Npy&Pyy in Teleost Food Intake

Subjects: Agriculture, Dairy & Animal Science

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Neuropeptide Y family (NPY) is a potent orexigenic peptide and pancreatic polypeptide family comprising neuropeptide Y (Npy), peptide YYa (Pyya), and peptide YYb (Pyyb), which was previously known as peptide Y (PY), and tetrapod pancreatic polypeptide (PP), but has not been exhaustively documented in fish. Nonetheless, Npy and Pyy to date have been the key focus of countless research studies categorizing their copious characteristics in the body, which, among other things, include the mechanism of feeding behavior, cortical neural activity, heart activity, and the regulation of emotions in teleost. In this review, we focused on the roles of *Npy* and *Pyy* in teleost food intake since feeding is essential in fish to ensure growth and perpetuation, being indispensable in the aquaculture settings where growth is prioritized.Therefore, a better understanding of the roles of these genes in food intake in teleost could help determine their feeding regime, regulation, growth, and development, which will possibly be fundamental in fish culture.

Keywords: neuropeptide Y (Npy) ; peptide YY (Pyy) ; anorexigenic ; orexigenic ; food intake ; teleost fish

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1. Introduction

Fish, the most distinguished group among vertebrates (over 30,000 species) [1], comprising approximately 95% teleost species, are the organisms most attracted for the study of the evolution of appetite-regulating systems in vertebrates [2][3]. This is due to their greater diversity in anatomy, ecology, behavior, and genomics [4][5][6]. Feeding is an important physiological activity in fish, necessary to ensure growth and survival. Food is one of the most authoritative external signals that can arouse fish feeding behavior and growth [7][8]. However, its availability and composition wield a precarious mechanism principally acting on the hormones responsible for their endocrine regulation [9]. Feeding is the outcome of an adjustment between starvation, appetite, and satiation. Starvation is the physiological requirement for food and comprises a solid stimulation to feeding conduct, including searching for food and feeding. Satiation is the physiological and mental sense of “fullness” that happens after eating, while appetite, on the other hand, is the longing to eat, which is ordinarily related to tactile (locate, scent, taste) perceptiveness of food [10].

In fish and other vertebrates, several hormones control feeding, including those produced by the brain and marginal organs [11][12]. It is known to be an intricate process that is vital to stimulate the survival of animals and the capacity to stay affected by elements, such as light, temperature, reproduction, and even the sort of food consumed. Food intake is governed by a fundamental and outlying nourishing scheme allied by a grid of peptides and hormones that control the sensitivity to eating and satiation [13][14][15].

Appetite and body weight control are multifaceted processes that involve extensive interactions between the brain and peripheral signals in all vertebrates. The brain (hypothalamus) produces key factors that either stimulate (orexigenic) or inhibit (anorexigenic) food intake in vertebrates (teleost) [12]. Knowledge about neuroendocrine control on food intake and regulation, including neuropeptide Y (*Npy*) and peptide YY (*Pyy*), explicitly concerning their roles, has significantly improved nowadays. Current studies have indicated that these peptides have impacts on the feeding behavior in vertebrates (teleost) [12][14][16][17][18] either as an orexigenic or anorexigenic factor.

Neuropeptide Y family (NPY) is a potent orexigenic peptide and pancreatic polypeptide family comprising neuropeptide Y (*Npy*), peptide YYa (Pyya), and peptide YYb (Pyyb), which was previously called peptide Y (PY), and tetrapod pancreatic polypeptide (PP) [19][20][21]. Both *Npy* and *Pyy* (Pyya and Pyyb) contain highly conserved amino acid sequences [19], whereas PP has evolved more rapidly but has fully not been recognized in fish [22][23][24]. Nonetheless, two peptides (*Npy* and *Pyy*) to date have been a key focus of countless research articles, categorizing their copious characteristics in the body, which, among other things, include the mechanism of feeding behavior (one playing the role of food inducer, while the other is a food inhibiter), cortical neural activity, heart activity, and the regulation of emotions [24][25][26][27][28][29][30][31][32].

Among all the roles that the neuropeptide Y family genes play in fish, this review focuses significantly on their functions in feeding. Feeding is essential to ensure growth and perpetuation in living organisms, including fish. Therefore, a better understanding of the roles of these genes and their effects on food intake in teleost could help determine their feeding regime, regulation, growth, and development, which will possibly be fundamental in fish culture. Herein, we examined the current studies on the roles of *Npy* and *Pyy* in the regulation of food intake in teleost, as well as information gaps and future research directions.

2. Fundamental Characteristics of Npy and Pyy in Teleost

Npy, a peptide with 36 amino acid (AA) residues that was first isolated from porcine brain [33], is one of the most highly conserved neuropeptides in vertebrates [34][35]. It is a 36-amino-acid peptide produced from a 96-amino-acid pre-pro-peptide containing a 28-amino-acid N-terminal signal peptide and a 32-amino-acid C-terminal extension. Two classes of *Npy* (Npya and Npyb) have been discovered in some teleosts. However, teleosts such as the goldfish (*Carassius auratus*) and zebrafish (*Danio rerio*) have only Npya [20][36]. *Npy* is known to be chiefly secreted by the hypothalamus' neurosecretory cells and is secreted in response to hunger [19][37]. Its primary function as a signaling factor is to regulate a variety of biological processes such as food intake, daily fixed cycle, neuroendocrine functions, and glucose homeostasis [38].

Pyy, conversely, belongs to a potent orexigenic peptide and pancreatic polypeptide (PP) family [19][20][39]. It is secreted from pancreatic endocrine cells (PP cells). *Pyy* has two endogenous forms: the full-length Pyy1–36 and the abridged form Pyy3–36 [40][41][42]. Both Pyy1–36 and Pyy3–36 can subdue appetite and food intake and delay gastric emptying [43]. *Pyy*, as an anorexigenic signal in teleost, is known to be a brain–gut peptide with its principal role as a satiety hint [27][29][44][45][46][47]. It has been approximated to be 70% homologous to *Npy* and PP; the configuration of amino acids for this peptide is also highly well-maintained within species [48]. It is secreted from the endocrine cells of the ileum and colon and functions by inhibiting *Npy* neurons in fish [49][50].

3. Expression of Npy and Pyy in Teleost

The Neuropeptide Y gene (*Npy*) has shown its expression in many tissues of several teleosts. It expresses itself in the central nervous system, intestine, liver, spleen, skeletal muscle, and fat tissue of several fish species, such as zebrafish (*Danio rerio*), goldfish (*Carassius auratus*), Atlantic salmon (*Salmo salar*), catfish (*Ictalurus punctatus*), and tilapia (*Oreochromis sp.*) [51][52][53]. It has also been detected in some teleost eyes but with little information [54][55].

Peptide YY mRNA (*Pyy)* also has shown expression in the kidney, gills, and within the brain—specifically the hypothalamus and pituitary—in some teleosts, including Atlantic salmon (*Salmo salar*), zebrafish (*Danio rerio*), goldfish (*Carassius auratus*), and Japanese eel (*Anguilla japonica*) [29][51][56][57]. It has also been identified in the gastrointestinal tract (GIT) of teleosts at the apparent highest levels in the stomach, pyloric caeca, foregut, and liver, and at lower levels in the hindgut [28][29][44][46][47][58].

In addition to this, our unpublished research study on the spotted scat (*Scatophagus argus*) revealed the expression of the *Npy* and *Pyy* genes in the central nervous system (brain) and some peripheral tissues (Assan et al., unpublished data).

4. Receptors of the Neuropeptide Y Family in Teleost

There is wide-ranging information about NPY and their receptors and neuro-endocrinological functions in non-mammalian vertebrates [22][23][24]. NPY is more intricate in teleost fish as compared to mammals. The NPY receptors of fish are articulated in the brain but can also be sited in marginal tissues, including the eye and intestine [59][60][61]. It is projected that the development of NPY peptides comprises the replication of a distinct congenital gene in an early vertebrate before the origination of vertebrates that possess jaws, ensuing in *Npy* and *Pyy* [62].

To date, seven types of receptors of NPY, known as the "Y receptors", have been identified: Y1, Y2, Y4, Y5, Y7, Y6, and Y8, of which five are present in mammals (Y1, Y2, Y4, Y5, and Y6) [20][63][64]. All of these belong to the G-protein-coupled receptor; they have been categorized into two groups: the Y1-Y4-Y6-Y8 and the Y2-Y7 groups (Matsuda et al., 2012). These receptors are chiefly expressed in neural tissue and receptors in instinctual organs (such as the kidney and intestine), respectively [63][64][65]. NPY receptors vary in their ligand affinity profiles, of which Y1, Y2, and Y5 have a high affinity for *Npy* [66][67]. According to Dumont et al. [68], *Pyy* commits to all of the Y receptors, but the utmost affinity is seen

for the Y2 receptor. Out of these seven NPY receptors, Y1 and Y2 have been consistently associated with the regulation of appetite with *Npy* [66][69].

According to Salaneck et al. [70] and Sundström et al. [20], Y1, Y2, Y4 (Ya), Y7, Y8a (Yc), and Y8b (Yb) have been traced in teleosts. They are pancreatic kinfolk polypeptides activated and characterized by NPY. The Y1 and Y5 receptors have been acknowledged to be intricate in the statute of orexins in mammals and fish [71]. The Y1 receptor-signaling pathway of NPY is known to stimulate food intake in teleost fish such as goldfish (*Carassius auratus*) and zebrafish (*Danio rerio*) [24][72][73]. The Y1 and Y2 receptor genes are comprehensively expressed in several expanses of the brain, but the expression of Y4 and Y5 receptor genes are constrained to precise loci involved in the directive of appetite, circadian rhythm, and apprehension [74]. There is a greater need for additional research that would help clarify the efficient rapport between the receptors of NPY, particularly that of fish.

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