
Temperature increase and its effects on fish stress physiology in the context of global warming

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Abstract :

The capacity of fishes to cope with environmental variation is considered to be a main determinant of their fitness and is partly determined by their stress physiology. By 2100, global ocean temperature is expected to rise by 1–4°C, with potential consequences for stress physiology. Global warming is affecting animal populations worldwide, through chronic temperature increases and an increase in the frequency of extreme heatwave events. As ectotherms, fishes are expected to be particularly vulnerable to global warming. Although little information is available about the effects of global warming on stress physiology in nature, multiple studies describe the consequences of temperature increases on stress physiology in controlled laboratory conditions, providing insight into what can be expected in the wild. Chronic temperature increase constitutes a physiological load than can alter the ability of fishes to cope with additional stressors, which might compromise their fitness. Besides, rapid temperature increases are known to induce acute stress responses in fishes and might be of ecological relevance in particular situations. This review summarizes knowledge about effects of temperature increases on the stress physiology of fishes, and discusses these in a context of global warming.

Keywords : heat, teleost, coping, cortisol, adaptive capacity, plasticity

1 | Introduction

The capacity of a fish to cope with environmental change is driven by its ability to mount an adequate stress response, through the activation of physiological systems, the reallocation of energy towards defensive mechanisms and a behavioural change in order to cope with or avoid the environmental threat. The physiological mechanisms underlying these responses involve the activation of two main neuroendocrine pathways: the hypothalamic-pituitary-interrenal (HPI) axis, and the brain–sympathetic–chromaffin cell (BSC) axis, responsible for the production and release of cortisol and catecholamines, respectively (Wendelaar Bonga, 1997).

As ectotherms, fish body temperature is equivalent to their water temperature, with profound effects on their physiology, metabolism and behaviour (Clarke & Johnston, 1999). Fish stress physiology is also affected by temperature in various ways. Firstly, the synthesis, release and actions of stress hormones are expected to be affected by temperature as a result of general thermodynamic effects on chemical reaction kinetics, according to the Boltzmann-Arrhenius model (Arrhenius, 1915; Boltzmann, 1972). In addition, a severe temperature increase can be a stressor in itself (Dengiz Balta *et al.*, 2017; Samaras *et al.*, 2018). Finally, acute or prolonged exposure to warm temperatures can alter function of the stress axes and responses to further stressors, possibly compromising the long-term coping capacity of the animal. This is particularly important because global warming is co-occurring with other elements of global change in aquatic habitats, such as ocean acidification and alterations in salinity (IPCC, 2014).

In the context of climate change, where seasonal water temperatures are increasing and thermal variations and extremes are becoming more frequent (Hoegh-Guldberg & Bruno, 2010; Vasseur *et*

al., 2014), a better understanding of the effects of temperature on stress physiology is crucial for predicting the consequences of global warming on the capacity of fish populations to persist. Little is known, however, about the impact of global warming on the two main stress axes, the HPI and BSC, in the wild. In this review, we provide an overview of the available information about the effects of temperature increase on fish stress physiology, mainly obtained in controlled laboratory conditions, and discuss the potential consequences for fitness and performance in a context of global warming.

2 | Global warming and fish stress physiology

2.1 | The fish stress response

In this review we adopt the functional definition of stress of Gorissen & Flik (2016), being “a condition induced by a factor (a stressor) that evokes an endocrine response that could be beneficial as well as disadvantageous”. Indeed, stress is not inherently bad and an acute stress response can be viewed as an effective way to promote a physiological and/or behavioural change to better adapt to an environmental challenge and regain homeostasis. However, the physiological and behavioural adjustments generated by the stress response could be inappropriate in conditions where the stress is repeated or sustained and cannot be avoided (Barton, 2002) and the animals cannot habituate to it.

Upon exposure to a stressor, various processes are initiated at different organizational levels (cells, tissue, organ, whole organism). The stress response is initiated by perception of a stimulus (internal or environmental) and its interpretation as a stressor (Schreck & Tort, 2016) by the brain “stress centers”, believed to be located in the forebrain (mostly in the hypothalamus and the telencephalon)

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in fishes (Gorissen & Flik, 2016). In the brain, the activity of monoaminergic neurotransmitters such as dopamine (DA), noradrenaline (NE) and, particularly, serotonin (5-HT), is likely involved in the organization and control of the stress state (Øverli *et al.*, 2005; Gesto *et al.*, 2013; Vindas *et al.*, 2018). The brain orchestrates an integrated stress response largely following two different neuroendocrine pathways. The first comprises direct neural stimulation of the chromaffin cells in the anterior kidney (brain-sympathetic-chromaffin cell axis – BSC) (Wendelaar Bonga, 1997), resulting in the release of catecholamines into circulation. A second neuroendocrine route, the hypothalamus-pituitary-interrenal (HPI) axis, is more complex. Briefly, it starts with the activation of corticotropin releasing factor (CRF) neurons that discharge CRF into the *pars distalis* of the anterior pituitary. In there, CRF and other peptides (e.g. vasotocin) stimulate the release of adrenocorticotrophic hormone (ACTH) into circulation, which in turn stimulates the production and release of cortisol (the main corticosteroid in teleosts) from the interrenal cells in the anterior kidney. (Sadoul & Geffroy, 2019). Together, both sets of stress hormones, catecholamines and cortisol, have secondary actions in various tissues and organs that aim to increase the chances of the animal overcoming the stressor threat. Those actions include catecholamine-induced responses that are mainly directed towards making energetic substrates readily available to be used by muscle and other tissues to facilitate a behavioural response (Fabbri & Moon, 2016), and cortisol-mediated changes (predominantly genomic, through the glucocorticoid (GR) and mineralocorticoid (MR) nuclear receptors), acting almost ubiquitously and believed to be directed towards mobilizing and reallocating energy substrates to facilitate adaptation (Faught *et al.*, 2016; Sadoul & Vijayan, 2016).

When the stress becomes chronic or repeated, the reallocation of energy substrates could become detrimental for normal function of the fish. In such cases, long-term tertiary effects can arise, including negative effects on the immune system, growth or reproductive success. The net result of those would depend on the severity of the sustained stressor, but they can have consequences that extend to fish populations (Adams, 1990; Barton, 2002). In addition, prolonged exposure to stress and changes in circulating corticosteroids (mainly cortisol) may have long lasting effects on the stress physiology of the organism that influence the coping ability of their progeny (Colson *et al.*, 2015, 2019; Redfern *et al.*, 2017), recently referred to as the “quaternary stress response” (Faught *et al.*, 2020).

2.2 | Acute warming as an acute stressor for fishes

Sudden exposure to high temperature is perceived as a stress by fishes, leading to the release of catecholamines and cortisol (LeBlanc *et al.*, 2011; Cockrem *et al.*, 2019). Cortisol responses during and after an acute temperature rise have been described for multiple species (**Table 1**), with only a few exceptions (e.g. LeBlanc *et al.* (2012); Chadwick *et al.* (2015)). Secondary stress responses are also observed upon acute temperature increase; glucose and lactate generally rise during acute thermal challenge, along with alterations in blood osmolality and other haematological variables (Dengiz Balta *et al.*, 2017; Bard & Kieffer, 2019). In addition, inhibitory effects on the fish immune system may be observed (Dengiz Balta *et al.*, 2017). At the cellular level, Heat Shock Protein (HSPs) release is also modulated by the endocrine stress systems (Maloyan & Horowitz, 2002; Currie *et al.*, 2008). Briefly, the adrenergic system potentiated the HSP response in red blood cells of rainbow trout *Oncorhynchus mykiss* (Walbaum 1792) (Currie *et al.*, 2008), while cortisol inhibited heat stress-induced levels of HSPs (Basu *et al.*, 2001) (**Figure 1**).

Global warming is increasing the frequency and severity of episodic and extreme marine heat waves (MHW; Meehl & Tebaldi, 2004; Hoegh-Guldberg & Bruno, 2010; Vasseur *et al.*, 2014; Frölicher *et al.*, 2018). It has been suggested that, in the context of global warming, these extreme events could be more relevant in driving population changes than a continuous increase in average temperatures (Vasseur *et al.*, 2014; Sandblom *et al.*, 2016). It is, however, difficult to know how frequently wild fish face abrupt changes in temperature. Fish are known to actively seek their preferred temperature (Larsson, 2005; Nivellet *et al.*, 2019) but that might not always be feasible, depending on habitat characteristics and species biogeography. Consequently, although we think that protocols investigating laboratory induced acute (within hours) thermal shocks are worth being conducted in a context of fundamental research (e.g. to describe coping mechanisms) or aquaculture (e.g. to describe effects on welfare or productivity), scientists should be cautious when interpreting such results in a context of global warming.

2.3 | Prolonged exposure to elevated temperature and coping with stress

2.3.1 | Effects of chronic exposure to elevated temperature on resting stress physiology

Living in warmer water has inherent effects on fish physiology since biochemical reaction rates are regulated by temperature (Somero, 2004). Therefore, physiological acclimation (or acclimatisation) to a higher temperature can be expected to enhance basal activity of HPI and BSC axes and basal release of stress hormones into cardiovascular circulation, as well as neurotransmitter activity. Such effects of temperature on biochemical reaction rates may be difficult to disentangle from effects generated by a chronic stress response. Nevertheless, we review evidence for the effects of prolonged increases in water temperature on the most common stress markers in fish.

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First, the brain catecholaminergic (noradrenergic and dopaminergic) systems may be altered under prolonged exposure to elevated temperature, which affects the synthesis, release and/or metabolization of their main neurotransmitters (NE and DA). For instance in common carp *Cyprinus carpio* L. 1758, both the level of a dopamine metabolite (3,4-dihydroxyphenylacetic acid, DOPAC) and the ratio between DOPAC and DA were greater in the hypothalamus and brain stem of fish held at elevated temperature for 2 weeks (30 vs 25°C) (De Boeck *et al.*, 1996), suggesting higher dopaminergic activity. In the Antarctic spiny plunderfish *Harpagifer antarcticus* Nybelin 1947, exposure to elevated temperature for 10 days (11 vs 2°C) induced an increase of DA in the brain (Vargas-Chacoff *et al.*, 2019). In the same study, however, temperatures of 5 and 8 °C had no effect on brain DA levels, when compared to fish reared at 2 °C. By contrast, exposure to higher temperature for two weeks (19 vs. 16 and 11 °C) induced a decrease of DA level in the brain of Chinook salmon *Oncorhynchus tshawytscha* (Walbaum 1792) (Giroux *et al.*, 2019). This suggests that the response of the dopaminergic system to a temperature shift may depend on various different factors, such as duration of exposure, extent of temperature change, and species under study. Concerning the noradrenergic system, chronic exposure to elevated temperature triggers various different changes, depending on sex and brain regions (Tsai & Wang, 1997). For instance, both males and females Mozambique tilapia *Oreochromis mossambicus* (Peters 1852) acclimated to 32 °C (3 weeks) displayed higher level of NE in the hypothalamus than those reared at 26 or 29 °C (Tsai & Wang, 1997). In the optic lobe, a similar increase in NE content was observed following acclimation to elevated temperature, but only in females. In the telencephalon, however, acclimation to high temperature lowered NE content in both males and females (Tsai & Wang, 1997).

The brain serotonergic system is believed to have an important role in organization of stress response in vertebrates (Winberg *et al.*, 1997; Gesto *et al.*, 2013; Puglisi-allegra & Andolina, 2015). Several studies have reported modification of serotonergic activity following prolonged exposure to elevated temperature. In *Cyprinus carpio*, for instance, the main metabolite of serotonin (5-Hydroxyindoleacetic acid, 5-HIAA) was higher in both hypothalamus and brain stem (as for DOPAC) under elevated temperature (De Boeck *et al.*, 1996). Consequently, greater serotonergic system activity was observed in brain stem of exposed fish (De Boeck *et al.*, 1996). In *Oreochromis mossambicus*, 5-HT levels were affected by temperature increase in a manner that depended on sex and brain region (Tsai & Wang, 1997). In *Harpagifer antarcticus*, the brain serotonin levels were enhanced upon exposure to both 8 and 11°C for 10 days, while the levels of the main metabolite of serotonin (5-hydroxyindole-3-acetic acid, 5HIAA) were not only dependent on temperature but also salinity (Vargas-Chacoff *et al.*, 2019). Taken together these studies demonstrate that, in fishes, activity of various neurotransmitters is influenced by water temperature. Since monoaminergic neurotransmitters are important for physiological and behavioural stress coping, temperature-driven effects on stress physiology could be partly mediated through alterations to these brain stress pathways.

Prolonged exposure to high temperature may also induce changes in basal levels of stress hormones. As far as we know, the few studies investigating blood catecholamines have all reported little effect of acclimation temperatures (Milligan *et al.*, 1989; Perry & Reid, 1994). However, catecholamine-induced secondary responses such as the enhancement of blood haemoglobin and haematocrit were often observed in fish exposed to increased temperatures (Houston & DeWilde, 1968; Houston & Cyr, 1974) suggesting that transient catecholamine surges could help the fish to

cope with a higher demand for oxygen. A putative negative feedback loop, consisting of catecholamines reducing sympathoadrenal activity, could be involved in the lack of changes in basal plasma catecholamines upon acclimation to high temperatures (Mravec, 2011), but the occurrence of such a loop remains to be demonstrated in fishes.

With regard to cortisol, basal blood levels are reported to be greater, overall, under prolonged exposure to elevated temperatures (Madaro *et al.*, 2018; Samaras *et al.*, 2018; Kim *et al.*, 2019) (**Figure 2**). However, alternative results have occasionally been observed, as for example in the Emerald rockcod *Trematomus bernacchii* Boulenger 1902 that showed no changes in cortisol basal values upon acclimation to warmer water (up to +3.8°C) (Hudson *et al.*, 2008) (**Table 1**). A negative feedback loop affecting cortisol production could underly the absence of increased basal cortisol in such cases (Mommsen *et al.*, 1999). In Senegalese sole *Solea senegalensis* Kaup 1858, following the stress response observed upon sudden exposure to elevated temperature (24 vs. 18°C), the cortisol level returned to basal level (i.e. similar to fish at 18°C) (Benítez-Dorta *et al.*, 2017). Cortisol levels then increased for a second time to a similar extent one week later. This midterm response was accompanied by an upregulation of glucocorticoid receptors and *crfbp* in the brain, acting as negative feedback on cortisol release (Benítez-Dorta *et al.*, 2017). High circulating levels of cortisol are generally observed in parallel with the secondary stress response, observed as a change in plasma osmolality or an increase in blood glucose and lactate (Ryan, 1995; Steinhausen *et al.*, 2008; Gallant *et al.*, 2017; Kandalski *et al.*, 2018; Samaras *et al.*, 2018), but exceptions to that general pattern have been observed (Davis, 2004; Samaras *et al.*, 2018).

Overall, living at warmer temperatures stimulates basal activity of monoamines in the central nervous system and the basal stress physiology of fishes. Whether these effects are the consequence

of increased metabolic rates at high temperature or of a prolonged state of mild stress is still unclear. This could be investigated by comparing metabolic rate and basal levels of stress indicators at multiple temperatures.

2.3.2 | Living in warmer environment alters stress coping capacities

Prolonged exposure to elevated temperature due to global warming may affect the stress coping abilities of fishes, by impairing BSC and the HPI responses to further stressors. For example, the response of monoaminergic neurotransmitters to additional acute stress has been shown to be affected by elevated temperature in *Cyprinus carpio*, where the activity of both the dopaminergic and serotonergic systems was enhanced in specific brain regions (mainly in telencephalon) in response to a salinity challenge under elevated temperature (De Boeck *et al.*, 1996), suggesting a temperature-induced shift of the stress response.

In response to hypoxia, catecholamines (E and NE) are released into the blood more rapidly and to higher levels in *Oncorhynchus mykiss* acclimated to 15°C compared to 5°C (Perry & Reid, 1994). Upon acute stress, the peak of cortisol release and the dynamic to recover baseline level after stress may also be affected by water temperature. Briefly, the cortisol peak is achieved more rapidly, and tends to be of larger magnitude (Ryan, 1995; Davis, 2004; Madaro *et al.*, 2018) (**Figure 2**). Other studies have however, found little effect of temperature on HPI responses (Lankford *et al.*, 2003; Meka & McCormick, 2005; Samaras *et al.*, 2018; Vargas-Chacoff *et al.*, 2020) (**Table 2**). This inconsistency could partly result from the difficulty of obtaining precise information on temporal response patterns for stress markers. Secondary stress response mechanisms are also generally

enhanced in fish reared at warmer temperatures (Davis, 2004; Meka & McCormick, 2005; Samaras *et al.*, 2018).

Overall, the fish stress response to a challenge is faster and greater at elevated temperatures. Again, whether this is the consequence of an increased overall metabolic rate or changes in coping ability is still unclear. Understanding the fitness consequences of such effects of warmer temperatures is primordial for investigating the impacts on fish populations, especially since fishes are exposed to a wide range of acute stressors during their life and more particularly in the context of global warming.

2.4 | Thermal imprinting and the fish stress response

Empirical studies in fishes have demonstrated that early exposure to other stressors induces plasticity of the HPI axis upon further stress exposure (Varsamos *et al.*, 2006; Auperin & Geslin, 2008). Since prolonged exposure to elevated temperature may be perceived as a stressor, exposure at early life stages, particularly during embryonic development, may trigger similar long-lasting effects on individual physiology and subsequent ability to cope with similar or novel environmental challenges. This phenomenon is generally known as ‘thermal imprinting’ (Steinbacher *et al.*, 2011; Mateus *et al.*, 2017a). Adult Gilthead seabream *Sparus aurata* L. 1758 reared at high temperatures during development (embryo and larvae) showed, for example, a reduced cortisol response to a confinement stress, despite an identical thermal history during the post-larval stage (Mateus *et al.*, 2017a). Their stress reactivity to a cold challenge was also greater in those reared at high temperature during the embryonic stage (Mateus *et al.*, 2017b). Changes in the transcription of key

genes involved in regulation of the HPI axis (e.g. *gr*, *pomca2*) were also observed in response to thermal imprinting, which may partly explain the changes in coping abilities (Mateus *et al.*, 2017a).

The biological processes by which stress physiology and the fish physiology in general are altered in the long term, due to prior exposure to elevated temperature, are not yet fully understood.

Sustained changes in brain monoaminergic signalling and neural plasticity in specific areas, or epigenetic modifications, may contribute to observed effects (Zhang *et al.*, 2010; Fokos *et al.*, 2017; Vindas *et al.*, 2018). In the context of global warming, epigenetic modifications may be induced by exposure to elevated temperature (Bizuayehu *et al.*, 2015; Anastasiadi *et al.*, 2017; Jonsson & Jonsson, 2019), that can later mediate the coping ability of individuals upon stress.

Prolonged exposure to elevated temperature at early life stages may therefore have long-term consequences for stress physiology, potentially modifying the ability to cope with additional stressors. Whether these modifications are adaptive in a context of global warming remains to be understood. Further research is also required to better understand the complex interrelationship between timing, amplitude and duration of the thermal increase during thermal imprinting in fishes, and the consequences for fitness traits.

Stress, energy and global warming: Potential consequences for fish populations

Global warming has already been demonstrated to alter fish populations, through changes in local abundance, extinctions or migrations towards colder areas (Payne, 2013; Burrows *et al.*, 2019; Free *et al.*, 2019). But what is the proximate cause of such alterations? Indirect effects of temperature increase, including alterations in prey-predator interactions or reduced oxygen availability (Breitburg *et al.*, 2018) also contribute to global warming-induced modifications of fish

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populations. However, a direct physiological effect of temperature is believed to be the primary mechanism behind population shifts (Pörtner & Knust, 2007; Pörtner & Farrell, 2008). This main direct effect seems to be related to global warming taking fish closer to, or beyond, their upper thermal-tolerance limits (Dillon *et al.*, 2010; Eliason *et al.*, 2011; Pinsky *et al.*, 2019). Furthermore, warming may particularly affect stenothermal species, typical of tropical or polar latitudes (Somero, 2010; Comte & Olden, 2017). For these species, an inability to tolerate temperature fluctuations and warming might be a particularly life-threatening challenge (Somero, 2010; Faught *et al.*, 2020). However, the physiological traits that determine thermal tolerance are not entirely understood. Protection against heat at the cellular level involves the synthesis of chaperone proteins, the HSPs, that are highly conserved in the animal kingdom (Margulis *et al.*, 1989). The HSPs prevent protein aggregation, refolding of stress-denatured proteins and apoptosis and cell death (Roberts *et al.*, 2010). Multiple studies have found a link between the ability to upregulate HSPs and thermal tolerance in aquatic species (Fangue *et al.*, 2006; Shatilina *et al.*, 2011; Feidantsis *et al.*, 2013; Blair & Glover, 2019), indicating a potential ecological relevance of HSPs in a context of global warming.

From an energetic point of view, warming is costly, for multiple reasons. Firstly, due to thermal acceleration of metabolic rates (Dell *et al.*, 2011), physiological and behavioural processes are stimulated, leading to faster development times, growth, or swimming activity (Pauly, 1980; Kent & Ojanguren, 2015; Tsoukali *et al.*, 2016). Together, this causes energy demands to increase, energy that must be more actively obtained from the environment (**Figure 3.b**). In general, these thermal conditions do not translate into energetic stress for the fish as long as the environment can provide sufficient food. Nevertheless, when temperature continues to increase, additional

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maintenance is needed at the cellular level (**Figure 3.c**), with the need to counteract the detrimental effects of temperature, including protein denaturation, DNA mutations, oxidative damage and ultimately cellular death (Lepock, 2005). Fish enters then a “stressed state”, with non-critical functions (reproduction, growth or immunity) slowed down to compensate for these new immediate needs (Sadoul & Vijayan, 2016).

Applying an additional stressor to this energetic framework can be expected to be particularly detrimental to the animal, since stress can reduce energy availability by lowering feeding activities and increasing somatic maintenance (Sadoul & Vijayan, 2016). Global warming can therefore be expected to exacerbate energetic constraints in a generally more stressful world, particularly because animal basal metabolic rates increase exponentially with temperature (Gillooly *et al.*, 2001; Dillon *et al.*, 2010), while maximum metabolic capacity often stops increasing or declines at high temperatures (Clarke & Johnston, 1999; Norin & Clark, 2016; Sandblom *et al.*, 2016). This ultimately leads to a reduced scope to support non-essential activities (Navarro *et al.*, 2019). This is suspected to be one of the main reason why local fish populations can be reduced or even extirpated from specific locations, particularly when populations or subpopulation are tightly adapted to specific environmental conditions (Eliason *et al.*, 2011). Chadwick *et al.* (2015) observed a concordance between upper thermal limit of Brook trout *Salvelinus fontinalis* (Mitchill 1814) and the temperature that induced a physiological stress response, suggesting that the stress threshold could be a major driver of fish distribution for this species. This highlights the pivotal role of stress physiology in the context of global warming (Chadwick & McCormick, 2017).

In addition, the effects of global warming on stress physiology can also have ramifications for other aspects of fish biology, such as reproduction or immunity. For example, changes in HPI regulation,

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and more particularly glucocorticoid levels during early life stages, may have profound long term consequences for the organism, including effects on sex determination (Geffroy & Douhard, 2019; Geffroy & Wedekind, 2020). Increased temperatures can also alter host-parasite interactions, resulting in higher occurrence and severity of infections (Marcos-Lopez et al., 2010). These effects can be partially mediated by stress-induced immune alterations (Tort, 2011; Yada & Tort, 2016). Those alterations include immune depression and higher susceptibility to infection and disease (Kandalski *et al.*, 2018; Martínez *et al.*, 2018; Kim *et al.*, 2019; Li *et al.*, 2019). In addition, it is important to note that global warming can lead to the emergence of novel infectious agents, triggering diseases for which fishes are not yet adapted (Marcos-López *et al.*, 2010).

Stress physiology is also involved in hydromineral balance and maintenance of ionic homeostasis (Barton & Schreck, 1987; Geering, 1990). Consequently, alteration in stress physiology due to global warming may have consequences for these regulatory homeostatic processes (Kandalski *et al.*, 2018), and the central role of cortisol in these effects was recently suggested (Samaras *et al.*, 2018; Vargas-Chacoff *et al.*, 2020).

In addition, the levels of cortisol and/or neurotransmitter activity are well known to mediate fish behaviour (Øverli *et al.*, 2002, 2004). Therefore, changes in fish behaviour can be expected at higher temperature, due to changes in stress physiology machinery, with potential cascading effect on populations. On the first hand, changes in neurotransmission may alter social behaviour of fish, affecting intra- and interspecies interactions that can affect the functioning of ecosystems under a warmer environment (Allan *et al.*, 2017; Paula *et al.*, 2019). On the other hand, an increase of locomotor activity, boldness and aggressive behaviour have been frequently observed for fish at higher temperature (Biro *et al.*, 2010; Angiulli *et al.*, 2020). It is suggested that these changes

allow fish to get higher access to food sources (for compensating higher metabolic rates), but this also makes them more vulnerable to predation (Biro *et al.*, 2007).

It is also worth mentioning that warmer temperatures can enhance the severity of other stressors. One example is the increase in the prevalence and/or severity of diseases commented above (Marcos Lopez *et al.*, 2010). Another example is the general increase in the toxicity of water-borne pollutants (Noyes *et al.*, 2009).

In summary, chronic temperature increase can act in three ways to affect fish populations, from the point of view of stress. It can be a stressor itself, altering responses to further stressors, and it can actually generate “new” or enhanced stressors for fish populations. Therefore, global warming will cause a multi-stressor environment for wild fish populations, potentially leading to serious reduction in their fitness. It has been hypothesized that, in the context of exposure to multiple stressors, fish populations could change coping strategy (shutting off stress response for maintaining growth and metabolic routines), negatively affecting fitness and survival (Petitjean *et al.*, 2019).

4 | Conclusions and perspectives

Global warming is now a reality challenging fishes with an increase in seasonal water temperatures and the occurrence of extreme heatwave events. Stress physiology has a pivotal role in coping with environmental changes, including global warming. We reviewed the effects of acute and chronic increases in water temperature on fish stress physiology. Upon chronic temperature increase, all metabolic reactions are enhanced in ectotherms. Nevertheless, the high levels of stress-related reactions observed during long term exposure to high temperature might be because the fish

perceives the conditions as a chronic stress. Very little information is available to disentangle whether high cortisol levels and changes in neurotransmitter activity are the consequences of increased metabolism or a response to chronic stress.

We explain in this review how global warming can lead to energy limitation through stress physiology, and ultimately modifies the sensitivity to other environmental stressors in fishes (Stiasny *et al.*, 2019; Cominassi *et al.*, 2020). This is of primary interest since, in addition to global warming, aquatic habitats are also suffering from acidification, hypoxia, chemical pollution, and so forth (Sih, 2013; Gordon *et al.*, 2018). Overcoming the load induced by a multi-stressor environment might be difficult under normal conditions, but will be even more complicated in a warmer world, due to limitations in energy available. Since the interactions between two or more stressors are complex to predict (Piggott *et al.*, 2015; Jackson *et al.*, 2016; Liess *et al.*, 2016), multi-stressors studies are needed to better understand how fish populations will be affected by global warming (Côté *et al.*, 2016).

The thermal experience of fish, especially during early life, can shape the HPI responsiveness upon further stressors (Mills *et al.*, 2015; Mateus *et al.*, 2017a). A research effort is needed to understand how exposure to elevated temperatures during early life may affect capacity to cope with the various threats caused by global warming (Whitney *et al.*, 2013; Mateus *et al.*, 2017a; Wassink *et al.*, 2019). Furthermore, in the context of global warming, recent multi-generational studies showed that, after acclimation of one or two generations to elevated temperatures, the progeny were often better able to tolerate higher temperatures, in particular by decreasing their metabolic rate (Donelson *et al.*, 2012; Bernal *et al.*, 2018; Ryu *et al.*, 2018; Pilakouta *et al.*, 2020). Further studies

must elucidate how this relates to stress physiology and further capacities to cope with additional stressors.

It is difficult to generalize about the vulnerability of fishes to global warming since their response will depend on multiple factors, including their natural distribution, their intrinsic metabolic capacities, their life history or genetic background (Somero, 2010; Comte & Olden, 2017; Colossi Brustolin *et al.*, 2019). Besides, fish species or individuals differ considerably in the magnitude of their responses to specific stressors, (Mommsen *et al.*, 1999; Barton, 2002), including increased temperature (LeBlanc *et al.*, 2012; Madeira *et al.*, 2013). Whether this differential sensitivity to stress might pose an advantage or disadvantage for certain individuals or species, in a warmer future, is not known. We argue that this requires a major research effort, to correctly predict consequences for ecosystems, fisheries and aquaculture (Froehlich *et al.*, 2018).

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Significance statement

Global warming is affecting fishes worldwide, through chronic temperature elevation and an increased frequency of extreme heatwaves. The consequences of these changes for stress physiology are, however, poorly addressed. This review provides an overview of information about the effects of temperature elevation (acute or chronic) on fish stress physiology, mainly obtained in controlled experimental conditions, and discusses the potential consequences for performance and fitness in the context of global warming.

Table 1. Cortisol release as a function of elevated temperature experience.

Common name (Scientific name)	Temperature experience	Cortisol release	Reference
Zebrafish (<i>Danio rerio</i>)	10 min - sudden change from 28.5 to 36 °C	Increased level	Yeh <i>et al.</i> , 2013
Senegalese sole (<i>Solea senegalensis</i>)	10 min - sudden change from 20 to 25 °C	Increased level	Conde-Sieira <i>et al.</i> , 2018
Black Sea trout (<i>Salmo trutta labrax</i>)	30 min - sudden change from 15 to 25 °C	Increased level	Dengiz Balta <i>et al.</i> , 2017
Haddock (<i>Melanogrammus aeglefinus</i>)	1 hour - sudden change from 10 to 15 °C	Increased level	Afonso <i>et al.</i> , 2008
Rainbow trout (<i>Oncorhynchus mykiss</i>)	1 hour - sudden change from 13 to 25 °C	Increased level	LeBlanc <i>et al.</i> , 2011
Rainbow trout (<i>Oncorhynchus mykiss</i>)	2 hour - sudden change from 10 to 22 °C	Increased level	Basu <i>et al.</i> , 2001
Mozambique tilapia (<i>Oreochromis mossambicus</i>)	2 hour - sudden change from 22 to 34 °C	Increased level	Basu <i>et al.</i> , 2001
Rohu (<i>Labeo rohita</i>)	2 hours - sudden change from 28 to 38 °C	Increased level	Kumar <i>et al.</i> , 2015
Goldfish (<i>Carassius auratus</i>)	1 hour - from 19 to 31°C (10°C per hour)	Increased level	Cockrem <i>et al.</i> , 2019
Atlantic cod (<i>Gadus morhua</i>)	2 hours - from 10 to 22 °C (2°C per hour)	Increased level	Pérez-Casanova <i>et al.</i> , 2008
Sockeye salmon (<i>Oncorhynchus nerka</i>)	From 15 to 24°C (2°C per hour)	Increased level	Steinhausen <i>et al.</i> , 2008
Brook trout (<i>Salvelinus fontinalis</i>)	6 hours - from 16 to 29°C	No change	Chadwick <i>et al.</i> , 2015
Sea bass (<i>Dicentrarchus labrax</i>)	4 days – gradual increase from 16 and 21°C	Increased level	Goikoetxea <i>et al.</i> , 2021
Sunshine bass (<i>Morone chrysops</i> × <i>Morone saxatilis</i>)	5 days - 5-30°C (by step of 5 °C)	No change	Davis, 2004
Senegalese sole (<i>Solea senegalensis</i>)	7 days - 24 vs 18 °C	Increased level at 1 h and 7 days but not within	Benítez-Dorta <i>et al.</i> , 2017
Olive Flounder (<i>Paralichthys Olivaceus</i>)	2 weeks - from 20, 22, 24, 26, 28 and 30 °C	Increased level at 1 and 2 weeks (28 and 30°C)	Kim <i>et al.</i> , 2019
European sea bass (<i>Dicentrarchus</i>)	2 weeks - 15,20 and 25°C	Increased level	Samaras <i>et al.</i> , 2018

<i>labrax</i>)			
Green sturgeon (<i>Acipenser medirostris</i>)	2 weeks - 19 vs 11°C	No change	Lankford <i>et al.</i> , 2003
milkfish (<i>Chanos chanos</i>)	3 weeks - 33 and 26°C	Increased level (scale)	Hanke <i>et al.</i> , 2019
Brook trout (<i>Salvelinus fontinalis</i>)	24 days - 16-24°C (by step of 2°C)	Increased level	Chadwick & McCormick, 2017
Atlantic salmon (<i>Salmo salar</i>)	4 weeks - 4, 8, 12 and 17 °C	Increased level (water)	Madaro <i>et al.</i> , 2018
Chinook salmon (<i>Oncorhynchus tshawytscha</i>)	4 weeks - 7.5, 12.5 and 21°C	No change	Barton & Schreck, 1987
<i>Trematomus bernacchii</i>	4 weeks - -1.9, 1.6 and 3,8°C	No change	Hudson <i>et al.</i> , 2008
European sea bass (<i>Dicentrarchus labrax</i>)	30 days - 8, 16, 24 and 32°C	Increased level at 8 and 32°C	Islam <i>et al.</i> , 2020
Sea bream (<i>Sparus aurata</i>)	35 days - 12, 19 and 26 °C	Increased level	Vargas-Chacoff <i>et al.</i> , 2020
Atlantic cod (<i>Gadus morhua</i>)	45 days - from 10 to 20°C (1°C every 5 days)	Increased level only at 30 days (16°C)	Pérez-Casanova <i>et al.</i> , 2008
Atlantic salmon (<i>Salmo salar</i>)	99 days - 12, 16 and 20°C	No change	Tromp <i>et al.</i> , 2018
European ea bass (<i>Dicentrarchus labrax</i>)	4 months - 16 and 21°C	Increased level	Goikoetxea <i>et al.</i> , 2021
Brook trout (<i>Salvelinus fontinalis</i>)	River - from 18 to 23.3°C	Increased level	Chadwick <i>et al.</i> 2015
Wild rainbow trout (<i>Oncorhynchus mykiss</i>)	River - 9.8, 12.2 and 13.2°C	Tendency for increased level	Meka & McCormick, 2005
Lake sturgeon (<i>Acipenser fulvescens</i>)	Embryo and larval - 18 vs 10 °C	Tendency for reduced level	Wassink <i>et al.</i> , 2019

Table 2. Cortisol release upon acute stress at elevated temperature.

Common name (Scientific name)	Temperature experience	Stressor	Cortisol release	Reference
Sockeye salmon (<i>Oncorhynchus nerka</i>)	From 15 to 24°C (2°C per hour)	Swimming trial	Increased level	Steinhausen <i>et al.</i> , 2008
Bald notothen (<i>Pagothenia borchgrevinki</i>)	Thermal stress up to 48 h - 5 vs -1.9°C	Confinement	Greater response and long lasting	Ryan, 1995
Sunshine bass (<i>Morone chrysops</i> × <i>Morone saxatilis</i>)	5 days - 5-30°C (by step of 5 °C)	Confinement	Faster and greater response	Davis, 2004
Green sturgeon (<i>Acipenser medirostris</i>)	2 weeks - 19 vs 11°C	Air exposure	Faster response	Lankford <i>et al.</i> , 2003
European sea bass (<i>Dicentrarchus labrax</i>)	2 weeks - 15, 20 and 25°C	Confinement	Faster response but reduced	Samaras <i>et al.</i> , 2018
Atlantic salmon (<i>Salmo salar</i>)	4 weeks - 4, 8, 12 and 17 °C	Confinement	Greater response (water)	Madaro <i>et al.</i> , 2018
Juvenile Chinook salmon (<i>Oncorhynchus tshawytscha</i>)	4 weeks - 7.5, 12.5 and 21°C	Handling	Faster recovery	Barton & Schreck, 1987
Lake sturgeon (<i>Acipenser fulvescens</i>)	Embryo and larval - 18 vs 10 °C	Alarm cue	Reduced response	Wassink <i>et al.</i> , 2019
Wild rainbow trout (<i>Oncorhynchus mykiss</i>)	River - 9.8, 12.2 and 13.2°C	Handling	Faster response	Meka & McCormick, 2005

Captions

Figure 1. Stress response upon acute exposure to a sudden elevation in temperature. The diencephalon orchestrates the primary stress response by releasing catecholamines (mostly adrenaline and noradrenaline) through activation of brain–sympathetic–chromaffin cell (BSC) axis, and cortisol through the hypothalamo-pituitary-interrenal (HPI) axis into the bloodstream. In the immediate term, these hormones (catecholamines, orange and cortisol, blue) enhance activity of the cardiovascular system (e.g. increased heart rate and blood pressure) and rapidly mobilize energy (i.e. glucose, lactate; secondary response). In parallel, the release of catecholamines enhances the production of heat shock proteins (HSPs) that prevent and repair oxidative damage linked to the warming. Several minutes later, the cortisol release occurs and inhibits the production of HSPs, and acts as negative feedback control of further cortisol release. In the long term, these stress responses inhibit energy allocation to biological processes such as immunity, growth and reproduction, also called tertiary responses). Normal arrows represent an activation while bar-headed arrows represent an inhibition.

Figure 2. The hypothalamic-pituitary-interrenal axis (HPI) response under (a) acute temperature (T°) increase, (b) chronic temperature elevation and (c) upon acute stressor at elevated temperature. Cortisol release (lower panel) is illustrated according to the temperature protocol (upper panel, green lines; normal temperature conditions and red lines; elevated temperatures). The cortisol responses displayed in this figure are based on the studies mentioned in Tables 1 and 2.

Figure 3. Effect of temperature increase on energy allocation in a fish. (a) Assimilated food is placed a reserve compartment and is then partitioned between structure and maturity after having paid for their respective maintenance costs (maint.). When temperature rises (b) all metabolic rates increase and physiological needs are met by increased food consumption. High temperature will put pressure on energy allocation (c) through increased costs for maintenance, leading to a reduction in allocation to structure and maturity.





