Regulators of Fish Reproduction: Dopamine and Melatonin

S. Selvaraj
Department of Aquaculture
Dr. MGR Fisheries College and Research Institute, Ponneri, Tamil Nadu, India

***Abstract*—** Fish exhibit seasonal reproduction and several neuroendocrine peptides modulate this event. Particularly, dopamine and melatonin produced in neuroendocrine tissues like pineal gland, brain and pituitary gland play an important role in controlling reproductive cycle. Dopamine that acts through dopamine receptors show drastic changes when fish undergo stress in captivity, and it has severe influence on progression of gametogenesis. Melatonin acting through melatonin receptors peak during night time in teleost fish and show seasonal fluctuation in response to changing photoperiod. These changes taking place in captive fish modulates gametogenesis by influencing different elements of reproductive brain-pituitary-gonad (BPG) axis.

Keywords: Dopamine, Melatonin, brain-pituitary-gonad (BPG)

I. Introduction

Dopamine is a catecholaminergic neurotransmitter that is widely expressed in the fish brain and plays an important role in central functions and behaviours, such as cognition, perception, emotion, motivation, reward, memory and decision making (Sibley et al., 1993; Jaber et al., 1996). The central dopaminergic system is comprised of four major pathways: the mesostriatial, mesolimbic, mesocortical and tuberoinfular systems, and tuberoinfundibular pathway, projects from the hypothalamus to the hypophysis where it is involved in neuroendocrine regulation (Missale et al., 1998; Messias et al., 2016).

Dopaminergic signalling is mediated by five distinct receptors that are organized in two separate clades based on their interaction with the enzyme adenylyl cyclase: D1-like receptors that include the D1 and D5 receptors; D2-like receptors including the D2, D3, and D4 receptors. D1-like receptors activate adenylyl cyclase while the D2-like receptors inhibits it. All of the receptors exhibit the typical seven-transmembrane domain α-helical G-protein coupled receptors structure (Sibley et al., 1993; Jaber et al., 1996). The central dopaminergic system, acting through dopamine-D2-type receptors forms an important inhibitory component of the regulation of reproductive brain-pituitary-gonad axis (Yu and Peter, 1990).

Pineal organ appears as an end vesicle attached to the roof of diencephalon by a slender stalk (Falcon et al., 2007, 2009). The three main cell types that make the pineal epithelium are pinealocytes or photoreceptors, glial or interstial or supporting, and ganglion type cells. Melatonin is produced at night by the photoreceptors and released into the cerebrospinal fluid and blood (Falcon et al., 2007, 2010). The melatonin biosynthesis in pineal photoreceptor cells involves four enzymatic stages: tryptophan hydroxylase catalyzes the conversion of tryptophan into 5-hydroxytryptophan; 5-hydroxytryptophan is decarboxylated by the aromatic aminoacid decarboxylase to produce serotonin; the arylalkylamine *N*-acetyltransferase converts serotonin to *N*-acetylserotonin; *N*-acetylserotonin is *O*-methylated by the action of the hydroxyindole-*O*-methyltransferase to produce melatonin (Klein *et al.*, 1997; Falcón *et al*., 2007). Pineal melatonin acts through G-protein coupled receptors (Emet et al., 2016).

II. Dopamine as Regulator of Fish Reproduction

Majority of dopamine neurons are localized to the diencephalon as opposed to the midbrain regions. Several studies in teleosts demonstrated that dopamine neurons responsible for the inhibitory control of reproduction originate in a specific nucleus of the preoptic area, and project directly to the region of the pituitary where gonadotrophic cells are localized (Dufour et al., 2010). The hypothalamus in fishes exerts its regulation on the release of the gonadotrophins via several neurohormones such as gonadotropin-releasing hormone (GnRH), dopamine, γ aminobutyric acid, kisspeptin, pituitary adenylate cyclase activating peptide, norepinephrine, neuropeptide Y, Insulin-like growth factor I, norepinephrine, leptin and ghrelin (Levavi-Sivan et al., 2010). In addition, gonadal sex steroids and peptides exert their effects on the gonadotropins either directly or via the hypothalamus. GnRH is considered as the major hypothalamic factor controlling pituitary gonadotrophins; however, its stimulatory action opposed by the potent inhibitory actions of dopamine in teleosts. This dual neuroendocrine control of reproduction by GnRH and dopamine has been demonstrated in several teleosts.

Both *in vivo* and *in vitro* experiments, as validated by molecular and biochemical studies indicate that the dopamine D2-like, but not D1-like, receptors inhibit gonadotropin secretion directly in the pituitary. This led to the development of methods to induce maturation and spawning in aquaculture, using a combined treatment with a GnRH agonist and a dopamine-D2 receptor antagonist such as domperidone (LINPE technique). Dopaminergic inhibition is especially significant in cyprinid fish. Hence, spawning induction in cyprinid fish in aquaculture requires the use of dopamine D2 receptor antagonists (pimozide, domperidone or metoclopramide) to promote a significant surge of LH, in response to GnRH that will lead to successful ovulation (Yaron, 1995; Levavi-Sivan et al., 2006, 2010).

Sex steroids have been shown to regulate dopaminergic systems in several teleost species, affecting both dopamine synthesis and dopamine receptor expression. In females, sex steroids play a major role in the regulation of dopaminergic activity by increasing the inhibitory tone during vitellogenesis, as demonstarted in silurids, salmonids, and percomorphs and resulting in ovarian follicular atresia of captive maintained fish broodstock (Senthilkumaran and Joy, 1995; Saligaut et al., 1999; Yaron et al., 2003).

III. Melatonin as Regulator of Fish Reproduction

Several experimental studies demonstrated that the pineal gland and/or melatonin control seasonal reproduction in finfish (Bromage et al., 2001; Bayarri et al., 2004; Francis et

al., 2004; Maitra et al., 2005). The effects of pinealectomy on gonadal activity shown to vary with photoperiod and/or season and pinealectomy promoted a daily cycle in serum gonadotropin levels in the goldfish, kept under short photoperiod (De Vlamming and Jo Vodicnik, 1978; Hontela and Peter, 1980). In an Indian catfish, pinealectomy accelerated ovarian recrudescence and vitellogenin synthesis, under short photoperiod (Garg, 1988). Pinealectomy in Asian catfish increased the glandular level of the thyroid hormones and stimulated vitellogenesis during preparatory and prespawning periods with no significant effect during spawning and post-spawning periods (Nayak and Singh, 1987; Ghosh and Nath, 2005). In Atlantic salmon, pinealectomy abolished the natural nocturnal rise in melatonin and did not influence the incidence or timing of early sexual maturation in the male parr (Mayer, 2000). Several other functional studies in other fish clearly indicate that pineal gland entrains photoperiodic information and regulate seasonal reproduction in finfish (Cowan et al., 2017).

Effects of melatonin on seasonal reproduction in fish depend on the photoperiod, duration of exposure to melatonin, and the site of melatonin synthesis. In carps, it is well demonstrated that melatonin plays a major role in the seasonal gonadal development and maturation. Chattoraj and his team for the first time demonstrated that prior incubation of rohu oocytes with melatonin accelerates the action of maturation inducing hormone on final oocyte maturation. Subsequently, Chattoraj et al. (2008) reported that serotonin is involved in modulating the action of melatonin on the final oocyte maturation in carp. Spotted snakehead exposed to melatonin water daily for 24 h had more vitellogenic follicles and fewer atretic follicles, in comparison to untreated control (Renuka and Joshi, 2010). Exogenous melatonin suppressed specific growth rate, gonadosomatic index, ovarian cellular activity, protein and lipid biosynthesis, in Nile tilapia (Singh et al., 2012). Also, Shellfish are also known to use the photoperiod as a temporal cue to initiate reproduction. Reproductive cycles of adult crustaceans are significantly influenced by moulting process (Adiyodi and Adiyodi, 1970; Nagaraju, 2011).

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