Chapter 7
Neuroendocrinology of Fishes

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Abstract The chapter includes information regarding neuroendocrinology in fishes particularly on the hypothalamohypophysial system, the organization of the telencephalon, preoptic region, hypothalamus, central neurohormones, hypophysiotropic peptides, steroid feedback regulation of stimulating and releasing hormones [luteinizing hormone (LH), *follicle*-stimulating hormone (FSH) and gonadotrophin-releasing hormone (GnRH)], hypothalamic neurotransmitters, hormonal targets of hypothalamus and pituitary as well as neuroendocrinology of fluid intake and fluid balance.

Keywords Fish hypothalamus · Endocrine regulation · Teleost · Fish neuroendocrinology

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7.1 Introduction

The secretory cells in the teleost fish brain were suggested by Scharrer (1928). The hormones secreted in the pars nervosa of the pituitary is governed by glandular nerve cells. Several studies revealed the presence of a hypothalamohypophysial system that links the endocrine and the central nervous systems (CNS) to regulate a wide variety of vital process. The hypothalamus, neurohypophysis and adenohypophysis are the three main areas of the hypothalamohypophysial system in fish. The hypothalamus is the part of the diencephalon; the adenohypophysis is the non-neuronal structure of the gland and the neurohypophysis is developed from the ventral diencephalon and characterizes the neural compartment of the pituitary (Pogoda and Hammerschmidt 2007). The cell bodies are present in the preoptic area of the nerve terminals and the pituicytes make up the neurohypophysis. Pituicytes have a supportive function. The neurohypophysis is divided into the pars nervosa and median eminence in non-teleost (Lagios 1968) and Elasmobranchs (van de Kamer and Zandbergen 1981). Adenohypophysis receives secretory products from hypothalamic neurons that have a network of blood capillaries which is the portal system. The portal system and median eminence are not found in teleost fishes. The diffusion distance between the region of adenohypophysis and hypothalamic neurons is reduced; hence the hypothalamic neurons control the adenohypophysis.

The endocrine system of the fishes consists of the thyroid gland, pituitary gland, corpuscles of Stannius, adrenal gland, urohypophysis, ultimobranchial glands, pineal gland and pancreatic islet. Thyrotropins release *thyroid-stimulating hormone (TSH)* that regulates the synthesis and secretion of triiodothyronine (T3), thyroxine (T4) and calcitonin and thyroid growth. Gonadotrophs triggers *luteinizing* hormone (LH) and *follicle-stimulating* hormone (FSH) hormones and thus control oogenesis, gonadal hormones and spermatogenesis. Somatotrophs trigger growth hormone (GH) and increase basal metabolic rates and growth of the fish body. Lactotrophs trigger prolactin (PRL) release that helps in melanogenesis and osmoregulation. Adrenocorticotropic hormone (ACTH) is triggered by corticotrophs and regulates corticotropin from the adrenal glands. Pigmentation and melanophores are regulated by melanocyte-stimulating hormone (MSH) and melanin-concentrating hormone (MCH) in the body and skin. Saltwater balance, mating/laying eggs and osmoregulation are regulated by oxytocin and arginine-vasotocin (AVT).

In bony fish, the thyroid arises as a median evagination from the floor of the pharynx. The thyroid hormones (TH) help in osmoregulation, migration, maturation, scale and bone development. The adrenal cortex and medulla are placed in two separate regions. Cortisol secretion, sodium retention and water metabolism are the responsibilities of adrenal glands. Hypocalcin is secreted by the corpuscles of Stannius, which regulates calcium balance. Calcitonin also regulates calcium levels that are secreted by ultimobranchial glands in the fish body. Urotensins control the metabolic regulation that is secreted by urohypophysis present at the end of the spinal cord. Insulin that regulates carbohydrate metabolism is produced by the pancreatic islets located in gut walls. Melatonin that controls photosensory or

secretory functions is secreted by the pineal gland. In fish, epinephrine, norepinephrine, and dopamine are produced by the chromaffin cells that present in the adrenal glands.

7.2 Telencephalon

The organization of the telencephalon is highly distorted in teleost fish. Evagination is the process through which the telencephalon develops at the earlier steps for the development of telencephalon in most of the vertebrates such as amniotes, cartilaginous fish, lampreys, and amphibians. As the telencephalon protrudes and expands, the lumen of the neural tube subsequently forms the telencephalic ventricles. The telencephalon comprises olfactory bulbs and telencephalic hemispheres. The telencephalic hemispheres are divided into two parts as ventralis telencephalic or subpallium and dorsalis telencephalic or pallium. The area ventralis telencephalic is structured into nuclei (Wullimann and Mueller 2004). In contrast, the dorsalis telencephalic is the largest region that exhibits a large number of histological distinct zones. The dorsal area is divided into three periventricular zones (pars dorsalis, pars medialis and pars lateralis) which is based on cytoarchitectonic criteria. The ventral area of the teleost telencephalon is a non-everted part that is rostrally placed on the preoptic area that is divided into precommissural and postcommissural nuclei. Precommissural nuclei are divided into lateral, dorsal and ventral whereas the post commissural portions contain supra commissural, post commissural, central, endopeduncular and intermediate nuclei.

7.3 Preoptic Area

The preoptic area is found in the hypothalamus. It is the functional and structural continuum with the basal forebrain. This area is responsible for thermoregulation. From the thermoreceptors in the skin, hypothalamus and mucous membrane it receives nervous stimulation. The preoptic periventricular recess is surrounded by the preoptic region that is located in between the anterior commissure and optic chiasm. The large neurosecretory cells of the magnocellular preoptic nucleus are further subdivided into magnocellular, gigantocellular and parvocellular parts. It is like an inverted plane, in the longitudinal plane, with a nucleus, rostrally located vertical rod and dorsocaudally extending horizontal rod. The larger dorsocaudal cells constitute the giganto- and magnocellular parts and the smaller rostroventral cells compose the parvocellular parts. The magnocellular and parvocellular preoptic nucleus is the parts of the preoptic area and the parvocellular preoptic nucleus is divided into posterior pars and anterior. The pars and anterior is known to be preoptic parvocellular nucleus, the division of magnocellular is called the preoptic nucleus and posterior pars, periventricular nucleus, in goldfish (*Carassius auratus*),

two salmonid species (Peter et al. 1991) and killifish (*Fundulus heteroclitus*). It is subdivided into the posterior and anterior periventricular nucleus.

7.4 Hypothalamus

Hypothalamus is found in caudal to the preoptic area under the thalamus that contains preoptic neuroendocrine fibres and hypothalamic fibres. It has densely stained and packed cells that surround the infundibular recess. Three main regions of the teleost hypothalamus are paired inferior lobes, periventricular region and tuberal region that is medially located separated by a deep ventral sulcus from the tuberal hypothalamus (Meek and Nieuwenhuys 1998). Hypothalamus is subdivided into ventral, caudal and dorsal according to other authors (Wullimann et al. 1996). Most of the median tuberal portion of the hypothalamus is constituted by caudal and ventral zones.

Periventricular cell population bordered by laterally migrated nuclei is displayed by all three subdivisions. Two laterally migrated populations, the anterior tuberal nucleus and the lateral hypothalamic nucleus, and two periventricular cell populations, the ventral and dorsal, occupy the rostral area of the hypothalamus region (Braford and Northcutt 1983). The hypothalamus of the teleost fish comprises Gomori-negative nucleus lateralis tuberis and Gomori-positive nucleus preopticus. The nucleus lateralis tuberis is situated caudally to the hypothalamus, and further it has been subdivided as pars rostralis, pars medialis, pars lateralis and pars ventrolateralis. In different teleost fishes, the nucleus lateralis tuberis subdivisions vary. The preoptic nucleus consists of pars magnocellularis and pars parvocellularis located on both sides of the preoptic recess. The preopticohypophysial tract is formed by the axons, which is originating from the preoptic nucleus. This tract penetrates through the pituitary gland and terminates in the neuro intermediate lobe.

7.5 Central Neurohormones

Isotocin is the nonapeptide homologous to mammalian oxytocin among bony fishes (Acher 1996). It belongs to the arginine vasopressin-oxytocin family of peptides and is exclusively produced in the preoptic area. Isotocin is produced in the pars and anterior and magnocellular in all fish species. The isotocin neurons cluster collectively to display the contact between the processes in the rainbow trout's magnocellular region. For local neuronal circuitry, the isotocin neurons can use electrical or chemical synapses. It plays an important role particularly in the aspect of reproductive behaviour and in fish reproduction. In rainbow trout (*Oncorhynchus mykiss*) and goldfish, it stimulates the release of ACTH from the pituitary. In the form of a non-covalent complex, the secretory granules store each hormone with its associated neurophysin, before secretion. By exocytosis, this complex is released

into the blood causing spontaneous dissociation. Neuropeptides, when released into the circulatory system, act as hormones, whereas in the CNS, it plays the role of neuromodulators as well as neurotransmitters. The hormones are stored in secretory as a non-covalent complex with its associated neurophysin. This complex is released into the blood by the exocytosis process.

The AVT, one of the main neurohypophysial hormones which is made by nine amino acid peptide (a nonapeptide), that belongs to the arginine vasopressin-oxytocin family of peptide and are homologous to arginine-vasopressin (AVP) and oxytocin in mammals (Acher 1996). It modulates the social behaviours of lower vertebrates (Goodson and Bass 2001). Their primary role is in the endocrine control of the vascular function, saltwater homeostasis (McCormick and Bradshaw 2006) and several physiological processes (Balment et al. 2006).

AVT is synthesized by preoptic neurons that are released into the vascular system by travelling through the preoptico-hypophysial tract via neurohypophysial axon terminals. The magnocellular and parvocellular neurons of the preoptic nucleus exclusively have the AVT-immunoreactive neurons. AVT-immunoreactive neurons in rainbow trout and many other fish species simultaneously project towards the extrahypothalamic and pituitary regions including the ventral telencephalon, mesencephalon and thalamus. In other vertebrates, these multiple projections are not known. Under different physiological challenges, these multiple projections are essential for coordinated control of central and peripheral output through the organization of the electrical activity (Saito et al. 2004). AVT neurons cluster together in the magnocellular of goldfish, eel (*Anguilla* sp.) and rainbow trout by soma-somatic apposition beside the ventricular wall. The function could be communication by changing somatodendritic peptide release or local field potential (Saito et al. 2004).

The MCH is a circulating cyclic heptadecapeptide that mediates the change of colour in the teleost fish (Kawauchi et al. 1983). It was initially purified from chum salmon pituitaries. The changes in the refractive index are mediated by the central accumulation of pigmentary organelles. This allows cryptic camouflage by making the scales appear paler (Kawauchi and Baker 2004). When the fish moves into a pale background, MCH is released into the fish blood in teleost fish. Some positive fibres of the MCH axons penetrate the pars distalis, which regulates the synthesis or release of adenohypophysial hormones (Baker and Bird 2002; Pandolfi et al. 2003). The lateral hypothalamic nucleus or the nucleus lateralis tuberis of fish contains the neuronal cell bodies that produce MCH.

7.6 Hypophysiotropic Peptides

Cholecystokinin (CCK) or gastrin immune reactive neurons belongs to the family of peptides (Chandra and Liddle 2007; Rehfeld et al. 2007) that is produced in the nervous system. This octapeptide of the C-terminus (Trp-Met-Asp-Phe-NH_2) of CCK is the same in chicken, mammals, turtle and frog and is a well-conserved structure during evolution with the substitution of one amino acid in the fish (Peyon

et al. 1998). Longer CCK peptides such as CCK 22, 33 and 58 are identified in the circulation and peripheral tissues (Rehfeld et al. 2007). In goldfish, the CCK is generally distributed in the hindbrain, forebrain and midbrain (Himick and Peter 1994). The inferior hypothalamic lobes and ventrolateral and ventromedial hypothalamus of goldfish have prominent, highly concentrated CCK/gastrin-immunoreactive perikarya and fibre systems (Himick and Peter 1994). In the hypothalamus of the goldfish brain, CCK mRNA that is similar to CCK-immunoreactive is widely expressed (Peyon et al. 1999). A large bundle of CCK/gastrin-immunoreactive fibres that originates in the central hypothalamus enters the hypophysis towards the neurohypophysis. In the preoptic recess proximal pars distalis (PPD), these large bundles of CCK/gastrin-immunoreactive fibres branch into smaller bundles and subsequently single fibres. The immunoreactive fibres separate neuro- from adenohypophysis by terminating on the basal lamina (Batten et al. 1999). The CCK-immunoreactive fibres have a strong relationship with GH release (Batten et al. 1999).

After the administration of amphetamine and cocaine in the rat, the cocaine- and amphetamine-regulated transcript (CART) mRNA expression was elevated in the rat (Douglas et al. 1995). A 116 or 129 amino acid having 27 amino acid signal peptides is the product of CART gene splicing in rat that results in pro-peptide do either long arm (102) or short arm (89) residues (Douglas et al. 1995). Rat long CART (55-102) or rat short CART (42-89) is released as a result of the pro-peptide process that depends on the precursor length (Dylag et al. 2006). Widely distributed CART immunoreactivity localized within the neuroendocrine territories is observed within the brain of catfish. Throughout the PPD, CART-immunoreactive terminals in neurohypophysis and long fibres were detected with a high concentration of thyrotropes and somatotropes. In fishes, four neuropeptides such as a binding protein (CRF-BP), urotensin I (UI) and two G-protein coupled receptors includes the corticotropin-releasing factor (CRF) (Bernier 2006) that plays an important role in the coordination of stress response. It can be modulating the activity of adenohypophysial ACTH and MSH cells; the CRF system regulates the pituitary-adrenal axis along with other physiological process regulation (Flik et al. 2006). In hypophysiotropic regions of the brain that include telencephalon, olfactory bulb, tuberal hypothalamus and preoptic area of zebrafish as well as a white sucker, the CRF is widely expressed (Alderman and Bernier 2007). A major site of CRF production is the preoptic area. Neuronal CRF circuits in the preoptic area differ depending on the species. In the vicinity of the ACTH cells along with of ACTH-releasing factor in the pars distalis of the sea bass is placed the CFR fibres. MSH secretion in teleost fish is stimulated by CRF.

Isolated from the porcine intestine, the 29 amino acid long N-terminal peptide, Galanin, is processed proteolytically from prepropeptide with a galanin message-associated peptide. This neuropeptide exhibits considerable differences in functional coupling and signalling process by binding to three different G-protein coupled receptors. It is usually distributed in the peripheral and CNS and has multiple biological effects including metabolism and feeding, water-intake and osmotic regulation, sleep regulation, nociception and reproduction (Lang et al. 2007). The

pituitary of many vertebrate groups contains galaninergic fibres that can help in the regulation and secretion of the pituitary gland (Anglade et al. 1994; Jadhao and Pinelli 2001). The occurrence of galanin-immunoreactive terminals in the central region of neurohypophysial was demonstrated in ultrastructural studies in fish. Some fibre is interlocked into PPD that ends in basal lamina opposite to GH, TSH, PRL, gonadotropins (GTH) and ACTH cells. ACTH and PRL adenohypophysial cells are directly innervated by galanin fibres. Somatolactin (SL), GH and PRL cells colocalize with the galanin-immunoreactive fibres. Confined galanin receptors are present in the region occupied by the PRL cells in the adenohypophysis particularly in the rostral part (Moons et al. 1991; Batten et al. 1999).

Gastrin-releasing peptide (GRP) is a set of peptides that are illustrated by a highly preserved C-terminus that is vital for many biological processes. It consists of 27-amino acid that is a part of the bombesin (BBS) and neuromedin B family of peptides. The exogenous BBS and endogenous GRP are structurally similar that reflects the functions of each other. Gastrointestinal and CNS is widely distributed with BBS/GRP peptides (McCoy and Avery 1990) which when administrated intraperitoneally or centrally acts as potent anorexigenic substances in fishes and mammals (Flynn 1991). Gut motility and visceral activity in fishes is regulated by BBS-like peptide. BBS-immunoreactive fibres are present in the posterior hypothalamus, tuberal hypothalamus, ventral telencephalon, preoptic area and assumed feeding centre associated areas in goldfish (Himick and Peter 1995).

The GnRH has an amide function at the carboxy terminus and pyro-glutamate modification in the amino terminus. GnRH is a decapeptide that has a cyclic structure and has been characterized into 24 molecular isoforms (Kah et al. 2007). GnRH is grouped into three types, namely, GnRH type I, GnRH type II and GnRH type III (White et al. 1998). GnRH type I is the hypophysiotropic GnRH variants, which includes mGnRH, cfGnRH and pjGnRH and sbGnRH. GnRH type II consists of cGnRH-II, which is localized in the midbrain. GnRH type III includes sGnRH (Lethimonier et al. 2004). The GnRH peptide is distributed from the olfactory bulb, throughout the ventral telencephalon in the forebrain (Pandolfi et al. 2005).

Studies suggest that the forebrain cGnRH-II in goldfish doesn't initiate ovulatory LH surge in comparison with the GnRH mRNA levels with LH levels at the time of ovulation and spawning (Canosa et al. 2008). GnRHs are classified into four types, which includes GnRH1, GnRH2, GnRH3 and GnRH4. The GnRH1, GnRH2 and GnRH3 are present in teleost fish, whereas the GnRH4 represents the lampreys. The structure of GnRH varies across vertebrate species, whereas in GnRH2 and GnRH3 the amino acid sequences are preserved. The GnRH may be considered the hypophysiotropic hormone when synthesized and secreted in the preoptic area of the hypothalamus. GnRH has additional neuroregulatory and neuromodulatory roles and is necessary for reproduction.

In teleosts, synthesis and secretion of LH and FSH are controlled by gonadal steroids. Actions at the level of the hypothalamus and pituitary involve the secretion of LH and FSH by sex steroid feedback regulation. The levels of GnRH and other neuroendocrine factors are affected by the effects on LH and FSH synthesis in the pituitary, testosterone and 17β-oestradiol that control LH synthesis and secretion.

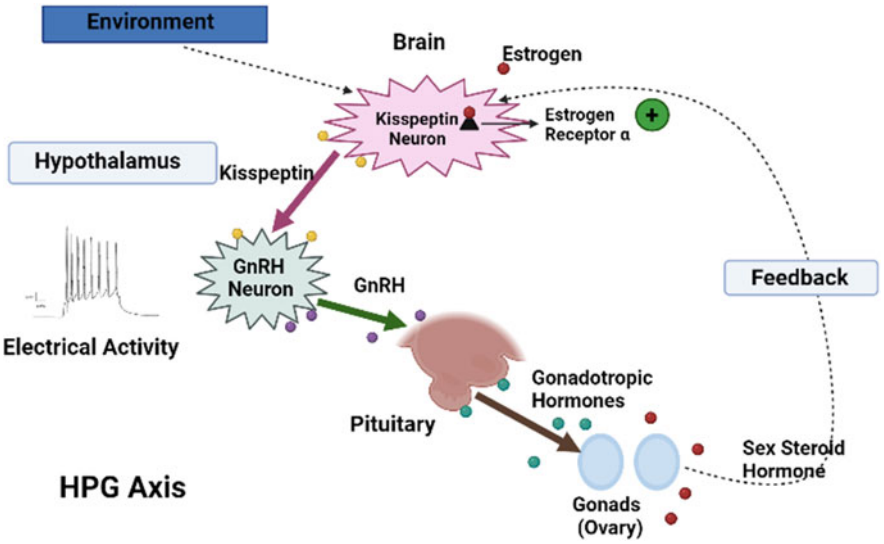

Fig. 7.1 Schematic representation of central regulation of reproduction in fishes. HPG axis: hypothalamic-pituitary-gonadal axis; GnRH; gonadotropin-releasing hormone

Through oestrogen receptors, the effects of testosterone are mediated through the receptor of androgen or result from metabolism to oestrogens. The synthesis and secretion of LH and FSH are implicated by maturation-inducing steroid 17, 20-β-dihydroxy-4-pregnen-3-one, corticosteroid and cortisol. These effects are secondary to the dominant actions of testosterone and 17β-oestradiol (Fig. 7.1).

Pituitary adenyl cyclase-activating polypeptide (PACAP) and growth hormone-releasing peptide (GHRH) have numerous similarities in structure and function. These belong to the family of glucagon/vasoactive intestinal peptide (VIP) and secretin superfamily of peptides (Sherwood et al. 2000). Molecules other than PACAP are formed by tandem exon duplication and gene duplication, whereas PACAP is a conserved, ancestral molecule from which other molecules are subsequently formed (Sherwood et al. 2000). Around 88-97% of the amino acid sequence is identical to PACAP across vertebrates whereas only 32-45% of amino acid sequence identity of GHRH exists between non-mammalian and mammalian vertebrates (Vaudry et al. 2000). GHRH stimulates the GH and it regulates physiological functions such as adaptation to different salinity growth and somatic growth by binding to growth hormone receptor (GHR). GH has diverse effects in vertebrates with multiple targets. It influences metabolism. The behaviour of fish is altered by GH by increasing appetite, aggression, and swimming activity and by reducing anti-predator behaviour. By the action of the peripheral mediator on the fish brain, the swimming activity is increased by GH. A secondary peripheral factor affects appetite. Immune functions that include non-specific defence such as haemolytic, cytotoxic, phagocytic and lysosome activities are enhanced by GH. Ceruloplasmin levels are elevated by a specific defence of immunoglobulin production by GH. In fish

models, gametogenesis, gonadal steroidogenesis and sexual maturation are contributed by the interaction of GH with the gonadotropic axis. The PRL and SL belong to the class I helical cytokines family that forms a family of pituitary hormones along with GH. The pituitary hormones signal via specific receptors, finally activating a similar intracellular signalling cascade. Except in the Chondrichthyes and Agnathans, both hormones have been identified in almost all classes of vertebrates whereas SLs are found only within the Osteichthyes. In the pituitary gland of teleosts, GH, SL and PRL are localized in three distinct areas such as PPD, pars intermedia and rostral pars distalis, respectively.

PRL has seven various functions such as growth and development, reproduction, immunoregulation and protection, endocrinology and metabolism, water and electrolyte balance, brain and behaviour and actions associated with disease conditions. Fish need to have PRL osmoregulatory actions to reside in water with different salinities. PRL, SL and GH interact with specific single transmembrane-domain receptors for exerting their biological effects. Hypothalamic neurohormones regulate the secretion and synthesis of the pituitary hormones. The hypothalamic neurohormones are classified generally into two categories such as releasing and inhibiting hormones. The presence of a highly specific receptor, which belongs to the G-protein coupled receptors (GPCR) on the target cell in the pituitary, determines the action of each hypothalamic neurohormone. GPCR are seven transmembrane segments that bind to either activate or inhibit G proteins.

7.6.1 Functions of Prolactin (PRL)

Water and Electrolyte Balance PRL stimulates the ion retention in teleosts, thereby preventing the water influx to the osmoregulatory organs for freshwater adaptation. Gills, skin, kidney, urinary bladder, gastrointestinal tract and opercular membrane are the principal osmoregulatory organs in fish. Fish acclimated to freshwater has high PRL cell activity than those in seawater. PRLRs expression ubiquitously in the osmoregulatory organs in euryhaline teleosts helps to adapt themselves for the sudden osmotic changes in the surrounding.

Growth and Development Somatotropic activity in tilapia was observed to cause stimulus of hepatic IGF-I mRNA expression and to cause an elevation in [H3] thymidine and [S35]sulphate incorporation into branchial cartilage. In climbing perch liver, PRL inhibited many enzymes involved in fatty acid biosynthesis. In juvenile coho salmon, lipid depletion was observed after PRL treatment. During embryogenesis and after hatching, the PRL gene was detected. Somatotropic action of PRL in teleosts was supported by the widespread tissue distribution of PRLR mRNA and protein in the developing pituitary gland during its embryonic and larval period.

Immunoregulation In several teleost fishes, the immune function is influenced by sex steroids, cortisol and pituitary hormones including PRL. Phagocytosis,

respiratory burst activity, and leukocyte mitogenesis are found to be stimulated by PRL and also increase the plasma IgM titres. Circulating lymphocytes, spleen and head of tilapia contains PRLP mRNA. The level of expression of PRL and PRL receptors were established to the higher concentration of salt in salt water (particularly, in seawater) acclimation fish than in freshwater fish, suggesting that the osmoregulatory action and the immunomodulatory actions of PRL are independent of each other.

Behaviour Administration of PRL in sexually mature male three-spined sticklebacks stimulates the parental fanning behaviour. Mucus is produced in tilapia by inducing the transformation of the skin gland by PRL for the nourishment of the offspring. In seawater eel, drinking water behaviour is affected by the administration of PRL into the fourth ventricle by inhibiting the water intake.

Reproduction Steroidogenesis is stimulated by PRL in the testes and ovary. During sexual maturation in salmonids, the plasma PRL and pituitary mRNA levels are elevated. In fishes, PRL release is stimulated by GnRH and E2 in both in vitro and in vivo models (Weber et al. 1997). In some teleosts, PRLR mRNA was detected in gonads suggesting the role of PRL in reproductive processes in fish.

7.6.2 Functions of Somatolactin (SL)

The SL is involved in adaptations to the background and decreased illumination, smoltification, adaptation to environmental changes, stress responses and control of some physiological aspects of reproduction, calcium and phosphate metabolism regulation, energy metabolism, growth and acid-base balance in fishes (Fig. 7.2). GHR1 expression was found to be higher in the skin consistent with SL functioning in chromophore regulation in rainbow trout and tilapia. SL levels in the plasma are not affected by the background colour in the rainbow trout. Water temperature causes seasonal changes in the SL secretion than to photoperiod. In teleosts, SL play a vital role in body colour regulation by the recognition of a gene, which is responsible for medaka colour interfere (ci) mutant. A significant increase in the number of leukophores and a decreased amount of visible xanthophores were exhibited by the medaka SL-deficient mutant colour interfere. During morphological body colour adaptation to different backgrounds, the SL transcription was dramatically changed showing the involvement of SL in chromatophore development.

Suggesting the metabolic function, tilapia GHR1 and rainbow trout SLR were highly expressed in liver, muscle and fat. Sea bass SL was injected into juvenile gilthead sea bream and found that it decreased the respiratory quotient by increasing the oxygen uptake and carbon dioxide output, but it does not modify the excretion of nitrogen-ammonia and circulating amount of IGF-I. The activity of hepatic acetyl-coenzyme A carboxylase was inhibited by SL, supporting the involvement of SL in the enhancement of lipid metabolism and energy homeostasis. Proopiomelanocortin (POMC)-expressing neurons, endogenous melanocortin antagonist expressing

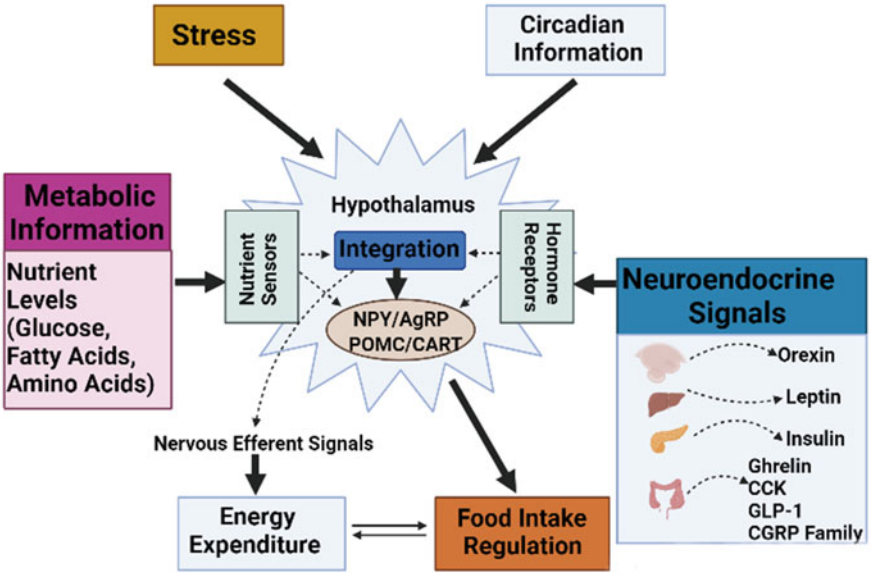

Fig. 7.2 Metabolic pathways of food intake. *NPY* neuropeptide Y, *AgRP* agouti-related protein, *POMC* proopiomelanocortin, *CART* cocaine- and amphetamine-regulated transcript, *CCK* cholecystokinin, *GLP-1* glucagon-like peptide-1, *CGRP* calcitonin gene-related peptide

neurons, agouti-related protein (AgRP) and central melanocortin receptor-expressing downstream targets of these neurons comprise the central melanocortin system. Three main domains containing MSH peptide are exhibited by a complex precursor encoded by the POMC gene. The α-MSH is the N-terminal sequence of ACTH that is found in the second domain (Cerda-Reverter et al. 2003). The pituitary produces POMC and its post-transcriptional modification occurs in a tissue-specific way. ACTH and β-lipoprotein are generated by the proteolytic cleavage by proconvertase 1 (PC1) in the corticotropes in the RPD. α-MSH and β-endorphin are generated by proconvertase 2 (PC2) and proconvertase 3 (PC3) in the melanotropes (Castro and Morrison 1997). A wide range of physiological functions are carried out by the melanocortins ACTH and MSH by binding to G-protein coupled receptor family. At the time of stress, the expression of POMC in magnocellular is upregulated while the function of ACTH in the brain of fish is unknown so far (Metz et al. 2004).

The neuropeptide tyrosine (NPY) family of peptides exhibits carboxy termination (C-terminal) amidation that consists of 36 amino acid. It is classified as three different peptides such as tyrosine-tyrosine peptide (PYY), pancreatic polypeptide (PP) and the NPY. Non-tetrapod vertebrates produce two kinds of peptides (NPY and PYY), whereas tetrapod species has all three peptides (PYY, PP and NPY). The NPY and PYY are synthesized in teleost fish, but PP is not synthesized (Sundstrom et al. 2008). The endocrine secretion of adenohypophysial cells is controlled by the involvement of NPY including GH and LH (Cerda-Reverter et al. 1999) in several

fishes. Gonadotropes (LH-FSH), GH and melanotropes have direct contact with NPY-immunoreactive neurosecretory vesicles (Pontet et al. 1989). Seasonal variations that support the regulation of the reproductive axis are exhibited by the neurohypophysial NPY innervations. NPY-immunoreactive gold particles that carry neurosecretory axons are seen occasionally in association with the GnRH-containing cells in the PPD. An important centre for the sex-steroid signal processing is the NPY neurons present in the central (Sakharkar et al. 2005).

Orexin or hypocretins is produced from a common precursor of the incretin family (de Lecea et al. 1998). They are excitatory neuromodulatory peptides. This exerts its function upon binding with G-protein receptors that showed a variable affinity for hypocretin and different distribution in CNS; the hypocretin 1 and 2 exert their biological functions (Sutcliffe and de Lecea 2000). In goldfish, orexins increase their locomotor activities (Nakamachi et al. 2006). Fasting increases the levels of the mRNA of orexin in the hypothalamus (Nakamachi et al. 2006) whereas hypocretins stimulate the intake of food (Novak et al. 2005). Insomnia-like phenotype is induced in zebrafish by the overexpression of orexin (Prober et al. 2006). Disruption in sleep/wake behaviour is disrupted in zebrafish that lacks a functional orexin receptor (Yokogawa et al. 2007).

Somatostatin (SS), also known as growth hormone inhibiting hormone (GHIH), is a peptide hormone and an effective inhibitor of basal and stimulated GH secretion in the teleost (Canosa et al. 2007). The peptide consists of three different SS precursors that are encoded by a variety of genes in teleost (Canosa et al. 2007) that includes PSS-I, PSS-II and PSS-III. The PSS-I is the most conserved form that has an identical amino acid sequence and codes for SS-14 at the C-terminus. PSS-II encodes for a variable length of SS proteins between 22 and 28 amino acids. PS-III encodes a peptide that bears the amino acid proline in the second place of 14 amino acid C-terminals. Numerous physiological processes are coordinated by SS and somatostatin receptors (SSTR) interaction. It plays an important role in regulating the metabolism and growth by inhibiting the release of hormones such as IGFs and GH in teleost fish. Thyrotropin-releasing hormone (TRH) may also stimulate several pituitary hormones such as GH (Canosa et al. 2007), PRL (Barry and Grau 1986) and MSH (Lamers et al. 1991) in teleost fish. It is the primary hypothalamic releasing factor that may be characterized chemically from the hypothalamus of sheep and pig (Guillemin, 1970). Its role in pituitary TSH release control is well established in tetrapods. In carp, TRH stimulates GH and PRL secretion and MSH in trout and goldfish. The adenohypophysis of the teleost fish produces a glycoprotein, thyrotropin by the action of TSH that secretes TH by stimulating the thyroid gland. TRH influences the thyroid activity and TSH cell activity in fishes.

7.7 Hypothalamic Neurotransmitters

7.7.1 Glutamate and Gamma-Aminobutyric Acid (GABA)

The main excitatory neurotransmitter in the CNS of vertebrate (Trudeau et al. 2000) is considered glutamate that is an important regulator involved in LH, PRL and GH control (Bellinger et al. 2006). Gamma-aminobutyric acid (GABA) is the most important inhibitory neurotransmitter in the CNS with a significant role in pituitary hormone secretion control (Martyniuk et al. 2007). A single enzymatic step that is catabolized by the glutamic acid decarboxylase (GAD) enzyme results in the synthesis of GABA. GAD is used as a marker for GABAergic fibres and cell bodies (Anglade et al. 1999). Telencephalon and olfactory bulbs of goldfish have GAD-immunoreactive cell bodies. LH secretion is regulated by GABA (Trudeau et al. 2000). GABA-containing cell bodies are found in the hypothalamus in tuberal and preoptic regions in the diencephalon.

7.7.2 Dopamine

Dopamine (DA) is one of the major neurotransmitters, which belongs to catecholamines in the CNS of the vertebrate that possesses hypophysiotropic functions. The dopaminergic system in the fish is extensively considered by using antibodies to identify the enzyme system involved in DA synthesis, tyrosine hydroxylase (Smeets and Gonzalez 2000; Rink and Wullimann 2001). In the posterior tuberculum and adjacent hypothalamic regions of fish, dopaminergic neurons are localized in the highest concentration (Ma 2003; Ma and Lopez 2003). In nuclei that are associated closely with ventricle and recesses, a large number of dopamine-containing neurons have been found. Dopaminergic neurons are located in the tuberal hypothalamus, the ventral regions of the preoptic area and olfactory bulbs. The dopaminergic neurons that innervate gonadotropes originating in the rostral region of pars and anterior are responsible for steroid hormones (Kah et al. 1986). D1 and D2 receptors are two DA receptor subtypes that are two distinct membranes that belong to the GPCR superfamily. The D1 receptor mediates the GH release and adenylate cyclase stimulation in the goldfish pituitary, whereas the D2 receptor inhibits PRL release in mammals and inhibits adenylate cyclase activity. In goldfish, there is significant hypertrophy and nuclear enlargement in cells of PRL was induced by the injection of DA agonists. A rise in the quantities of rough endoplasmic reticulum and reduce in the quantities of the secretory granules in PRL cells were induced by the treatment with DA in tilapia.

7.7.3 Serotonin

Serotonin or 5-hydroxytryptamine (5-HT) consists of the monoamine with neurotransmitters DA and NA. This is an indoleamine neurotransmitter that has both neuroendocrine (Trudeau 1997; Canosaet al. 2007) and behavioural functions (Johansson et al. 2004). 5-HT system contains two main localizations in the brain region of the teleost fish such as one anterior and posterior localization. The response of neurotransmitters during gonadal development in yellow snapper was analysed using 5-hydroxy indole acetic acid (5-HIAA) and found that both 5-HIAA and 5-HT were not detectable at any gonadal development in the pituitary. It works as a neuromodulator with multiple functions in fish and other vertebrates. The function of fish reproduction is modulated by serotonin through a variety of pathways including through peripheral (gonads) and central (preoptic-hypothalamic area and pituitary) actions.

7.8 Endocrine Targets of the Hypothalamus and Pituitary

7.8.1 Sex Steroid Production in the Fish Brain

The regulation of reproduction and energy balance is an important role of gonadal steroid hormones. Steroid production in gonads is stimulated by pituitary tropic hormones, GTH. These steroids control the secretion of tropic hormones to adapt their activity to the current physiological situation by feedback onto the neuroendocrine systems. The brain itself is a steroidogenic organ that produces several steroids with their functions less understood. Two enzymes that convert testosterone into dihydrotestosterone and oestradiol are the product of 5-α reductase and the cyp19a1b, P450 aromatase B (A or B), respectively. P450 aromatase B is evidence of steroidogenic enzymes for brain expression in fish. The presence of P450scc is required to cleave the lateral chain of cholesterol to form pregnenolone. There are two key steroidogenic enzymes including cytochrome P450c17 (CYP17) and 3-β-hydroxysteroid dehydrogenase/D4-D5 isomerase (3βHSD) performing further metabolization of pregnenolone. The 3βHSD is involved in dehydrogenation and isomerization of pregnenolone to progesterone. Hydroxylation of C21 steroids (17-α-hydroxylase activity) is caused by CYP17 followed by the cleavage of the two-carbon side chain. The C19 steroids dehydroepiandrosterone or androstenedione are generated. Histological differentiation of gonads is achieved by the steroid biosynthetic capacity in the brain. The asynchronous peak was shown by mRNAs of these genes, indicating the formation of oestradiol locally in the forebrain as well as the midbrain after 120 days of hatching, in the black porgy. In the zebrafish brain, oestrogen production might be associated with neurogenesis. By the action of oestrogen 2-hydroxylase, the oestrogens can be metabolized into catechol-oestrogens. Oestrogen effects on neuroendocrine and behavioural functions are

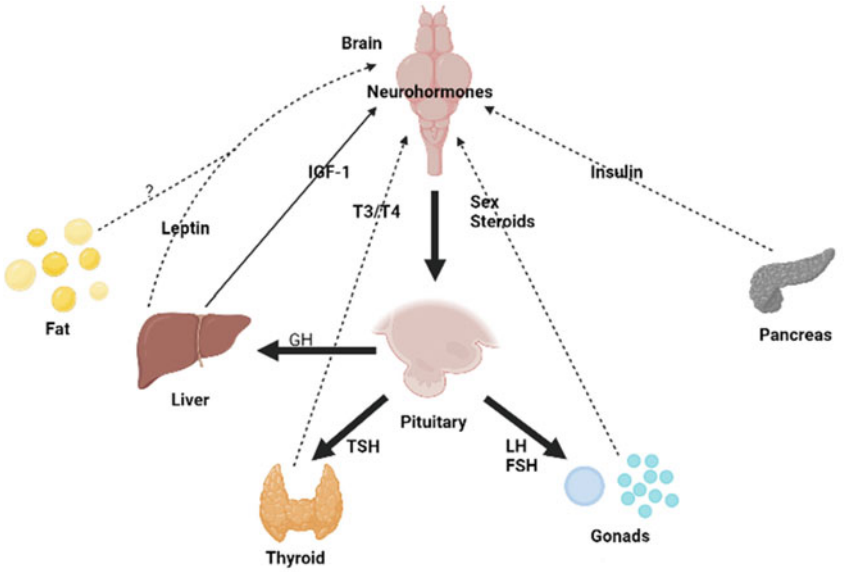

Fig. 7.3 Schematic representation of brain-hormone relationships in fishes. *LH* luteinizing hormone, *FSH* follicle-stimulating hormone, *TSH* thyroid-stimulating hormone, *GH* growth hormone, *IGF-1* insulin-like growth factor-1, *T3* triiodothyronine, *T4* thyroxine

mediated by potentially bifunctional, oxidized 2-hydroxy oestrogen molecules. Tyrosine hydroxylase activity is non-competitively inhibited by catechol-oestrogens through modifying catecholamine metabolism in fishes (Fig. 7.3).

7.8.2 Metabolic Hormones

Sensing of metabolic signals by neuroendocrine circuits that involve neuropeptides, cocaine and amphetamine-regulated transcript, KiSS or GnRH ensures the signal between the reproductive axis and energy status through several neuropeptide hormones. Mandatory signals are required for normal gonadal function and pubertal maturation that is emerged by kisspeptins, which is encoded by the gene named KiSS-1 and its receptor GPR54. Changes in fertility may be linked to disturbed energy balance in fish are explained by the negative feedback inputs on the GnRH systems through the KiSS neurons.

7.8.3 Leptin

Leptin levels have been roughly proportional to fat stores that are produced by the adipose tissue. It stimulates the appetite centre, which is located in the ventromedial nucleus of the hypothalamus to regulate food intake. Leptin works by stimulating α-MSH activity and by inhibiting AgRP and NPY. The brain uses leptin as a parameter to assess the energy levels to proceed with highly demanding reproductive function. In fish, the liver is the primary source of leptin.

7.8.4 Insulin-Like Growth Factor and Insulin

The hormone insulin regulates the glucose homeostasis in the vertebrates that are produced from proinsulin precursor molecule of the pancreas under the action of prohormone convertases. It is also involved in survival factor during early morphogenesis by expressing in the developing brain. The proliferation and cell survival of the developing retina and brain are stimulated by the unprocessed proinsulin. Insulin is secreted from Brockmann bodies in the teleost fish as well as in the pituitary gland and the brain of tilapia but with low concentration. GH stimulates the formation of IGF-I and it binds to specific IGF receptors present especially on bone, liver, muscle, kidney, lungs, skin, brain, cartilage, hippocampus, cerebellum and olfactory bulb. Embryonic growth and development are regulated by IGF-I signalling by promoting the progression of cell survival and cell cycle. GH cells release IGF-I that serves as a mediator of a negative feedback system. The formation and secretion of pituitary hormones are regulated by local IGF-I in a paracrine or autocrine manner. It stimulates the proliferation of endocrine cells and prevents apoptosis. Depending on the reproductive stages, IGF-I affects the sGnRH-induced GTH subunit gene expression differently.

7.8.5 Receptors for Thyroid Hormone

Pleiotropic effects on growth, differentiation, metamorphosis and reproduction are exerted by TH through thyroid hormone receptors (TRs). TH belong to the superfamily of nuclear receptors and there are two major forms as thyroxin and tri-iodothyronine. They are iodinated derivatives of tyrosine. Thyroxin contains four iodine residues whereas tri-iodothyronine, the most potent and the major biological TH, contains only three iodine residues. The feedback of TH to the brain pituitary is due to some of these effects. In fish and amphibians, it plays an important role in metamorphosis and parr-smolt transformation on salmon. In teleost fish, there are two forms of TH, as TRα and TRβ regulate the development, growth and metabolism. Hindbrain patterning is disrupted by the overexpression of TRα1

form during embryogenesis that causes the repression of retinoic acid receptors in hox gene expression control.

7.9 The Neuroendocrinology Regulation of Fluid Intake and Fluid Balance

7.9.1 Mechanism of Fluid Exchange and Balance

A thin respiratory epithelium separates fish body fluids from the surrounding area. The osmolarity range of these environments ranges from a few to 1000 mOsm kg-1. Regulation of their body fluids autonomously of the surrounding area for their survival is necessary. Maintenance of the composition of extracellular fluid and its volume during the continuous process of osmotic gain of water from the dilute environment associated with a stable diffusion loss of major fluid ions, in particular, Na^+ and Cl^- are the major challenges for fish in fish water. For the excretion of water in large volumes of urine, the glomerular kidney filters the blood and carries out tubular reabsorption of ions and other solutes. The reabsorptive ability of the ion by the fish urinary bladder supports this process. Dietary intake and gut absorption support the balance of the ion losses (Fig. 7.4). The ion actively taken up from the environment by the cells rich in mitochondria in the gill leaflets also supplements for balancing ion loss. H^+-ATPase with synergetic action of Na/K-ATPase facilitates the active uptake (Lin et al. 2000).

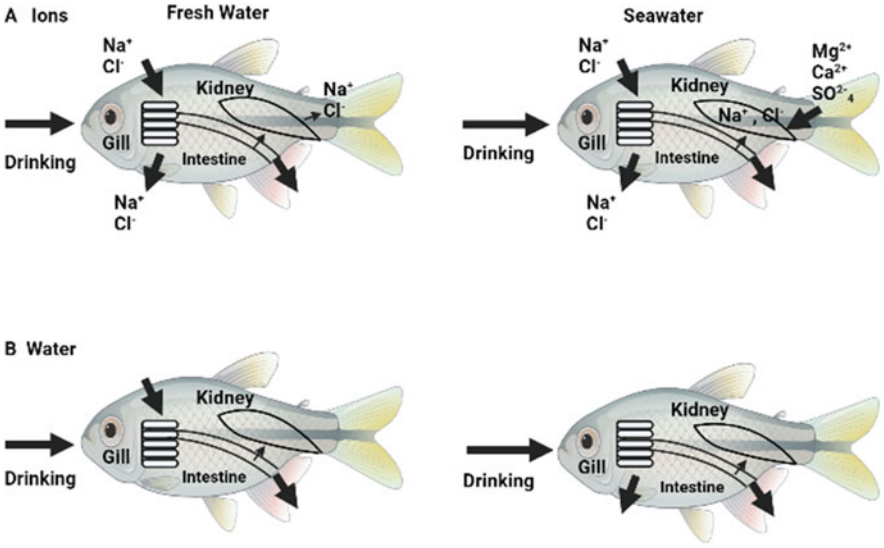

Fig. 7.4 Movement of ions (**a**) and water (**b**) between environment and body in starved teleost fish

7.9.2 Regulation of Fluid Intake

The oral intake of free water, water from the food, water released by the oxidation by cell metabolism of carbohydrates, proteins and lipids are the main sources by which animals gain body fluids. The oral water intake of terrestrial animals and fish differ greatly as fish live in water. To avoid overhydration, the freshwater teleost fish frequently drinks only a little amount of water through the gills by the osmosis process. Water must be ingested orally to compensate for the osmotic loss in marine teleost fish.

7.10 Hormonal Regulation of Drinking in Fish

7.10.1 Hormones That Induce Drinking

Neural mechanisms play an important role in the regulation of drinking habit in the fishes. The dynamic component of the renin-angiotensin system (RAS) is the best known dipsogenic hormone, Angiotensin II (ANG II) and it induces abundant water intake in all vertebrates. In euryhaline species, on moving into hypertonic waters the ANG II increases the drinking habit. In various stenohaline species that are restricted to live in either saline water or freshwater, the ANG II did not induce drinking. The water can passively enter into the oesophagus, and through the coordinated movement of muscles concerned with swallowing, the ANG II induces a burst of drinking. Therefore, in saline water fish, in constant drinking, the ANG II may not be concerned. The infusion of antiserum induces the removal of free ANG II from plasma, but the drinking rate was not suppressed by ANG II in saline water eels. The increased bradykinin in plasma or captopril treatment results in the inhibition of drinking.

Papaverine, a relaxant of the smooth muscles, may activate the endogenous RAS. In flounder, it also increases drinking rates. To induce drinking, increased circulation of ANG II acts on the target cells in the brain that lack the blood-brain barrier as shown in birds and mammals. After "decerebration" that is the removal of the complete forebrain and most of the midbrain, the ANG II was still effective, or rather more effective in the eel. Another circumventricular organ in the hindbrain, the area postrema (AP) that faces the fourth ventricle, is the most possible site of the mechanism of ANG II (Mukuda et al. 2005).

7.10.2 Hormones That Inhibit Drinking

Natriuretic Peptides (NPs) In teleost fish, the Natriuretic peptide family consists of seven members as B-type, four C-type NPs such as CNP1, CNP2, CNP3 and CNP4,

atrial and ventricular NP such as atrial natriuretic peptide (ANP), BNP, and Ventricular NP (VNP). VNP is majorly produced in the heart and C-type NPs are synthesized in the brain, which lacks a C-terminal "tail" sequence extending from the intramolecular ring having common structural characteristics. In the eel, ANP and VNP are potent anti-dipsogenic hormones. The abundant drinking of saline water eels was almost terminated at 3 pmol kg min-1, and at a rate of 0.3–-3 pmol kg min-1, ANP dose-dependently reduced the drinking rate when introduced into the circulation. The infusion takes place at 3 pmol kg min-1, in which the plasma endogenous ANP concentration was increased to the level. CNP was 50 times more potent in drinking inhibition than in elasmobranch with the stimulatory effect of ANG II. In saline water eels, plasma ANG II concentration is decreased by dose-dependent ANP infusion which amplifies its anti-dipsogenic effect.

To survive in the hypotonic saline water environment, it is indispensable for teleost fish to drink saline water. As fish lives in water, overdrinking is a susceptible factor; when they are in seawater it leads to hypernatremia. In less than 1 min in feedback to the elevated Cl^- ion concentration in saline water, vigorous drinking occurs after the transfer of eels from freshwater to saline water. The excessive and acute intake of water stopped in 15 minutes and suppressed drinking was continued at a decreased rate than the constant saline water drinking rate for a few hours. An inhibitory signal, such as stomach distension, is an inhibitory signal formed after the initial robust drinking that causes such transient inhibition, whereas the inhibition time course coincides with a short-term increase in ANP concentration in plasma once after the transfer of saline water. When encountering saline water, ANP likely suppresses excessive drinking to enhance an abrupt increase in Na^+ concentration in plasma and to encourage fish to adapt to saline water. In freshwater and saline water adapted eels, there is no difference in plasma ANP concentration. To maintain plasma Na^+ concentration in saline water eels higher than in freshwater, the excessive drinking in seawater adapted eels are chronically inhibited by ANP, because ANP antiserum introduction to remove the ANP that is circulating resulted in increased plasma Na^+ concentration and cause a surge in drinking.

Ghrelin Ghrelin is a 19–28 amino acid residue long, a linear peptide with fatty acids addition that includes decanoic acid, octanoic acid and so on at the third Thr or Ser residue that has been identified in two species of elasmobranchs and 11 species of teleosts. In the rainbow trout and channel catfish, two different genes have been identified. GH secretion was stimulated when ghrelin was administrated into the periphery.

When ghrelin was injected in the eel into regions such as the brain and periphery, it was found to have potent anti-dipsogenic actions on body fluid regulation. Likewise when ghrelin was injected into the fourth ventricle of saline water eels, ghrelin is even more potent than ANP. Swallowing is inhibited by the action on the AP by ANP. In the ventricular surface, a change in the potential to cross the ependymal layer was observed when ghrelin is acylated with fatty acid. In many vertebrate species including fishes, ghrelin has stimulatory actions on GH production and orexigenic effects. During fasting and energy metabolism, the changes in plasma

ghrelin concentration were measured. In plasma, ghrelin exists in active form which is acylated and the inactive form which is non-acylated. At a rate of 50 fmol $mL^{-}1$, the acylated form of ghrelin circulates in eels. Once after 6 h of the transfer of eels from freshwater to saline water, the concentration increases. The GH/insulin-like growth factor-I (IGF-I) axis is stimulated and the in vitro GH secretion is increased by homologous ghrelin in the tilapia.

Bradykinin Bradykinin is the active linear nonapeptide hormone and final product of the kallikrein-kinin system (KKS) that have strong inflammatory and cardiovascular functions. There are two kallikrein types such as tissue KKS and plasma KKS. The low molecular weight kininogen associates with the tissue kallikrein to secrete kallidin, [Lys0]-bradykinin, whereas the high molecular weight kininogen and plasma kallikrein together act to produce bradykinin.

The RAS and the KKS are closely related because they share ACE for activation and inactivation of the system, respectively. The ACE is also known as kininase II which degrades bradykinin. Bradykinin degradation is inhibited by the treatment of captopril to inhibit ACE. When administered as a bolus or introduced at a rate in a way such that the arterial pressure is unchanged, the homologous [Arg0]- bradykinin acts as a potent anti-dipsogenic hormone in the eel. Plasma ANG II concentration was increased when [Arg0]-bradykinin was injected into the circulation. Bradykinin injection increased the ACE activity that may cause an elevation in plasma ANG II concentration. In anti-dipsogenic effect, [Arg0]-bradykinin is more potent than bradykinin or [Arg0]-des-Arh9-bradykinin (Fig. 7.5).

7.10.3 Other Hormones That Regulate Drinking

Hypertensive substances are anti-dipsogenic and hypotensive substances are dipsogenic. In the eel, β-adrenergic agonist, such as histamine, acetylcholine and isoproterenol, that acts as vasodepressor aredipsogenic, while vasopressor α-adrenergic agonist, such as adrenaline or noradrenaline, oxytocin, AVT, and uropygial extract (probably urotensin II), are all anti-dipsogenic. In saline water adapted eels, the intestinal pentapeptide, a VIP and CCK depressed the drinking. In saline water eels, when injected centrally, serotonin, GABA, AVT, PRL, noradrenaline and VIP obstruct drinking along with ghrelin and ANP, while isoproterenol, acetylcholine, and substance P intensified drinking along with ANG II. When fish migrate to hyperosmotic media, in salmonids and teleosts, the cortisol and GH boost the drinking rate and cortisol and GH are important saline water adapting hormones.

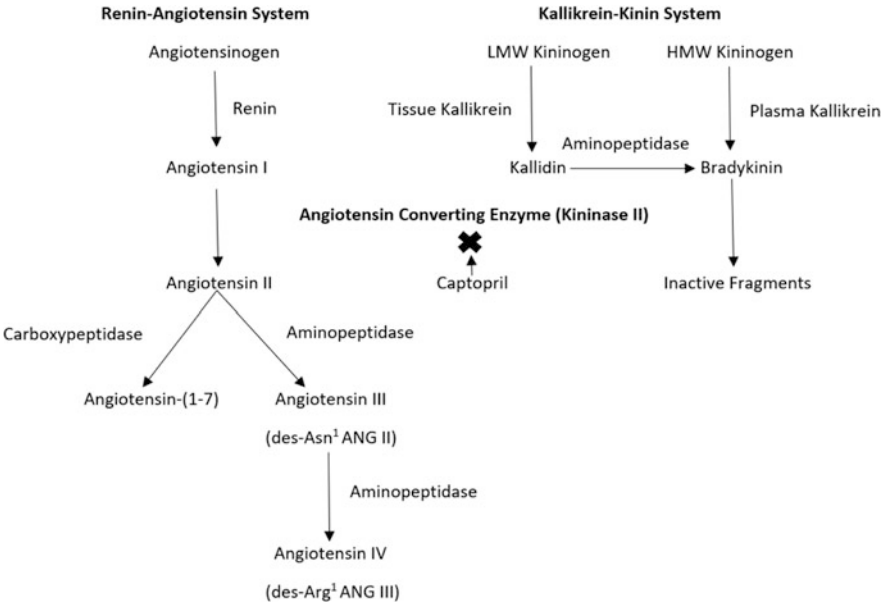

Fig. 7.5 Cascade components of Renin-Angiotensin and Kallikrein-Kinin and its relationship with the ACE. ANG I to ANG II conversion is inhibited by captopril by inhibiting the ACE, but the truncation of bradykinin into its inactive fragments are reduced by the inhibition of this enzyme. *LMW* low molecular weight, *HMW* high molecular weight

7.10.4 Neural Mechanisms of Drinking in Fish

In saline water eels, copious drinking is not influenced by the forebrain removal and the majority of the midbrain. Hindbrain regulates drinking in fish. In eels whose cerebrum is removed, ANG II acts on the hindbrain because the ANG II-induced drinking is observed to be survived. For the act of drinking, the tenth cranial nerve, the vagus nerve plays an important role as a bilateral transverse section of the vagus nerve terminate both induced drinking by ANG-II and saline water-induced drinking.

The different skeletal muscles, third brachial, fourth brachial, oesophageal sphincter, opercular, pharyngeal, the sternohyoid, different skeletal muscles and oesophageal body muscles are involved in swallowing movements that are supplied by glossopharyngeal and/or vagus nerve. The different regions of the glossopharyngeal-vagal motor complex (GVC) which elongate anterior-posteriorly through each side of the medulla oblongata give rise to each muscle. The upper oesophageal sphincter muscle (UES) is composed of skeletal muscle which functions as a gate for ingestion that is compressed by cholinergic control. Catecholamines inhibit the GVC neuronal activity which affects swallowing, indicating adrenergic innervations from the commissural nucleus of AP and/or Cajal. Water is blocked from entering into the oesophagus when boosted UES is constricted

constantly by stimulatory signals through the vagus. The GVC neurons that transmit signals to the UES are inhibited when the adrenergic innervations to the GVC are activated, resulting in UES relaxation followed by water ingestion.

7.10.5 Fluid Balance Regulation

The loss and build-up of ions and water are balanced through dietary uptake and exchange with the surrounding environment; by which the body fluids are regulated in fish. To establish the body fluid osmolality and absolute volume balance of intracellular and extracellular fluid compartments, a close relation between ion balances with body water content is observed. The transporting epithelia of the gill, kidney, rectal gland and gut contributes to the fluid balance.

7.10.5.1 Fluid Balance by Arginine-Vasotocin (AVT)

In all jawed vertebrates, two neurohypophysial hormones homologous to mammalian vasopressin and oxytocin are present. AVP in mammals is replaced by AVT in all non-mammalian species (Acher 1996). AVT is concerned with the regulation of body fluid composition and volume. Rather than a reduction in blood volume, increased osmolality is also a strong stimulant for AVT secretion in the euryhaline flounder, *Platichthys flesus*. To the osmotic challenge as well as long-term adaptation, AVT contributes acute feedback. In the initial days after the fish is transferred between saline water and fresh water, the expression of hypothalamic AVT mRNA surges, plasma AVT levels are raised and pituitary AVT content reduced. In the initial hours after the fish enter into freshwater, the plasma AVT concentration falls, and when fishes are transferred to saline water, the plasma AVT concentration elevates along with the elevated plasma osmolality. Once after 2 days of fish kept in concentrated saline water (130%), the amount of the expression of AVT mRNA in plasma and AVT mRNA in the hypothalamus were notably elevated. In fish, both renal and extra-renal target tissues are involved in the AVT actions that contribute to body fluid balance. Studies in freshwater eels reported an antidiuresis or a clear fall in urine flow alongside a lower, non-pressor dose of AVT while high doses of AVT associated with a pressor response produce a diuresis.

7.10.5.2 Fluid Balance by Renin-Angiotensin System (RAS)

Throughout the vertebrates, osmoregulatory mechanisms are modulated by one of the major endocrine systems, the RAS. Gill that produces a notable amount of converting enzyme and the kidney that produces the hormone renin are involved in the regulation of RAS activity and themselves being the target tissues for the active ANG II. RAS is activated by hypotension or hypovolemia that is usually

caused by salinity transfer or haemorrhage and other challenges that causes hypotension and hypovolemia. Teleost fish acclimatize the movement in between the media of contrastive salinities. The inter-renal product cortisol is essential for long-term acclimatory adjustments, including mitochondria-rich cell functions and gut transport capacity. The level of plasma cortisol and ANG II are parallelly changed when the sea beam was adapted to variable salinities, whereas in flounder, the ANG II introduction elevates the level of plasma cortisol. Captopril, which is a converting enzyme, when administrated, blocks the production of cortisol following freshwater to saline water transfer of eels.

A drop in GFR and antidiuresis is caused by the exposure of fish to dehydrating conditions. During dehydration, a direct renal effect of ANG II and RAS activation cause vasoconstriction of renal microvasculature. When there is a drastic loss in blood volume or a drop in blood pressure, the RAS is considered to contribute to blood pressure. The unique elasmobranch mineralocorticoid, 1-hydroxycorticosterone secretion is stimulated by the involvement of indirect osmoregulatory actions. In elasmobranchs and in teleosts, the presence of macula densa and juxtaglomerular cells, along with RAS is involved in the glomerular filtration rate control.

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