Introducing the Amphibious Mudskipper Goby as a Unique Model to Evaluate Neuro/Endocrine Regulation of Behaviors Mediated by Buccal Sensation and Corticosteroids

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Abstract: Some fish have acquired the ability to breathe air, but these fish can no longer flush their gills effectively when out of water. Hence, they have developed characteristic means for defense against external stressors, including thirst (osmolarity/ions) and toxicity. Amphibious fish, extant air-breathing fish emerged from water, may serve as models to examine physiological responses to these stressors. Some of these fish, including mudskipper gobies such as Periophthalmodon schlosseri, Boleophthalmus boddarti and our Periophthalmus modestus, display distinct adaptational behaviors to these factors compared with fully aquatic fish. In this review, we introduce the mudskipper goby as a unique model to study the behaviors and the neuro/endocrine mechanisms of behavioral responses to the stressors. Our studies have shown that a local sensation of thirst in the buccal cavity—this being induced by dipsogenic hormones—motivates these fish to move to water through a forebrain response. The corticosteroid system, which is responsive to various stressors, also stimulates migration, possibly via the receptors in the brain. We suggest that such fish are an important model to deepen insights into the stress-related neuro/endocrine-behavioral effects.

Keywords: stressors; thirst; angiotensin II; corticosteroids; amphibious fish

1. Introduction

Water–land transition necessitates many important physiological and biochemical adaptations to the terrestrial environment. In particular, fish that routinely emerge from water, such as mudskippers (class Actinopterygii, order Perciformes, family Gobiidae; e.g., Periophthalmodon schlosseri, Boleophthalmus boddarti and our Periophthalmus modestus) commonly found in estuaries of the Indo-Pacific and evolutionarily many other fish taxa [1], cannot effectively flush their body surfaces (primarily gills) due to a lack of water. Hence, these fishes are amphibious and have developed ways to ameliorate terrestrial stress (e.g., endogenous ammonia) during emersion. They are equipped with strategies on land, such as modified nitrogen metabolism (Figure 1), and amphibious behavior to defend against ammonia toxicity, whereas most aquatic animals excrete ammonia in water. Therefore, these fish, as well as ammonia-tolerant nonamphibious fish such as the Gulf toadfish and a gobiid fish (Mugilogobius abei) [2–6], may serve as unique models to examine the effects of stressors such as ammonia, but their characteristic adaptational behaviors and neuro/endocrine mechanisms have only been minimally studied [7–13].
Figure 1. Glutamine synthesis adopted by amphibious fish to defend against ammonia toxicity. Level of glutamine synthetase mRNA in mudskippers exposed for 1 day ($n = 6$). Bars represent the mean ± SEM. * $p < 0.05$ vs control. This strategy involves the detoxification of ammonia to glutamine, whereas the glutamine synthetase activity is generally undetectable or low in nonureosmotic fishes [14,15].

*Periophthalmus modestus* spend a significant amount (70–90%) of time out of water (0–40 parts per thousand) [16,17], as a means of predator avoidance and to forage (Supplementary Video S1), which appears to be ecologically diverse across the families [1]. They have evolved numerous physiological and behavioral traits of locomotion, gas exchange, nitrogen excretion, ionoregulation and osmoregulation associated with amphibious lives [7,8,18–22]. For example, they can store water in the buccal and opercular cavities when they are on land, because their opercula are closed without ventilation of the gills [17]. The aquatic preference and rolling behavior on wet land are also notable for moistening the dorsal skin [23]. The emersion is very easy to score as an individual is either in or out of water, which makes the mudskipper an interesting model to examine the effects of external stressors such as ammonia and dehydration (Figure 2), and may provide novel avenues for investigations of the neuro/endocrine systems, since some of these have recently been analyzed [16].
Figure 2. Schematic of the experimental setup used to examine amphibious behavior in mudskippers. The hashed area represents land and is easily accessible to the mudskipper placed in the water area. Treatment with stressors and hormones allows the observation of the period of time in water and the frequency of migration. Plastic mesh on the land area facilitates drainage of water. Water in the tank is constantly aerated [17,24–26].

In this review, we focus on two topics relevant to the neuro/endocrine regulations of stress-related behavioral changes. First, we discuss the behavior motivated by dipsogenic hormones via a buccal local sensation of thirst and external factors such as eating. Then, we introduce the roles of corticosteroids that are responsive to various external stressors [27,28] in the amphibious behavior. We hope that this review will create further interest in the neuro/endocrine regulation of this behavior not only among fish endocrinologists, but also for those working on other animals.

2. Migration to Water Motivated by Local Sensation in the Buccal/Opercular Cavity

On land, mudskippers continually search for water (Supplementary Video S1), in much the same way as tetrapods [16]. Indeed, we recently demonstrated that artificial removal (e.g., by piercing holes in the opercula) of buccal water stored on land by the mudskipper resulted in a strong behavioral preference for a water environment, suggesting the presence of thirst (defined as a conscious sensation of a need for water and a desire to drink, which is followed by a search for water in terrestrial animals such as mammals [29,30]) in fish [17]. Furthermore, administration of the most potent dipsogenic hormone known in many vertebrate species, angiotensin II [31–33], resulted in a swallowing action of water held in the buccal cavity of the mudskipper that was regulated by the area postrema (AP) in the hindbrain, as in aquatic fish (Figure 3a,b; [17,24]). Migration of the mudskipper to water following the loss of buccal water by swallowing is indicative of the seeking behavior exhibited by tetrapods in a local thirst (dry mouth) response [16,17]. This behavior is considered to be an anticipatory thirst in mice and is regulated before changes in blood chemistry and/or humoral factors such as angiotensin II [34–36].
Buccal water is also used for sucking food when mudskippers eat on land [37,38]. Water volume accumulation is essential for the intraoral transport of food on land, and eating appears to be a potent stimulus for buccal thirst. Indeed, ad libitum eating “naturally” induces immediate migration to water for refilling the buccal/opercular cavity with water (our unpublished data). Many mammalian species similarly drink during meals [34,39,40].
Figure 3. A theoretical model illustrating regulatory mechanisms of drinking behavior in amphibious mudskippers, aquatic fish and terrestrial mammals. The area postrema (AP), organum vasculosum of the lamina terminalis (OVLT) and subfornical organ (SFO) are collectively referred to as the circumventricular organs (CVOs) in the brain. The AP and OVLT have been identified in fish and tetrapods, but the SFO has only been identified in tetrapods. (a) Comparatively simple mechanisms in
mudskippers. Sensory regions in the buccal cavity of mudskippers monitor the contents (e.g., ion content, water and toxins). Changes in the chemistry of the buccal contents initiates behavioral responses for drinking. Information is processed by afferent vagus/glossopharyngeal nerves, possibly leading to the forebrain initiating migratory behavior to water. The specific region in the forebrain has yet to be identified, but vasotocin nerves in the parvocellular preoptic nucleus (PP) may be involved in the neural basis. Increases in circulatory levels of angiotensin II elicit AP neurons to fire and induce a swallowing response mediated by the medulla oblongata. Loss of buccal water subsequently evokes water-seeking behavioral responses in the forebrain, whereas systemic angiotensin II is perceived by forebrain neurons in mice and motivates a move to water. (b) In aquatic fish, the forebrain is not involved in drinking behaviors. Increases in circulatory levels of angiotensin II elicit AP neurons to fire and induce a swallowing response mediated by the medulla oblongata. (c) Complex mechanisms in mice. Signals from buccal receptors act through neuronal connections with the forebrain center (e.g., SFO) via visceral afferent neurons in spinal or vagal pathways. These signals are relayed to the thalamus, paraventricular (PVN) and supraoptic (SON) nuclei to promote expression of vasopressin, a mammalian homolog of vasotocin. With the lack of a blood–brain barrier, circulating angiotensin II is perceived by neurons in the SFO and OVLT. The sensation of thirst and subsequent behavioral responses likely involve the activation of the cortex, and these signals may be transmitted to neurons in the medial region of the thalamus. The role of the vagal afferents in regulating behavior relevant to local sensation appears to be conserved among vertebrates. Dashed lines, dashed arrow, and red arrow indicate possible neural signaling, established neural signaling, and hormonal actions, respectively.

In fully aquatic fish, the anadromous or diadromous migratory behavior induced by local/peripheral sensation is challenging to study; however, work in eels has shown that increases in the buccal Cl\(^-\) concentration rather than osmoreception or baroreception stimulate a swallowing reflex [41]. This “chloride response” was presumed to prevent the dehydrating effect of life in seawater for hypo-osmotic regulating marine teleosts and was also described as an anticipatory drinking response [41], similar to that described for tetrapods and mudskippers. Additionally, in a basal vertebrate, the river lamprey (*Lampetra fluviatilis*), transfer from seawater to freshwater rapidly decreased the drinking rate without a change in plasma osmolality [42], suggesting that the mechanism of anticipatory drinking by local sensation may be widely distributed among vertebrates. A complex network of the endocrine system also responds to the fluctuation of internal solute concentrations [43]. The integration of hormonal and anticipatory information has recently been shown in mammals [30], but remains to be examined in fish. Recent suggestions of osmosensitive mechanisms in the gill [44,45], as well as in the brain and pituitary [46–48], may lead to understanding of the comprehensive mechanisms.

Similarly to osmoregulatory/feeding purposes, these behavioral responses may also protect body surfaces such as gills by flushing with water from external stressors such as ammonia and toxins [23]. Buccal local stimuli are thought to be sensed by afferent fibers of the vagus and/or glossopharyngeal nerves in fish [49]. The input signals for thirst and food consumption are relayed rapidly to neurons in the sensory circumventricular organ (CVO) of the forebrain in mammals (Figure 3c; [35,50–52]). The mammalian CVO also monitors blood factors including angiotensin II [31,51,53–60] and orchestrates a motivation for water by engaging the medial thalamic–cortex network [30,61,62]. Given this complex mechanism in mammals, the mudskipper with its simpler brain architecture might be a useful model to investigate neuronal mechanisms of systemic hormone actions separately from local sensation.

### 3. Corticosteroid-Regulated Amphibious Behavior

In vertebrates, corticosteroids released from adrenal or analogous tissue can result in a glucocorticoid or mineralocorticoid response. Tetrapods have evolved responses to two unique hormones: cortisol or corticosterone (species-dependent) primarily regulates energy balance and acts through glucocorticoid receptors (GRs), whereas aldosterone primarily regulates mineral balance and acts through the mineralocorticoid receptor (MR) [63]. In teleosts, aldosterone is unlikely to be present or to act through either receptor [64]; however, circulating 11-deoxycorticoesterone (DOC)
has been shown to stimulate a MR, but not a GR [64–67], whereas cortisol appears to act through the GR and MR [64,66–71]. In addition to their role in regulating metabolic balance, including the important osmoregulatory role of GRs, GRs and MRs are involved in regulating responses to stress in the brain [28,72–74]. For example, the mRNA expression patterns of teleost MR are relatively modest in organs associated with ionoregulation, such as the gills, but are considerably higher in the brain and eyes of most teleosts examined to date (e.g., [67,75–77]). This suggests that MR signaling may be involved in facilitating behavioral responses to external stimuli.

Mudskippers migrate into water when treated with DOC and cortisol [25]. Cortisol may act as an endogenous ligand for brain MRs as well as GRs to stimulate this migration naturally, because plasma cortisol, rather than DOC, is increased in dehydrated mudskippers under terrestrial conditions (Figure 4; [22]) and the cortisol-stimulated behavior is not completely inhibited by a specific GR blocker, RU-486. Thus, the aquatic preference of mudskippers, induced by cortisol-brain MR/GR signaling, appears to be a stress response. There are limited data available on such corticosterone responses in amphibians [78].

![Figure 4](image-url)

**Figure 4.** Hypothalamus–pituitary–interrenal axis activation by stress and behavioral modification in fish. The magnocellular preoptic nucleus (PM) and parvocellular preoptic nucleus (PP) of the hypothalamus are stimulated to express corticotropin-releasing hormone (CRH) and possibly vasotocin/isotocin following exposure to stressful stimuli. Binding of CRH causes release of adenalcorticotropic hormone (ACTH) from the pituitary gland, which then induces release of cortisol from the interrenal gland. Cortisol binds to GR/MRs in the commissural and subcommissural nuclei of the telencephalon (V; putative fish homologue to the mammalian amygdala) and the ventral parts of the lateral zone of the dorsal telencephalon (DI; putative fish homologue of the mammalian hippocampus) to modulate behaviors such as the aquatic preference of mudskippers. In the central nervous system, cortisol also functions at the level of the pituitary gland and the PP/PM. Dashed lines indicate possible signaling.

In addition to being key components of the stress axis, GR is expressed ubiquitously and MR is expressed in several important areas (Table 1) in the fish central nervous system, with likely correspondence to regions of expression in other vertebrates [4,66,77,79–83]. MR is highly expressed in telencephalic regions, which include the ventral parts of the lateral zone of the dorsal telencephalon (putative fish homologue of the mammalian hippocampus [84]), and commissural and subcommissural nuclei of the telencephalon (putative fish homologue of the mammalian amygdala [84]). In the diencephalon, several hypothalamic nuclei and the glomerulus complex of the thalamus exhibit MR expression, as do the mesencephalic tegmentum and granular layer of the optic tectum. MR is
expressed markedly in some regions of the cerebellum and eyes. These findings suggest that GRs/MRs are critical for many physiological and behavioral responses, such as the regulation of salt intake, mood, appetite, exploratory behavior and visual responses [77,85–87]. Indeed, zebrafish and medaka models with constitutive GR or MR knockout fail to integrate these brain behavior and visual responses as well as regulate the stress axis, although they can grow and osmoregulate [77,80,88–97]. The simple aquatic preference of mudskippers may also reflect these behaviors. Furthermore, most GR/MR-expressing PM and PP nuclei produce vasotocin and its paralogue, isotocin [82], and the cortisol-GR system regulates the expressions of vasotocin and isotocin [98]. These neuropeptides also promote migration to water in mudskippers, similarly to angiotensin II [26]. In the mammalian brain, neurons in CVOs such as the SFO and AP also express MR [99]. “Crosstalk” among these systems in the brain may be affected by stress. Regardless, the dual-label brain regions for corticosteroid receptors and Fos in mudskippers after the stress-induced aquatic preference suggest their targets.

**Table 1.** Distribution of mineralocorticoid receptor (MR) mRNA in the teleost fish brain.

| Brain Region                          | MR       |
|---------------------------------------|----------|
| Stress axis                           | ++       |
| Forebrain pallial area                 | ++       |
| Corticotrophin-releasing hormone cells in preoptic nucleus | +       |
| Adrenocorticotrophic hormone-containing cells in pituitary pars distalis | +       |
| Ventral parts of the lateral zone of dorsal telencephalon (presumed hippocampus) | ++       |
| Commissural and subcommissural nuclei of telencephalon (presumed amygdala) | ++       |
| Several hypothalamic nuclei           | ~ ++     |
| Glomerulus complex of thalamus        | +        |
| Mesencephalic tegmentum               | ++       |
| Granular layer of optic tectum        | +++      |
| Cerebellum                            | +++      |

For details, see Sakamoto et al. [99] and Sakamoto and Sakamoto [80].

### 4. Summary and Perspectives

Extant amphibious fish may offer an opportunity to detect stress-related behavior and to examine its neuro/endocrine regulation. These fish can emerge from water and make an excursion onto land, as a means of predator avoidance and to forage. During this emersion, they would have difficulties flushing their gills effectively. Hence, they are equipped with behavioral strategies to defend against terrestrial stressors such as dehydration and ammonia. Assessment of the distinct amphibious behavior of mudskippers as simple methods for detection of stress-related behavioral outcomes is possible compared with fully aquatic fish, and some neuroendocrine regulations of this behaviors have been described here. These studies have demonstrated the potential effects on behavior regulated by dipsogenic hormones via local sensation in the buccal cavity and by the corticosteroid system. Further analyses of natriuretic peptides and gastrin-releasing peptide in mudskippers may elucidate the itch sensation by the dry dorsal skin moistened by aquatic preference or rolling behavior on wet land, and the unknown evolution of the itch sensation in vertebrates. These peptides are currently known as key molecules to transmit the itch sensation to the central nervous system in rodents [100–104]. The factors such as stressors driving many amphibious fish to water have been reviewed, and these factors can also be triggered in cyprinodontiforms, including in model species (e.g., *Kryptolebias marmoratus*) [105,106]. The mode of action can be assessed through neurohistological methods of labeling of Fos and neuro/endocrine transmitter systems in the less complicated fish brain [16], since these species have sequenced genomes [7,107–109].
Supplementary Materials: Supplementary materials can be found at http://www.mdpi.com/1422-0067/21/18/6748/s1. Supplementary Video S1 (Periophthalmus modestus: Amphibious behavior).

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References

1. Ord, T.J.; Cooke, G.M. Repeated evolution of amphibious behavior in fish and its implications for the colonisation of novel environments. *Evolution* 2016, 70, 1747–1759. [CrossRef] [PubMed]
2. Barimo, J.F.; Steele, S.L.; Wright, P.A.; Walsh, P.J. Dogmas and controversies in the handling of nitrogenous wastes: Ureotely and ammonia tolerance in early life stages of the gulf toadfish, *Opsanus Beta*. *J. Exp. Biol.* 2004, 207, 2011–2020. [CrossRef] [PubMed]
3. Ip, A.Y.; Chew, S.F. Ammonia production, excretion, toxicity, and defense in fish: A review. *Front. Physiol.* 2010, 1, 134. [CrossRef] [PubMed]
4. Wilkie, M.P. Ammonia excretion and urea handling by fish gills: Present understanding and future research challenges. *J. Exp. Zool.* 2002, 293, 284–301. [CrossRef] [PubMed]
5. Iwata, K.; Kajimura, M.; Sakamoto, T. Functional ureogenesis in the gobid fish *Mugilogobius abei*. *J. Exp. Biol.* 2000, 203, 3703–3715.
6. Ip, Y.K.; Chew, S.F.; Wilson, J.M.; Randall, D.J. Defences against ammonia toxicity in tropical air-breathing fishes exposed to high concentrations of environmental ammonia: A review. *J. Comp. Physiol. B* 2004, 174, 565–575. [CrossRef]
7. You, X.; Sun, M.; Li, J.; Bian, C.; Chen, J.; Yi, Y.; Yu, H.; Shi, Q. Mudskippers and Their Genetic Adaptations to an Amphibious Lifestyle. *Animals* 2018, 8, 24. [CrossRef]
8. Ip, Y.K.; Chew, S.F. Air-breathing and excretory nitrogen metabolism in fishes. *Acta. Histochem.* 2018, 120, 680–690. [CrossRef]
9. Sayer, M.D.J. Adaptations of amphibious fish for surviving life out of water. *Fish Fish.* 2005, 6, 186–211. [CrossRef]
10. Rossi, G.S.; Tunnah, L.; Martin, K.E.; Turko, A.J.; Taylor, D.S.; Currie, S.; Wright, P.A. Mangrove Fishes Rely on Emersion Behavior and Physiological Tolerance to Persist in Sulfidic Environments. *Physiol. Biochem. Zool.* 2019, 92, 316–325. [CrossRef]
11. Cochrane, P.V.; Rossi, G.S.; Tunnah, L.; Jonz, M.G.; Wright, P.A. Hydrogen sulphide toxicity and the importance of amphibious behaviour in a mangrove fish inhabiting sulphide-rich habitats. *J. Comp. Physiol. B* 2019, 189, 223–235. [CrossRef] [PubMed]
12. Livingston, M.D.; Bhargav, V.V.; Turko, A.J.; Wilson, J.M.; Wright, P.A. Widespread use of emersion and cutaneous ammonia excretion in Aplocheiloid killifishes. *Proc. Biol. Sci.* 2018, 285, 20181496. [CrossRef] [PubMed]
13. Blewett, T.A.; Simon, R.A.; Turko, A.J.; Wright, P.A. Copper alters hypoxia sensitivity and the behavioural emersion response in the amphibious fish *Kryptolebias Marmoratus*. *Aquat. Toxicol.* 2017, 189, 25–30. [CrossRef] [PubMed]
14. Randall, D.; Wood, C.; Perry, S.; Bergman, H.; Maloiy, G.; Mommsen, T.; Wright, P. Urea excretion as a strategy for survival in a fish living in a very alkaline environment. *Nature* 1989, 337, 165–166. [CrossRef] [PubMed]
15. Chew, S.F.; Ip, Y.K. Excretory nitrogen metabolism and defence against ammonia toxicity in air-breathing fishes. *J. Fish Biol.* 2014, 84, 603–638. [CrossRef]
16. Katayama, Y.; Sakamoto, T.; Takanami, K.; Takei, Y. The amphibious mudskipper: A unique model bridging the gap of central actions of osmoregulatory hormones between terrestrial and aquatic vertebrates. *Front. Physiol.* 2018, 9. [CrossRef]
17. Katayama, Y.; Sakamoto, T.; Saito, K.; Tsuchimochi, H.; Kaiya, H.; Watanabe, T.; Pearson, J.T.; Takei, Y. Drinking by amphibious fish: Convergent evolution of thirst mechanisms during vertebrate terrestrialization. *Sci. Rep. UK* 2018, 8, 625. [CrossRef]
18. Clayton, D.A. Mudskippers. *Oceanogr. Mar. Biol.* 1993, 31, 507–577.
19. Graham, J.B. *Air-Breathing Fishes: Evolution, Diversity, and Adaptation*; Academic Press: Cambridge, MA, USA, 1997.
20. Sakamoto, T.; Amano, M.; Hyodo, S.; Moriyama, S.; Takahashi, A.; Kawauchi, H.; Ando, M. Expression of prolactin-releasing peptide and prolactin in the euryhaline mudskippers (*Periophthalmus modestus*): Prolactin-releasing peptide as a primary regulator of prolactin. *J. Mol. Endocrinol.* 2005, 34, 825–834. [CrossRef]
21. Brunt, E.M.; Turko, A.J.; Scott, G.R.; Wright, P.A. Amphibious fish jump better on land after acclimation to a terrestrial environment. *J. Exp. Biol.* 2016, 219, 3204–3207. [CrossRef]
22. Sakamoto, T.; Yasunaga, H.; Yokota, S.; Ando, M. Differential display of skin mRNAs regulated under varying environmental conditions in a mudskipper. *J. Comp. Physiol. B* 2002, 172, 447–453. [CrossRef] [PubMed]
23. Ip, Y.K.; Chew, S.F.; Tang, P.C. Evaporation and the turning behavior of the mudskipper, *Boleophthalmus boddarti*. *Zool. Sci.* 1991, 8, 621–623.
24. Katayama, Y.; Takei, Y.; Kusakabe, M.; Sakamoto, T. Hormonal regulation of thirst in the amphibious ray-finned fish suggests the requirement for terrestrialization during evolution. *Sci. Rep.* 2019, 9, 16347. [CrossRef]
25. Sakamoto, T.; Mori, C.; Minami, S.; Takahashi, H.; Abe, T.; Ojima, D.; Ogoshi, M.; Sakamoto, H. Corticosteroids stimulate the amphibious behavior in mudskippers: Potential role of mineralocorticoid receptors in teleost fish. *Physiol. Behav.* 2011, 104, 923–928. [CrossRef]
26. Sakamoto, T.; Nishiyama, Y.; Ikeda, A.; Takahashi, H.; Hyodo, S.; Kagawa, N.; Sakamoto, H. Neurohypophysial Hormones Regulate Amphibious Behaviour in the Mudskipper Goby. *PLoS ONE* 2015, 10, e0134605. [CrossRef] [PubMed]
27. Pankhurst, N.W. The endocrinology of stress in fish: An environmental perspective. *Gen. Comp. Endocrinol.* 2011, 170, 265–275. [CrossRef] [PubMed]
28. Marketon, J.I.; Sternberg, E.M. The glucocorticoid receptor: A revisited target for toxins. *Toxins (Basel)* 2010, 2, 1357–1380. [CrossRef]
29. Denton, D.; Shade, R.; Zamarippa, F.; Egan, G.; Blair-West, J.; McKinley, M.; Lancaster, J.; Fox, P. Neuroimaging of genesis and satiation of thirst and an interoceptor-driven theory of origins of primary consciousness. *Proc. Natl. Acad. Sci. USA* 1999, 96, 5304–5309. [CrossRef]
30. Gizowski, C.; Bourque, C.W. The neural basis of homeostatic and anticipatory thirst. *Nat. Rev. Nephrol.* 2018, 14, 11–25. [CrossRef]
31. Fitzsimons, J.T. Angiotensin, thirst, and sodium appetite. *Physiol. Rev.* 1998, 78, 583–686. [CrossRef]
32. Takei, Y. Comparative physiology of body fluid regulation in vertebrates with special reference to thirst regulation. *Jpn. J. Physiol.* 2000, 50, 171–186. [CrossRef] [PubMed]
33. McKinley, M.J.; Johnson, A.K. The physiological regulation of thirst and fluid intake. *Physiology* 2004, 19, 1–6. [CrossRef] [PubMed]
34. Berridge, K.C. Motivation concepts in behavioral neuroscience. *Physiol. Behav.* 2004, 81, 179–209. [CrossRef] [PubMed]
35. Zimmerman, C.A.; Lin, Y.-C.; Leib, D.E.; Guo, L.; Huey, E.L.; Daly, G.E.; Chen, Y.; Knight, Z.A. Thirst neurons anticipate the homeostatic consequences of eating and drinking. *Nature* 2016, 537, 680–684. [CrossRef]
36. Zimmerman, C.A.; Leib, D.E.; Knight, Z.A. Neural circuits underlying thirst and fluid homeostasis. *Nat. Rev. Neurosci.* 2017, 18, 459–469. [CrossRef] [PubMed]
37. Michel, K.B.; Heiss, E.; Aerts, P.; Van Wassenbergh, S. A fish that uses its hydrodynamic tongue to feed on land. *Proc. R. Soc. Lond. B Biol. Sci.* 2015, 282, 20150057. [CrossRef]
38. Heiss, E.; Aerts, P.; Van Wassenbergh, S. Aquatic–terrestrial transitions of feeding systems in vertebrates: A mechanical perspective. *J. Exp. Biol.* 2018, 221, jeb154427. [CrossRef]
39. Fitzsimons, J.; Simons, B.J. The effect on drinking in the rat of intravenous infusion of angiotensin, given alone or in combination with other stimuli of thirst. *J. Physiol.* 1969, 203, 45–57. [CrossRef]
40. Oatley, K.; Toates, F. The passage of food through the gut of rats and its uptake of fluid. *Psychon. Sci.* 1969, 16, 225–226. [CrossRef]
41. Hirano, T. Some factors regulating water intake by the eel, *Anguilla japonica*. *J. Exp. Biol.* 1974, 61, 737–747.
42. Rankin, J. Drinking in hagfishes and lampreys. *Symp. Soc. Exp. Biol.* 2002, 54, 1–17.
43. Takei, Y.; Hiroi, J.; Takahashi, H.; Sakamoto, T. Diverse mechanisms for body fluid regulation in teleost fishes. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2014, 307, R778–R792. [CrossRef] [PubMed]

44. Inokuchi, M.; Breves, J.P.; Moriyama, S.; Watanabe, S.; Kaneko, T.; Lerner, D.T.; Grau, E.G.; Seale, A.P. Prolactin 177, prolactin 188, and extracellular osmolality independently regulate the gene expression of ion transport effectors in gill of Mozambique tilapia. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2015, 309, R1251–R1263. [CrossRef] [PubMed]

45. Kültz, D. Physiological mechanisms used by fish to cope with salinity stress. *J. Exp. Biol.* 2015, 218, 1907–1914. [CrossRef] [PubMed]

46. Liu, S.-T.; Chou, M.-Y.; Wu, L.-C.; Horng, J.-L.; Lin, L.-Y. Transient receptor potential vanilloid 4 modulates ion balance through the isotocin pathway in zebrafish (*Danio rerio*). *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2020, 318, R751–R759. [CrossRef] [PubMed]

47. Seale, A.; Watanabe, S.; Grau, E. Osmoreception: Perspectives on signal transduction and environmental modulation. *Gen. Comp. Endocrinol.* 2012, 176, 354–360. [CrossRef]

48. Katayama, Y.; Wong, M.K.-S.; Kusakabe, M.; Fujio, M.; Takahashi, N.; Yaguchi, M.; Tsukada, T. Seawater transfer down-regulates C-type natriuretic peptide-3 expression in prolactin-producing cells of Japanese eel: Negative correlation with plasma chloride concentration. *Mol. Cell. Endocrinol.* 2020, 507, 110780. [CrossRef]

49. Mayer-Gostan, N.; Hirano, T. The e...
67. Sturm, A.; Bury, N.; Dengreville, L.; Fagart, J.; Flouriot, G.; Rafestin-Oblin, M.; Prunet, P. 11-deoxycorticosterone is a potent agonist of the rainbow trout (Oncorhynchus mykiss) mineralocorticoid receptor. *Endocrinology* 2005, 146, 47–55. [CrossRef] [PubMed]

68. Baker, M.E.; Katsu, Y. 30 YEARS OF THE MINERALOCORTICOID RECEPTOR: Evolution of the mineralocorticoid receptor: Sequence, structure and function. *J. Endocrinol.* 2017, 234, T1–T16. [CrossRef] [PubMed]

69. Baker, M.E.; Funder, J.W.; Kattoula, S.R. Evolution of hormone selectivity in glucocorticoid and mineralocorticoid receptors. *J. Steroid Biochem. Mol. Biol.* 2013, 137, 57–70. [CrossRef]

70. Baker, M.E.; Katsu, Y. Evolution of the Mineralocorticoid Receptor. *Vitam. Horm.* 2019, 109, 17–36. [CrossRef]

71. Baker, M.E.; Chandsawangbhuwana, C.; Olikainen, N. Structural analysis of the evolution of steroid specificity in the mineralocorticoid and glucocorticoid receptors. *BMC Evol. Biol.* 2007, 7, 24. [CrossRef]

72. Gjerstad, J.K.; Lightman, S.L.; Spiga, F. Role of glucocorticoid negative feedback in the regulation of HPA axis pulsatility. *Stress* 2018, 21, 403–416. [CrossRef]

73. Myers, B.; McKlveen, J.M.; Herman, J.P. Glucocorticoid actions on synapses, circuits, and behavior: Implications for the energetics of stress. *Front. Neuroendocrinol.* 2014, 35, 180–196. [CrossRef]

74. Takahashi, H.; Sakamoto, T. The role of ‘mineralocorticoids’ in teleost fish: Relative importance of glucocorticoid signaling in the osmoregulation and ‘central’actions of mineralocorticoid receptor. *Gen. Comp. Endocrinol.* 2013, 181, 223–228. [CrossRef]

75. Arterbery, A.S.; Deitcher, D.L.; Bass, A.H. Corticosteroid receptor expression in a teleost fish that displays alternative male reproductive tactics. *Gen. Comp. Endocrinol.* 2010, 165, 83–90. [CrossRef] [PubMed]

76. Greenwood, A.K.; Butler, P.C.; White, R.B.; DeMarco, U.; Pearce, D.; Fernald, R.D. Multiple corticosteroid receptors in a teleost fish: Distinct sequences, expression patterns, and transcriptional activities. *Endocrinology* 2003, 144, 4226–4236. [CrossRef]

77. Sakamoto, T.; Yoshiki, M.; Takahashi, H.; Yoshida, M.; Ogino, Y.; Ikeuchi, T.; Nakamachi, T.; Konno, N.; Matsuda, K.; Sakamoto, H. Principal function of mineralocorticoid signaling suggested by constitutive knockout of the mineralocorticoid receptor in medaka fish. *Sci. Rep.* 2016, 6, 37991. [CrossRef] [PubMed]

78. Cockrem, J.F. Individual variation in glucocorticoid stress responses in animals. *Gen. Comp. Endocrinol.* 2013, 181, 45–58. [CrossRef] [PubMed]

79. Kikuchi, Y.; Hosono, K.; Yamashita, J.; Kawabata, Y.; Okubo, K. Glucocorticoid receptor exhibits sexually dimorphic expression in the medaka brain. *Gen. Comp. Endocrinol.* 2015, 223, 47–53. [CrossRef]

80. Sakamoto, T.; Sakamoto, H. ‘Central’ Actions of Corticosteroid Signaling Suggested by Constitutive Knockout of Corticosteroid Receptors in Small Fish. *Nutrients* 2019, 11, E611. [CrossRef]

81. Kolber, B.J.; Wieczorek, L.; Muglia, L.J. Hypothalamic-pituitary-adrenal axis dysregulation and behavioral analysis of mouse mutants with altered glucocorticoid or mineralocorticoid receptor function. *Stress* 2008, 11, 321–338. [CrossRef] [PubMed]

82. Teitsma, C.A.; Anglade, I.; Toutirais, G.; Muñoz-cueto, J.a.; Saligaut, D.; Ducouret, B.; Kah, O. Immunohistochemical localization of glucocorticoid receptors in the forebrain of the rainbow trout (Oncorhynchus mykiss). *J. Comp. Neurol.* 1998, 401, 395–410. [CrossRef]

83. Kolber, B.J.; Muglia, L.J. Defining brain region-specific glucocorticoid action during stress by conditional gene disruption in mice. *Brain Res.* 2009, 1293, 85–90. [CrossRef]

84. Wood, C.M.; McDonald, M.D.; Sundin, L.; Laurent, P.; Walsh, P.J. Pulsatile urea excretion in the gulf toadfish: Mechanisms and controls. *Comp. Biochem. Physiol. B Biochem. Mol. Biol.* 2003, 136, 667–684. [CrossRef]

85. Geerling, J.C.; Loewy, A.D. Aldosterone in the brain. *Am. J. Physiol. Renal. Physiol.* 2009, 297, F559–F576. [CrossRef]

86. Kawata, M.; Nishi, M.; Matsuda, K.; Sakamoto, H.; Kaku, N.; Masugi-Tokita, M.; Fujikawa, K.; Hirahara-Wada, Y.; Takanami, K.; Mori, H. Steroid receptor signalling in the brain—lessons learned from molecular imaging. *J. Neuroendocrinol.* 2008, 20, 673–676. [CrossRef] [PubMed]

87. Rozeboom, A.M.; Akil, H.; Seasholtz, A.F. Mineralocorticoid receptor overexpression in forebrain decreases anxiety-like behavior and alters the stress response in mice. *Proc. Natl. Acad. Sci. USA* 2007, 104, 4688–4693. [CrossRef] [PubMed]

88. Ziv, L.; Muto, A.; Schoonheim, P.J.; Meijting, S.H.; Strasser, D.; Ingraham, H.A.; Schaaf, M.J.; Yamamoto, K.R.; Baier, H. An affective disorder in zebrafish with mutation of the glucocorticoid receptor. *Mol. Psychiatry* 2013, 18, 681. [CrossRef] [PubMed]
89. Sakamoto, T.; Hyodo, S.; Takagi, W. A possible principal function of corticosteroid signaling that is conserved in vertebrate evolution: Lessons from receptor-knockout small fish. *J. Steroid Biochem. Mol. Biol.* 2018, 184, 57–61. [CrossRef]

90. Faught, E.; Vijayan, M.M. Loss of the glucocorticoid receptor in zebrafish improves muscle glucose availability and increases growth. *Am. J. Physiol. Endocrinol. Metab.* 2018, 316, E1093–E1104. [CrossRef]

91. Faught, E.; Vijayan, M.M. The mineralocorticoid receptor is essential for stress axis regulation in zebrafish larvae. *Sci. Rep.* 2018, 8, 18081. [CrossRef] [PubMed]

92. Chatzopoulou, A.; Heijmans, J.P.; Burgerhout, E.; Oskam, N.; Spanik, H.P.; Meijer, A.H.; Schaaf, M.J. Glucocorticoid-Induced Attenuation of the Inflammatory Response in Zebrafish. *Endocrinology* 2016, 157, 2772–2784. [CrossRef]

93. Filosa, A.; Barker, A.J.; Dal Maschio, M.; Baier, H. Feeding State Modulates Behavioral Choice and Processing of Prey Stimuli in the Zebrafish Tectum. *Neuron* 2016, 90, 596–608. [CrossRef]

94. Mosser, E.A.; Chiu, C.N.; Tamai, T.K.; Hirota, T.; Li, S.N.; Wang, A.; Singh, C.; Giovanni, A.; Kay, S.A.; et al. Identification of pathways that regulate circadian rhythms using a larval zebrafish small molecule screen. *Sci. Rep. UK* 2019, 9, 12405. [CrossRef]

95. Sireeni, J.; Bakker, N.; Jaikumar, G.; Obdam, D.; Slabbe Koorn, H.; Tudorache, C.; Schaaf, M. Profound effects of glucocorticoid resistance on anxiety-related behavior in zebrafish adults but not in larvae. *Gen. Comp. Endocrinol.* 2020, 292, 113461. [CrossRef] [PubMed]

96. Morbiato, E.; Frigato, E.; Dinarello, A.; Maradonna, F.; Facchinello, N.; Argenton, F.; Carnevali, O.; Dalla Valle, L.; Bertolucci, C. Feeding Entrainment of the Zebrafish Circadian Clock Is Regulated by the Glucocorticoid Receptor. *Cells (Basel)* 2019, 8, 1342. [CrossRef] [PubMed]

97. Lee, H.B.; Schwab, T.L.; Sigafoos, A.N.; Gauerke, J.L.; Krug, R.G., 2nd; Serres, M.R.; Jacobs, D.C.; Cotter, R.P.; Das, B.; Petersen, M.O.; et al. Novel zebrafish behavioral assay to identify modifiers of the rapid, nongenomic stress response. *Genes Brain Behav.* 2019, 18, e12549. [CrossRef]

98. Kalamarz-Kubiak, H.; Kleszczynska, A.; Kulczykowska, E. Cortisol stimulates arginine vasotocin and isotocin release from the hypothalamo-pituitary complex of round goby (*Neogobius melanostomus*): Probable mechanisms of action. *J. Exp. Zool. Part A Ecol. Genet. Physiol.* 2015, 323, 616–626. [CrossRef]

99. Coirini, H.; Marusici, E.T.; De Nicola, A.F.; Rainbow, T.C.; McEwen, B.S. Identification of mineralocorticoid binding sites in rat brain by competition studies and density gradient centrifugation. *Neuroendocrinology* 1983, 37, 354–360. [CrossRef] [PubMed]

100. Kiguchi, N.; Sukhtankar, D.D.; Ding, H.; Tanaka, K.-i.; Kishioka, S.; Peters, C.M.; Ko, M.-C. Spinal functions of B-type natriuretic peptide, gastrin-releasing peptide, and their cognate receptors for regulating itch in mice. *J. Pharmacol. Exp. Ther.* 2016, 356, 596–603. [CrossRef]

101. Liu, X.-Y.; Wan, L.; Huo, F.-Q.; Barry, D.M.; Li, H.; Zhao, Z.-Q.; Chen, Z.-F. B-type natriuretic peptide is neither itch-specific nor functions upstream of the GRP-GRPR signaling pathway. *Mol. Pain* 2014, 10, 1. [CrossRef]

102. Mishra, S.K.; Hoon, M.A. The cells and circuitry for itch responses in mice. *Science* 2013, 340, 968–971. [CrossRef]

103. Sun, Y.-G.; Chen, Z.-F. A gastrin-releasing peptide receptor mediates the itch sensation in the spinal cord. *Nature* 2007, 448, 700–703. [CrossRef]

104. Lozano-Vilano, M.L.; De La Maza-Benignos, M. Diversity and status of Mexican killifishes. *J. Fish Biol.* 2017, 90, 3–38. [CrossRef]

105. Turko, A.J.; Wright, P.A. Evolution, ecology and physiology of amphibious killifishes (*Cyprinodontiformes*). *J. Fish Biol.* 2015, 87, 815–835. [CrossRef] [PubMed]

106. Kim, B.M.; Lee, B.Y.; Lee, J.H.; Rhee, J.S.; Lee, J.S. Conservation of Hox gene clusters in the self-fertilizing fish *Kryptolebias marmoratus* (*Cyprinodontiformes; Rivulidae*). *J. Fish Biol.* 2016, 88, 1249–1256. [CrossRef]
108. Lins, L.S.F.; Trojahn, S.; Sockell, A.; Yee, M.C.; Tatarenkov, A.; Bustamante, C.D.; Earley, R.L.; Kelley, J.L. Whole-genome sequencing reveals the extent of heterozygosity in a preferentially self-fertilizing hermaphroditic vertebrate. Genome 2018, 61, 241–247. [CrossRef] [PubMed]

109. Rhee, J.S.; Lee, J.S. Whole genome data for omics-based research on the self-fertilizing fish Kryptolebias marmoratus. Mar. Pollut. Bull. 2014, 85, 532–541. [CrossRef] [PubMed]

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