypothalamo-neurohypophysial complex of the European eel, *Anguilla anguilla* L. *Gen. Comp. Endocrinol.*, **7**: 234-244.

MacLeod, R. M. (1976). Regulation of prolactin secretion. *In* "Frontiers in neuroendocrinology" (L. Martini and W. F. Ganong, eds.) Vol. 4, pp. 169-194. Raven, New York.

Maetz, J. and Lahlou, B. (1974). Actions of neurohypophysial hormones in fishes. *In Handbook of physiology,* Sect. 7, Vol. IV, Pt. 1. pp. 521-544. American Physiological Society, Washington, D. C.

Matsuo, H., Baba, Y., Nair, R. M. G., Arimura, A. and Schally, A. V. (1971). Structure of the porcine LH- and FSH-releasing Hormone. I. The proposed amino acid sequence-Biochem. *Biophys. Res. Communic.*, **43**: 1334-1339.

Millar, R. P. and King, J. A. (1983). Synthesis, luteinizing hormone-releasing activity, and receptor binding of chicken hypothalamic luteinizing hormone-releasing hormone. *Endocrinology.*, **113**: 1364-1369.

Miyamoto, K., Hasegawa, Y., Igarashi, M., Kangawa, K. and Matsuo, H. (1983). Structural determination of the second gonadotropin releasing hormone (GnRH II) in chicken hypothalamus. In "Peptide Chemistry" (E. Munekata, ed.) pp. 94-104 The Protein Research Foundation.

Moss, R. L. and McCann, S. M. (1973). Induction of mating behavior in rats by luteinizing hormone-releasing factor. *Science.*, **181**-177-179.

Nozaki, M. and Kobayashi, H. (1979). Distribution of LH-RH-like substance in the vertebrate brain as revealed by immunohistochemistry. *Arch. Histol. Japon.*, **42**: 201-219.

Olivereau, M. (1967a). Notions actuelles sur le contrôle hypothalamique des fonctions hypophysaires chez les poissons. *Rev. Eur. Endocrinol.*, **4**: 175-196.

_______. (1971). Action de la réseɹpine chez l'anguille. I. Cellules à prolactine de l'hypophyse du mâle. *Z. Zellforsch. Mikrosk. Anat.*, **121**: 232-243.

Omeljaniuk, R. J., Shih, S. H. and Peter, R. E. (1987). *In vivo* evaluation of pituitary dopamime receptor mediated inhibition of gonadotropin secretion in the goldfish, *Carassius auratus. J. Endocrinology.*, (in print).

Pang, R. K. T. (1967). The effect of pinealectomy on the adult male killifish, *Fundulus herteroclitus. Ann. Zool.*, **7**: 525 (abstr).

Pang, R. K. T. (1977). Osmoregulatory functions of neurohypophysial hormones in fishes and amphibians. *Ann. Zool.* **17**: 739-749.

Perks, A. M. (1969). The neurohypophysis. *In* "Fish Physiology" (W. S. Hoar and D. J. Randall eds.), Vol. 2, pp. 111-205. Academic press, New York.

Peter, R. E. (1970). Hypothalamic control of thyroid gland activity and gonadal activity in the goldfish, *Carassius auratus. Gen. Comp. Endocrinol.*, **14**: 334-356.

Peter, R. E. and Crim, L. W. (1978). Hypothalamic lesions of goldfish: Effects on gonadal recrudescence and gonadotropin secretion. *Ann. Biol. Anim. Biochim. Biophys.*, **18**: 819-823.

Peter, R. E. (1983a). Evolution of neurohormonal regulation of reproduction in lower vertebrates. *Amer. Zool.* **23**: 685-695.

Peter, R. E. (1983b). The brain and neurohormones in teleost reproduction. *In* "Fish Physiology Vol. IX" (W. S. Hoar, D. J. Randall, and E. M. Donaldson, eds.), pp. 97-135. Academic Press, New York.

Peter, R. E. and Billard, R. (1976). Effects of third ventricle injection of prostaglandins on gonadotropin secretion in goldfish, *Carassius auratus. Gen. Comp. Endocrinol.*, **30**: 451-456.

Peter, R. E. and Hontela, A. (1978). Annual gonadal cycles in teleosts: Environmental factors and gonadotropin levels in blood. *In* "Environmental endocrinology" (D. S. Farner and I. Assenmacher, eds.), pp. 20-25. Springer-Verlag, Berlin.

Peter, R. E. and Nagahama, Y. (1976). A light and electron microscopic study of the structure of the nucleus preopticus and nucleus lateral tuberis of the goldfish, *Carassius auratus. Can. J. Zool.* **54**: 14231437.

Peter, R. E., Crim, L. W. Goos, H. J. Th. and Crim. J. W. (1978). Lesioning studies on the gravid female goldfish: Neuroendocrine regulation of ovulation. *Gen. Comp. Endocrinol.*, **35**: 391-401.

Peter, R. E., Chang, J. P., Nahorniak, C. S., Omeljaniuk, R. I., Sokolowska, M., Shih, S. H. and Billard, R. (1986). Interactions of catecholamines and GnRH in regulation of gonadotropin secretion in teleost fish. *Recent Prog. Horm. Res.* **42**: 513-545.

Peter, R. E., Nahorniak, C. S., SHIH, S. H., King, J. A. and Millar, R. P. (1987). Activity of position-8-substitute analogs of mammalian gonadotropin-releasing hormone (mGnRH) and chicken and lamprey gonadotropin-releasing hormone in goldfish. *Gen. Comp. Endocrinol.*, **65**: (in print).

Pohl, C. R. and Knobil, E. (1982). The role of the central nervous system in the control of ovarian function in higher primates. *Ann. Rev. Physiol.*, **44**: 583-593.

Schreibman, M. P., Halpern, L. R., Goos, H. J. Th. and Morgolis-Kazan, H. (1979). Identification of luteinizing hormone-releasing hormone (LH-RH) in the brain and pituitary gland of a fish by immunocytochemistry. *J. Exp. Zool.* **210**: 153-160.

Sherwood, N., Eiden, L., Brownstein, M., Spiess, J., River, J. and Vale, W. (1983). Characterization of a teleost gonadotropin-releasing hormone. *Proc. Natl. Acad. Sci., U. S. A.*, **80**: 2794-2798.

Sherwood, N. M. (1986). Evolution of a neuropeptide family: Gonadotropin-releasing hormone. *Amer. Zool.* **26**: 1041-1054.

Shih, S. H. (1980). Pituitary changes and reproductive cycles in the common goby, *Pomatoschistus microps* (Krϕyer). *Biol. Bull. NTNU.* **15**: 39-54.

Shih, S. H. (1981). Reproductive cycles in teleost fishes. *Hormones and Reproduction*, NSC and BRC, Academia Sinica, ROC. **11**: 149-163.

Stell, W. K., Walker, S. E., Chohan, K. S. and Ball, A. K. (1984). The goldfish nervus terminalis: An LHRH and FMRF amide-immunoreactive olfactoretinal pathway. *Proc. Natl. Acad. Sci. U. S. A.*, **81**: 940-944.

Sundararaj, B. I. and Vasal, S. (1976). Photoperiod and temperature control in the regulation of reproduction in the female catfish, *Heteropneustes fossilis*. *J. Fish. Res. Board. Can.* **33**: 959-973.

Sundararaj, B. I. and Goswami, S. V. (1869). Role of interrenal in LH-induced ovulation and spawning in catfish, *Heteropneustes fossilis*. *Gen. Comp. Endocrinol. Suppl.*, 2: 374-384.

Vale, W., Rivier, C. and Brown. M. (1977). Regulatory peptides of the hypothalamus. *Annu. Rev. Physiol.*, **39**: 473-527.

Van Oordt, P. G. W. J. and Peute, J. (1983). The cellular origin of pituitary gonadotropins in teleosts. *In* "Fish Physiology" (W. S. Hoar, D. J. Randall and E. M. Donaldson eds.), Vol. IX-A, pp. 137-186. Academic Press, New York.

Vigh-Teichmann, I., Vigh, B. and Aros, B. (1976). Cerebrospinal fluid-contacting neurons, ciliated perikarya and "peptidergic" synapses in the magnocellular preoptic nucleus of teleostean fishes. *Cell. Tissue Res.*, **165**: 397-413.

Weil, C., Breton, B. and Reinaud, P. (1975). Etude de la réponse hypophysaire à l'administration de Gn-RH exogène au cours du cycle reproducteur annuel chez la carpe *Cyprinus carpio* L. *C. R. Hebd. Seances Acad. Sci. Ser. D*: *Sci. Nat.*, **280**: 2469-2472.

Zambrano, D. (1970a). The nucleus lateralis tuberis system of the gobiid fish *Gillichthys mirabilis*. I. Ultrastructural and histochemical characterization of the nucleus. *Z. Zellforsch. Mikrosk. Anat.* **110**: 9-26.

________. (1970b). The nucleus lateralis tuberis system of the gobiid fish *Gillichthys mirabilis*. II. Innervation of the pituitary. *Z. Zellforsch. Mikrosk. Anat.*, **110**: 496-516.

Zambrano, D. (1971). The nucleus lateralis tuberis system of the gobiid fish, *Gillichthys mirabilis.* III Functional modification of the neurons and gonadotropic cells. *Gen. Comp. Endocrinol.*, **17**: 164-82.

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# The Hypothalamic regulation of the Gonadotropin Secretion in Teleosts

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The morphological organization of the pituitary gland in teleosts is reviewed. As in the eel, *A. anguilla,* there are three types of hormone-producing cells, TSH-, prolactin, and ACTH cells are located in the rostral pars distalis (RPD) of the adenohypophysis, somatotropes (STH) as well as gonadotropes (GtH) are in the proximal pars distalis (PPD); however, the PbH+ve, MSH cells and one PAS+ve cells are distributed in the pars intermedia (PI) of this master gland.

The hypophysis has a separate vascular system supply to the pars distalis (PD) and the PI. In teleosts, a common pattern of rete mirabile-like arteriolar loops at interface between the PD and the pars nervosa (NH) is served as a humoral transmission system involved the pituitary hormone secretion. Another distinct neurosecretory system is the preoptic nucleus and its axonal terminalis where two types of hormone, arginine vasotocin and isotocin are released from.

Neuroendocrine regulation of the secretion of pituitary hormones in fish is reviewed. ACTH secretion is regulated by a corticotropin-releasing factor originating from the NLT and preoptic nucleus, and negative feedback effects of ACTH on hypothalamus and hypophysis. Gonadotropin secretion is regulated by GtH-releasing hormone (GnRH) and also the release-inhibitory factor; the GnRH invalues the NLT, while the inhibitory factors, at least, including dopamine compound. GtH secretion in animals is regulated by various types of GnRH(s), on which, three types of carp GnRH-like substances, one type of salmon GnRH are found in teleosts. The secretion of GtH is also influenced by the catecholamine, pineal activity, prostaglandins, and positive feedback as well as nagative feedback effects of the concentration of gonadal steroid hormones.

Several anti-dopamine drugs are high potent for the stimulation of GtH secretion and could be used as powerful agents for the induction of the gonadal maturation and spawning in the bony fishes.

Pituitary prolation is regulated by a release-inhibitory factor, possibly dopamine, from the NLT and changes in environmental osmolarity during reproductive migration.

Various types of innervation of GtH cells and the secretion of nerve-endings, type A and B, are discussed.