Evolution of the hormonal control of animal performance: Insights from the seaward migration of salmon

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Synopsis The endocrine system is the key mediator of environmental and developmental (internal) information, and is likely to be involved in altering the performance of animals when selection has favored phenotypic plasticity. The endocrine control of performance should be especially pronounced in animals that undergo a developmental shift in niche, such as occurs in migratory species. By way of example, I review the developmental and environmental control of the preparatory changes for seawater entry of juvenile salmon (known as smolting) and its hormonal regulation. There is a size threshold for smolt development in juvenile Atlantic salmon that results in greater sensitivity of the growth hormone and cortisol axes to changes in daylength. These hormones, in turn, have broad effects on survival, ion homeostasis, growth and swimming performance during entry into seawater. Migratory niche shifts and metamorphic events are extreme examples of the role of hormones in animal performance and represent one end of a continuum. A framework for predicting when hormones will be involved in performance of animals is presented. Endocrine involvement in performance will be more substantial when (1) selection differentials on traits underlying performance are high and temporally discontinuous over an animal's lifetime, (2) the energetic and fitness costs of maintaining performance plasticity are less than those of constant performance, (3) cues for altering performance are reliable indicators of critical environmental conditions, require neurosensory input, and minimize effects of lag, and (4) the need for coordination of organs, tissues and cells to achieve increased performance is greater. By examining these impacts of selection, endocrinologists have an opportunity to contribute to the understanding of performance, phenotypic plasticity, and the evolution of life-history traits.

Introduction: hormones as integrators of developmental and environmental change

The neuroendocrine system is a key mediator of environmental and developmental information in most complex organisms (Scharrer and Scharrer 1963). It has the capacity to ''sense'' and interpret internal conditions such as energetic state or developmental stage, external changes such as daylength, temperature, or salinity, integrate these cues, and communicate them to all parts of the body to bring about coordinated, tissue-specific responses. The resulting biochemical, physiological, morphological, and behavioral changes can have a profound impact on the performance of animals, and ultimately on the survival and reproductive capacity of an organism. The complex attributes of the endocrine system and their control of performance have likely been shaped by a long evolutionary history, and unraveling the selective forces that have shaped them will be challenging (Bern 1967).

There are several properties of the neuroendocrine system that are critical for the integration of environmental and developmental information. First is the ability to respond to the external environment. Photoperiod, circadian rhythms, water, organic compounds (denoting the presence of food, predators, or noxious conditions), and temperature can be sensed by the eyes, pineal gland, olfactory tissue, or skin, then processed by the central nervous system that in turn signals the hypothalamus, pituitary, and other endocrine organs (Norris 2005). A few environmental changes may be able to directly signal all cells in the body, such as temperature in ectotherms (Feder and Hofmann 1999b), but many, such as changes in daylength, or external chemicals, may not be available to the interior of complex organisms, and thus require recognition and

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processing by the nervous system. Some environmental factors are themselves the agents of selection, such as salinity or temperature, whereas others are surrogate cues that indicate the presence of selection agents (Nijhout 2003; West-Eberhard 2003).

In addition to the capacity for sensing the external environment, the neuroendocrine system provides regulation of development and metabolism, and feedback from the internal state of the animal. In fish, cells of the pituitary that produce the hormone prolactin (which controls ion and water balance) are directly responsive to the osmotic concentration of blood, secreting more prolactin as osmotic concentration decreases (Nagahama et al. 1975). Control of plasma insulin and glucagon levels are highly sensitive to the circulating levels of glucose and thus provides a signal for the short-term metabolic state of an animal (Norris 2005). Leptin is produced by adipose tissues and provides a potential signal for the body's energy stores (Flier 1997). The hormone ghrelin, produced by the stomach, provides a signal for fullness of the gut, which in turn provides feedback to peptides controlling appetite and growth (St Pierre et al. 2003). In fish, release of growth hormone by the pituitary may be impacted by at least a dozen hypothalamic factors that are themselves responsive to the internal state of the animal (Björnsson et al. 2002; Canosa et al. 2007). These metabolic regulatory systems provide many pathways for feedback and are clearly involved in developmental decisions such as metamorphosis and puberty (Chehab et al. 1997), although many of the details of the integration of internal developmental signals involved in critical life-history events are still lacking (Ketterson and Nolan 1992; Stearns 1992).

The most common pathway for endocrine effects is hypothalamic production of a peptide causing release of a pituitary hormone that moves through the blood and has actions at distant parts of the body through highly specific receptors (Fig. 1). Many hormones are accompanied by binding proteins that can affect their stability (half-life) and interaction with a receptor. Most vertebrates possess at least five binding proteins for insulin-like growth factor I (IGF-I) that maintain free IGF-I at very low levels (Wood et al. 2005). Some make the hormone more readily available to the membrane receptor, and some inhibit receptor binding; each of these binding proteins can be independently regulated. Membrane or intracellular receptors provide highly specific responsiveness to hormones at target tissues. Abundance of receptors or alteration of affinity through expression of different receptor isoforms determine whether a tissue or cell type responds to a given hormone and at what level of hormone they become responsive. The presence of hormone-specific enzymes in some tissues, such as the 11β-hydroxystreroid dehydrogenase which degrades cortisol but not aldosterone, provides more tissue-specific regulation of hormonal response (Funder et al. 1988).

Hormone-receptor signaling pathways may have relatively rapid impacts, such as phosphorylation of existing proteins or their insertion into membranes. Long-term impacts occur through up- or down-regulation of gene expression, and in many cases the transcriptional response of a large number of genes is induced by a single hormone. By altering genes involved in regulatory pathways such as the differentiation of cell types, the endocrine system can have impacts that persist long after the increased hormone levels have disappeared. These are not limited to the individual organism but can be passed on to the next generation through maternal effects of hormones on eggs and, in placental mammals, on early development (Dufty et al. 2002).

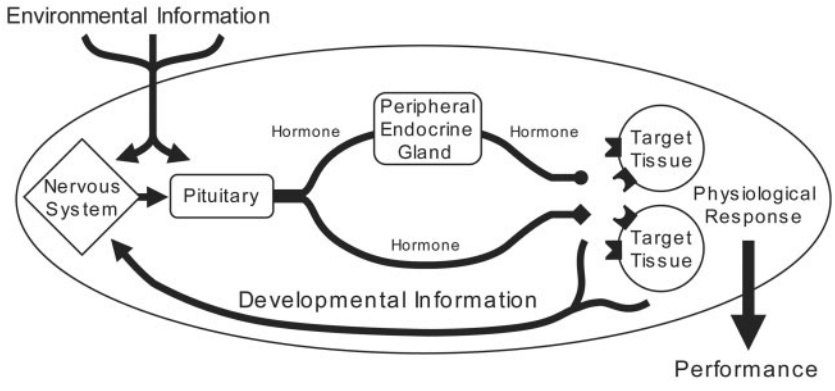

Figure 1 The endocrine system as a mediator of environmental and developmental information, resulting in coordinated changes in behavioral, physiological, and morphological traits that affect performance.

This brief summary demonstrates some of the complexity of the endocrine system. Its numerous components, each controlled by a gene and many regulating the expression of multiple downstream genes, present substantial opportunity for selection to act on those aspects of the endocrine system that affect survival, growth, and reproductive success (West-Eberhard 2003). Because they may be involved in controlling multiple organ systems and are known to be involved in complex traits, hormones have been implicated in the control of animal performance, which can be defined as a quantitative measure of how well an organism accomplishes some ecologically relevant task (Husak et al., 2009). Dramatic niche shifts resulting from migration are often associated with metamorphic or transformational events that are clear examples of the hormonal control of performance. In these instances individuals are moving to new habitat that requires fundamental shifts in how they cope with their environment, often including how they move, breathe, regulate water and ions, eat, and reproduce. Familiar examples include the movement from water to land (amphibian metamorphosis) and water to air (aerially breeding aquatic insects). Less well-known is the transition of anadromous fish from fresh water to seawater. In the next section, I will show how hormones are involved in the capacity of one species of anadromous fish, Atlantic salmon (*Salmo salar*), to move from fresh water to seawater while maintaining high growth and swimming capacity. I will summarize differences in smolt development among salmonids and how these relate to life history and migratory behavior. While migratory species are clear, perhaps extreme, cases of endocrine alteration of performance, I will discuss other more subtle examples of the integration of developmental and environmental information by the endocrine system. Finally, I will present a framework for understanding and potentially predicting when hormones are involved in performance.

Transformation of parr–smolt and performance in seawater

> ''Smolting is an adaptation not just to survive in seawater, but to thrive in seawater'' (Richard L. Saunders, personal communication).

During their normal life history all anadromous species, while juveniles, make at least one migratory movement from fresh water to seawater. Juvenile Pacific and Atlantic salmon undergo a parr–smolt transformation that include behavioral, morphological, and physiological changes that increase their capacity for downstream migration and entry into the ocean (Hoar 1988). Smolts lose their positive rheotaxis and develop schooling behavior and a preference for high salinity. Morphological changes include the loss of cryptic parr marks on their sides, development of silvering and a darkening of the margins of the fins, characteristic of many schooling fish. In addition to the acquisition of salinity tolerance, physiological changes include altered retinal pigmentation, olfactory sensitivity, buoyancy, and increased metabolic rate (McCormick and Saunders 1987; Hoar 1988).

Of clear importance to the movement of anadromous fish from freshwater to seawater is the capacity to survive in the increased salinity of the ocean (~35 ppt). Like most freshwater fish, Atlantic salmon parr have only a limited capacity for salt secretion, and direct transfer from freshwater to seawater (above 25 ppt) results in mortality (S.D. McCormick, unpublished manuscript). During the period of migration downstream in spring, smolts acquire an increased capacity for salt secretion that results in an ability to withstand direct transfer to seawater with virtually no ion perturbation (Clarke 1982). Many of the mechanisms for the increased capacity of smolts for salt secretion have been determined. Branchial chloride cells, which are responsible for salt secretion, increase in number and size during smolt development (Pisam et al. 1988). Two transport proteins present in chloride cells and directly responsible for salt secretion, Na^+/K^+-ATPase (NKA) and the Na^+/K^+, $2Cl^-$ contransporter (NKCC), increase in abundance during smolting (Pelis et al. 2001). The intestine of marine teleosts takes up both water and salt, and the uptake capacity of the intestine for both water and salt increases during smolting (Collie and Bern 1982). The kidney is involved in secreting excess divalent ions (Ca^{2+}, Mg^{2+}, and SO_4^{2-}) in seawater, but to date we know little about changes in renal function that occur during smolting.

In most euryhaline fish, the physiological changes described above are those that occur in response to exposure to seawater, but in salmon smolts these develop *prior* to exposure. By decreasing the osmotic perturbations that might normally occur during exposure to seawater, this increased capacity for salt secretion may have impacts on many other aspects of performance, especially during the initial entry into seawater. Coho salmon (*Oncohrhynchus kisutch*) parr exposed to 26.5 ppt seawater had reduced maximum swimming capacity (measured as U_{crit}) relative to fresh water controls, and there

was a strong negative correlation between plasma ions and swimming capacity (Brauner et al. 1992). In a simulated predation arena, Atlantic salmon juveniles with larger osmotic perturbations after transfer to seawater suffered greater predation (Handeland et al. 1996). Growth rates in seawater also appear to be influenced by smolt development, as fish that have been prevented from smolting by continuous light have normal growth in freshwater but much lower growth than smolts after transfer to seawater (McCormick et al. 1987).

These differences in salt secretory capacity and associated differences in growth and swimming are likely to have strong influence on survival in seawater, although to date there is only indirect evidence for this relationship. Several studies have demonstrated that smolts released at the peak of their osmoregulatory ability have higher returns than do fish released before or after (see summary in McCormick et al. 1998). These studies are of course confounded by the fact that the release times at peak smolt development also coincide with normal timing of smolt migration, and thus may be as much determined by an "ecological" smolt window (timing of favorable environmental conditions for smolt survival) as by a "physiological" smolt window (timing of individuals ability to secrete salt, swim, and grow in seawater). Exposure to moderately acidified water has been shown to reverse the seawater tolerance of smolts, and the release of acid-exposed smolts results in substantially lower return rates of adults (Kroglund et al. 2008). Although exposure to acid may affect other aspects of physiology than just salinity tolerance, taken together, these studies indicate that there is a strong relationship between smolt development and the capacity to perform and survive in an oceanic environment.

The role of growth hormone and cortisol in smolt development and performance in seawater

> "Hormones are the unsung heroes of the nature–nurture field of study" (Pigliucci 2001, p. 124).

Atlantic salmon spend from 1 to 5 years in fresh water before undergoing the parr–smolt transformation in spring. This variation in age at migration is largely due to the size-dependent nature of smolting in this species, which occurs at ~12–13 cm fork length in early spring. Atlantic salmon in regions with short growing seasons (such as high latitude or elevation) may take several years to reach this critical size threshold, whereas fish in regions with longer or better growing seasons may reach this threshold within one or two years (Metcalfe and Thorpe 1990). The evolutionary forces that have shaped this dependency on size appear to involve predation and/or availability of prey favoring survival of larger smolts (Holtby et al. 1990; Saloniemi et al. 2004). The proximate mechanism by which salmon determine this size-related development is currently unknown, but may involve feedback from lipid content or other aspects of metabolic state that are size-dependent (McCormick et al. 1998), assessment of previous growth rate (Dickhoff et al. 1997), or some combination of these.

There are a number of hormonal changes that occur during the parr–smolt transformation, the most prominent of which are increases in circulating levels of thyroxine, cortisol, growth hormone, insulin-like growth factor I, and insulin. All of these hormones are known to have positive effects on various aspects of smolt development (see reviews by Hoar 1988; Dickhoff et al. 1997). Plasma prolactin levels increase early in smolt development and decline at the peak (Prunet et al. 1989; Young et al. 1989), and this hormone is generally thought to be inhibitory to the development of salinity tolerance (Madsen and Bern 1992). Because growth hormone and cortisol are most clearly involved in controlling the capacity for ion regulation (detailed below) and for the sake of brevity, I will focus on the role of these two hormones. In spite of this emphasis, it is important to keep in mind that other hormones interact with growth hormone and cortisol and are involved in the many changes that occur during smolt development.

The size-dependency of smolt development in Atlantic salmon has been used to examine the interaction of photoperiod and development in controlling the parr–smolt transformation (McCormick et al. 2007). Parr that are <11 cm in January and kept under normal daylength have low levels of growth hormone and cortisol in late spring and do not develop increased gill Na^+/K^+-ATPase activity or salinity tolerance (Fig. 2). Juveniles that are larger than 12 cm in January show increased levels of growth hormone and cortisol in late spring and large increases in gill Na^+/K^+-ATPase activity. This difference in development can be directly linked to the difference in responsiveness to photoperiod between large and small juveniles. When exposed to an advanced photoperiod of 16 h light in February, large juveniles show increased levels of plasma growth hormone after 1 week and increased

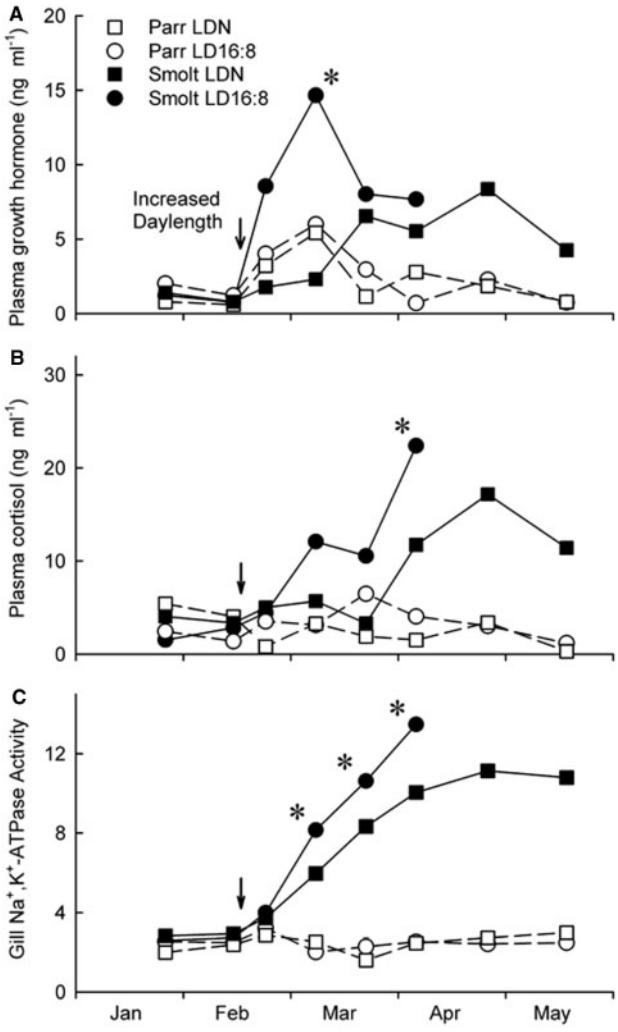

Figure 2 The interaction of size-related development and photoperiod in the control of (**A**) plasma growth hormone, (**B**) cortisol, and (**C**) gill Na^+/K^+-ATPase activity in juvenile Atlantic salmon (McCormick et al. 2007). Juveniles of the same age that were smaller than 11 cm (parr) or larger than 12 cm (smolt) in January were separated and exposed to normal daylength (LDN) or long daylength (16:8) in mid-February. Smolts respond to increased daylength with increased levels of plasma growth hormone and cortisol, whereas parr do not show a photoperiodic response for these hormones. Asterisk indicates a significant difference from the LDN group at the same time point.

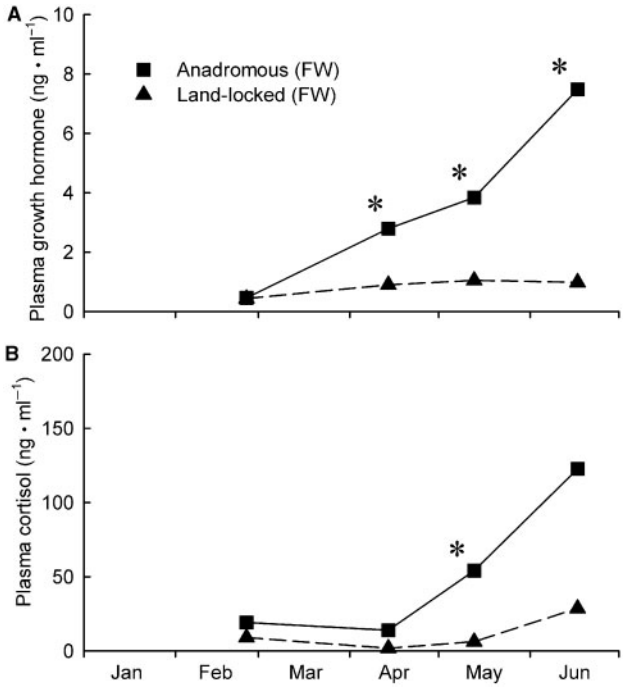

Figure 3 Levels of (**A**) plasma growth hormone and (**B**) cortisol of anadromous and landlocked strains of Atlantic salmon reared under identical conditions (Nilsen et al. 2008). Asterisk indicates a significant difference of the anadromous from the landlocked strain at the same time point.

levels of plasma cortisol after three weeks, and these increases are followed by an advanced development of gill Na^+/K^+-ATPase activity. In contrast, plasma growth hormone and cortisol in small juveniles is not responsive to increased daylength in February. The mechanism for the size-related increase in sensitivity of growth hormone and cortisol to daylength has not been established, but one possible pathway is an increase in retinal innervation of the hypothalamus in larger juvenile Atlantic salmon in early spring (Ebbesson et al. 2003).

Further evidence of the importance of growth hormone and cortisol in regulating smolt development can be seen in the comparison of anadromous and landlocked strains. "Landlocked" strains of Atlantic salmon have developed in many lakes and are generally thought to have been derived from anadromous forms. The landlocked Bleke strain from southern Norway has been isolated for ~10,000 years; juveniles reside in rivers and then migrate into the lake at a similar size as anadromous smolts. Thus, the marine life-history phase is absent in these landlocked strains, resulting in relaxed selection on demands imposed by the marine environment such as salt secretion. When reared under the same conditions, smolts of the anadromous strain from the Vosso River had substantial increases in levels of plasma growth hormone and cortisol during the spring, whereas fish of the same size from the landlocked strain had only moderate increases (Fig. 3). The anadromous strain also had larger increases in gill Na^+/K^+-ATPase activity, and when each strain was exposed to seawater in early May the anadromous strain had no mortality whereas the landlocked strain experienced 40% mortality over 3 weeks (Nilsen et al. 2003). Interestingly, the landlocked fish that do

survive the initial exposure to seawater show increased levels of growth hormone, cortisol and greater branchial Na^+/K^+-ATPase activity in the gills, suggesting an increased capacity for salt secretion after exposure to seawater (Nilsen et al. 2008).

In addition to the strong correlations between increased plasma levels of growth hormone and cortisol and the development of salinity tolerance, there is direct evidence for these hormones' involvement based on treatment with exogenous hormones. A number of studies have shown that growth hormone and cortisol can independently affect tolerance to seawater in salmonids, and that salinity tolerance comparable to that of smolts can be achieved if the two hormones are injected together (McCormick 2001). The number and size of branchial chloride cells and the abundance of Na^+/K^+-ATPase and NKCC are similarly upregulated individually by growth hormone and cortisol, and together act additively or synergistically (Madsen 1990; Pelis and McCormick 2001). The intestine is also a target of endocrine control of homeostasis of ions and water during smolt development (Veillette et al. 1995), and although the renal tissue is also likely to be affected, this has not been examined. There are several pathways through which growth hormone and cortisol may interact in promoting development of seawater tolerance to seawater. Growth hormone increases the abundance of gill cortisol receptors, which will make gill tissue more responsive to any level of endogenous cortisol (Shrimpton and McCormick 1998a). Growth hormone has also been shown to increase the sensitivity of the interrenal tissue to adrenocorticotrophic hormone (Young 1988).

The evidence outlined above indicates that there is a size-related, heightened sensitivity for growth hormone and cortisol to respond to increased daylength, and this is an important foundation for smolt development in Atlantic salmon (Fig. 4). These changes, in turn, result in an increased capacity for survival after transfer to seawater with less ionic and osmotic perturbations, an example of ''regulatory performance'' (Husak et al. 2009). Are these hormones also involved in other ecologically relevant aspects of performance, such as growth and swimming capacity, after entry into seawater? We treated Atlantic salmon parr with growth hormone, cortisol and the two hormones together for 12 days in fresh water (McCormick 1996), and examined their impact on growth and swimming performance after exposure to salinity. Prior treatment of Atlantic salmon parr with cortisol for 12 days in freshwater significantly improved growth rate for the first 3 weeks following transfer to seawater ($P = 0.04$); growth hormone by itself had no detectable effect, but the greatest impact on growth in seawater was when the two hormones were combined (S.D. McCormick, unpublished manuscript). Prior treatment with growth hormone ($P = 0.02$) and to a lesser extent cortisol ($P = 0.09$) in freshwater for 12 days improved the maximum sustained swimming capacity (U_{crit}) of salmon parr after exposure to elevated salinity, and the combined hormone treatment had the greatest effect, increasing U_{crit} by 25%. The effect of hormones on U_{crit} was not seen in fish tested in freshwater, indicating that the effect is likely due to the influence of these hormones on the capacity to secrete salt, but we are examining whether they may also act through other tissues such as blood, heart, or muscle.

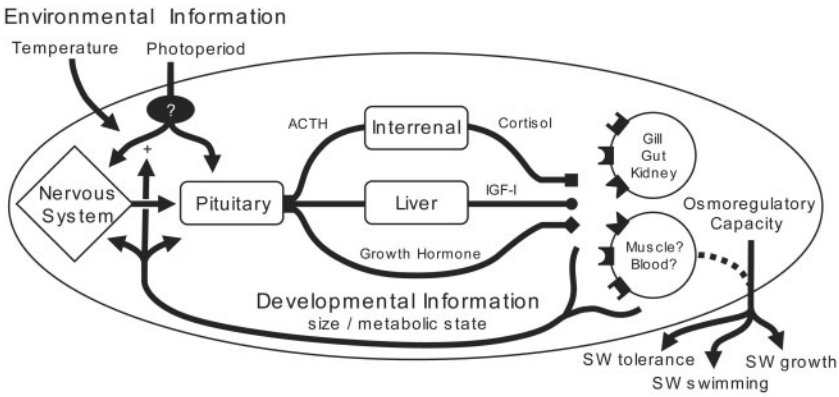

Figure 4 Interaction of size-related development and photoperiod (along with other environmental factors) in the endocrine control of performance of juvenile salmon in seawater. Size-related development causes increased responsiveness of the GH/IGF-I and cortisol axes to photoperiod. Growth hormone, IGF-I, and cortisol interact at the osmoregulatory organs (and perhaps other tissues) and increase performance in seawater.

Variations among salmonids in the timing and control of performance in seawater

> "It is diversity among lineages in physiology and development that hold the key to understanding the comparative patterns of life-history variation" (Stearns 1992, p. 204).

Salmonids are generally recognized as having a freshwater ancestry, with many of the basal groups being restricted to freshwater (Wilson and Li 1999; Crespi and Fulton 2004). Within the more advanced subfamily Salmoninae, containing the genera *Salvelinus*, *Salmo*, and *Oncorhynchus*, there is variation in the degree and timing of anadromy within and among species. Brook trout (*Salvelinus fontinalis*), brown trout (*Salmo trutta*), and rainbow trout (*O. mykiss*) have mainly freshwater populations, but with anadromous populations present in many coastal rivers. In brook trout there appears to be no preparatory phenotypic plasticity, and the ability to move into seawater is gradually acquired by larger individuals through exposure to intermediate salinity (McCormick et al. 1985). Anadromous populations of brown trout and rainbow trout (the latter known as steelhead) show some preparatory increases in salinity tolerance, which are absent in nonanadromous populations (Mcleese et al. 1994; Pirhonen and Forsman 1998). Recent phylogenetic analysis indicates that increased anadromy in more recently derived species has occurred independently in *Salmo* and *Oncorhynchus* (Crespi and Fulton 2004). Atlantic and coho salmon spend at least a year in freshwater, whereas pink and chum salmon (*O. gorbusha* and *keta*) develop tolerance to seawater and migrate downstream soon after hatching. Thus, there is a heterochrony in development of salinity tolerance among salmonids, with the most advanced species showing earlier development that involves a shift in both timing of development and the environmental factors that cue salinity tolerance (McCormick 1994). In the most primitive forms with facultative anadromy, such as brook trout, salinity itself acts as an important cue for the development of the capacity for salt secretion. In species such as Atlantic salmon in which anadromy is the norm, there has been a shift to using photoperiod as the primary cue to develop mechanism for salt secretion in advance of entry into seawater. In pink and chum salmon, salinity tolerance appears to be driven solely by development (and occurs much earlier than in other salmonids), and is largely independent of environmental conditions (Clarke et al. 1989).

The capacity to respond to salinity in non-anadromous forms appears to involve both growth hormone and cortisol. As with Atlantic salmon, exogenous growth hormone and cortisol can affect salinity tolerance in non-anadromous forms (Bolton et al. 1987; Almendras et al. 1993). Plasma cortisol, metabolic clearance rate, and gill cortisol receptors increase after brook trout are exposed to seawater (Weisbart et al. 1987). Although circulating growth hormone does not consistently increase in response to seawater in trout, metabolic clearance rates and number of gill receptors increase, indicating increased hormone production and utilization by receptors (Sakamoto et al. 1990; Sakamoto and Hirano 1991). As noted above, landlocked Atlantic salmon have retained the capacity to respond to exposure to salinity with increased growth hormone and cortisol. In anadromous forms that show clear smolt development, changes in circulating levels of growth hormone appear to be primarily responsible for developmental and environmental regulation of smolting. Levels of cortisol receptors in the gill are high in both parr and smolt (Shrimpton and McCormick 1998b), and parr are responsive to growth hormone and cortisol treatment many months before smolt development (McCormick 1996). However, receptors and tissue responsiveness may be involved in the early development of salinity tolerance that occurs in pink and chum; gill tissue of chum salmon can respond to changes in level of cortisol by increasing gill Na^+/K^+-ATPase activity soon after hatching, whereas chinook and coho salmon are unresponsive at the same developmental stage (McCormick et al. 1991). Thus, it would appear that both circulating levels and changes in receptors for growth hormone and cortisol are involved in the shifts in environmental and developmental control that accompany the heterochrony in salmonid anadromy.

A predictive framework for endocrine control of performance: the discontinuous selection hypothesis

It is clear from the discussion above and from other papers presented in this symposium that hormones often play a role in both dynamic and regulatory performance (Husak et al. 2009). Migration and metamorphic events appear to be universally driven by hormones that integrate developmental and environmental information, and likely represent one end of a continuum in which hormones are critical for performance. Is it possible to predict when hormones will be involved in animal performance

and their underlying traits? In the following section, I will present arguments that endocrine involvement in performance will be more likely when (1) selection differentials on traits underlying performance are high and temporally discontinuous over an animal's lifetime, (2) the energetic and fitness costs of maintaining performance plasticity are less than those of constant performance, (3) cues for altering performance are reliable indicators of critical environmental conditions, require neurosensory input, and minimize effects of lag, and (4) the need for coordination of organs, tissues and cells to achieve increased performance is greater.

Continuous and discontinuous selection

For many animals the presence of environmental factors that affect fitness may be relatively continuous over their lifetime. They may reside in relatively constant environments that we might view as benign, such as the tropics, or more extreme environments, such as deserts or hot springs, which place extreme but constant demands on an organism. In both of these cases, selection for dynamic and regulatory performance will be nearly constant over an animal's lifetime, driving a relatively constant physiology and morphology (Fig. 5). Most oceanic fish do not have the capacity to survive in freshwater, and most freshwater fish cannot survive for long in salinities higher than their own internal osmotic pressure (one-third seawater) (Evans 1984). Although a completely fixed phenotype is rarely realized, low phenotypic plasticity is a likely consequence of reduced environmental variability. During long (evolutionary) periods of environmental stasis, adaptive plasticity will be lost (Masel et al. 2007).

Animals that experience significant changes in environmental conditions that affect fitness as part of their normal life history will gain a selective advantage by altering their capacity for survival under those conditions. Migration and metamorphic events present a special case of niche shift in which there is a developmentally and/or temporally driven change in habitat (Denver 1997). These species represent clear examples in which hormones control changes in performance (performance plasticity) with strong consequences for fitness (it seems unlikely we need to test the relative ability of tadpoles and frogs to survive on land). Many animals that do not migrate will nonetheless experience alterations in environmental conditions that affect survival and reproduction. Seasonal changes in temperate and sub-arctic habitats seem the most obvious of these, as animals in these habitats will experience large changes in temperature, availability of water and food, predation pressure, physical habitat, and many other factors. Moran (1992) argued that temporal changes are much more likely to promote phenotypic plasticity (and by extension performance plasticity) than are spatial changes. There are many examples of seasonal changes in capacity of animals

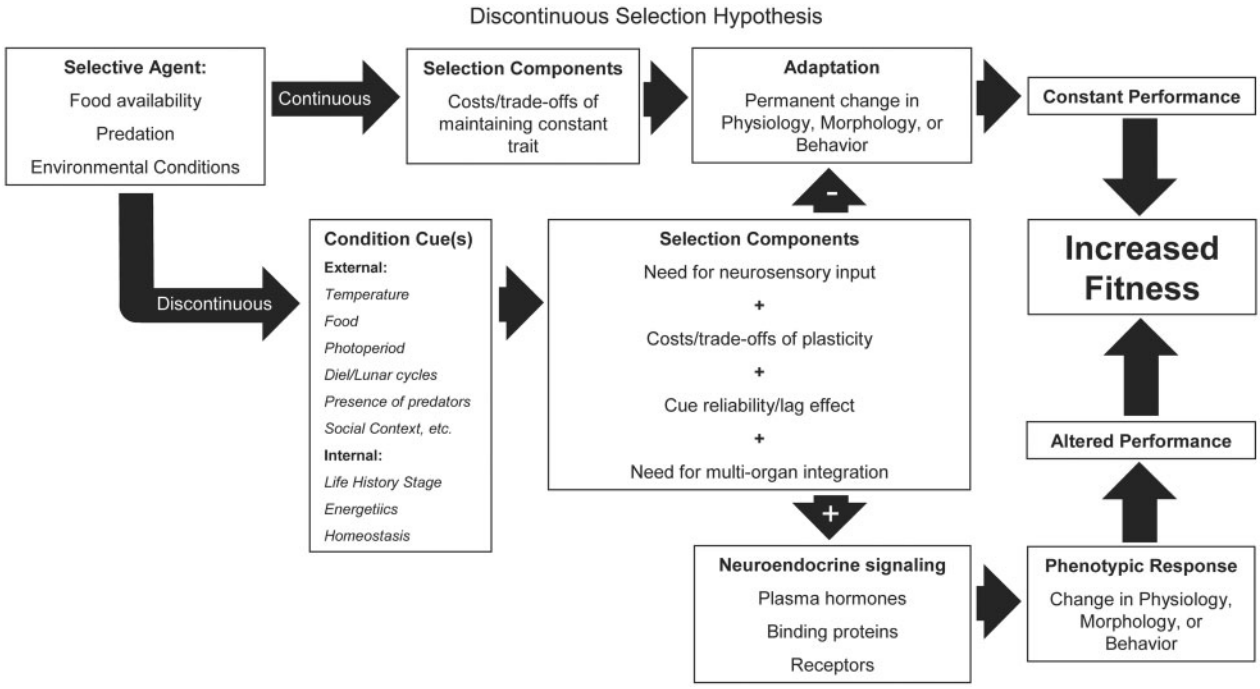

Figure 5 The discontinuous selection hypothesis for the endocrine control of changes in performance.

to digest food and grow or to withstand high temperature or freezing conditions (Willmer et al. 2005). In fish, prior exposure to low temperature improves swimming performance and growth at that temperature (Brett and Groves 1979). Thus, both regulatory and dynamic performance can be altered seasonally.

In addition to the many aspects of seasonality, other temporal changes in environmental conditions may be associated with endocrine-controlled alterations in performance. Lunar periodicity is important for many animals, especially for intertidal and reef dwellers, and even terrestrial animals that may be exposed to increased predation during full moon. Lunar rhythms of activity and reproduction occur in many species (Takemura et al. 2004), and may be associated with altered performance. Circadian rhythms control a number of motivational behaviors including the classic wheel-running behavior of hamsters, and cognitive performance in humans. Similar rhythms may exist in many animals and have important consequences for nocturnal-diurnal behavior and survival. Although many hormones, including melatonin, display diurnal cycles, the relationship between these and performance has not been fully established (Blatter and Cajochen 2007).

In addition to the alterations in selection imposed by environmental change, life-history events will also impose discontinuities in the factors that impact survival and reproduction. The shift from an actively growing juvenile to a reproductively mature adult has been shaped by prior selection and has been the focus of much theoretical and empirical work (Stearns 1992; Pigliucci 2001). There appear to be trade-offs in relative fitness between allocating resources to offspring versus those needed by the parent for continued survival and growth. The alteration in selection imposed by competition for mates and by allocation of resources to young can be viewed as a discontinuous selection that occurs when moving from a nonreproductive to a reproductive state. It is becoming increasingly apparent that hormones are involved in assessing the energetic state of the individual and in determining the timing of critical life-history events (Ketterson and Nolan 1992; Zera and Harshman 2001; Wingfield 2008; Lessells and Kate 2008; Ketterson ED, Atwell JW, McGlothlin JW, submitted for publication; Moore and Hopkins, submitted for publication). Especially for seasonal breeders, there appear to be critical periods during the year in which assessment of energetic stores may determine whether reproduction takes place (Rowe and Thorpe 1990; Silverstein et al. 1997). In addition, internal and external stressors may be a means of assessing risk and causing delay or abandonment of reproductive effort (Cyr and Romero 2007). This capacity for assessing environmental information applies not just to abiotic factors such as photoperiod and temperature, but also to biotic factors such as the presence and size of conspecifics or predators. A particularly compelling example is the sex change that occurs in bluehead wrasse (*Thalasoma bifasciatum*) in which territories are held by the largest male; if all large males are removed, the largest female will become the dominant male (Warner et al. 1975).

The ontogenetic development of performance traits is nearly universal in vertebrates with an inherently complex early development, likely due to the evolutionary constraints imposed by the development of size and complexity (Gould 1977). Hormones are involved in many aspects of embryological development (West-Eberhard 2003), and one can hypothesize that this may have been their earliest evolutionary function. Indeed, the importance of hormones in development may have provided the ''raw material'' for hormones to be involved in phenotypic plasticity. As noted above, constantly extreme habitats should result in high performance under the conditions present in that habitat, and the underlying traits may be fixed by hormones early in development. For instance, muscle mass or limb length varies greatly among species and is linked to higher running performance; in many cases these differences are established early in development and controlled by hormones. Thus, the absence of changes in performance over an animals' postembryonic lifetime does not preclude the involvement of hormones, but rather that the capacities have to a great degree already been established early in development.

Fitness and energetic costs in altered performance

There is a robust literature on the costs and trade-offs involved in maintaining phenotypic plasticity that directly relates to the capacity to alter performance (see references in Via et al. 1995; Dewitt et al. 1998; Pigliucci 2001). Some confusion exists about these terms that I hope to avoid in the following discussion. There are fitness costs, associated with the effects of selection for one adaptation (the growth of spines enhancing avoidance of predation) affecting other aspects of fitness (e.g. the presence of a spine decreasing ability to capture food). There are also energetic costs, which have the potential to affect fitness through a number of pathways including growth and reproduction.

The presence of performance plasticity will be strongly influenced by the fitness costs of altered

performance relative to constant performance. If there are strong fitness costs associated with constant high performance (e.g., if the presence of anti-freeze proteins compromises swimming ability at warm temperatures), then selection should favor a variable phenotype in which performance appears at a time appropriate for the environmental challenge. This will be balanced by a number of factors. There will often be a lag between the time increased performance is needed and when it can be constructed (Dewitt et al. 1998; Nishimura 2006) (discussed in greater detail below). There is evidence that phenotypic plasticity is associated with developmental instability, which can decrease fitness (Scheiner et al. 1991). In some cases of altered performance there may be an ''epiphenotype'' problem, in which a structure that develops late in ontogeny (an ''add-on device'') is inferior to those that develop early (Dewitt et al. 1998).

Both constant performance and variable performance will have energetic costs associated with building and maintaining the underlying traits. Building costs are presumably greater for plastic traits in which construction may occur several times during the animal's lifetime. The energetic costs of both building and maintenance may also vary as a function of when they occur during development. For variable performance there may also be costs associated with removing traits. Maintenance costs will also accrue to both constant and altered performance, although these are presumably less for plastic traits which exist for shorter periods of time. Finally, there may also be energetic costs associated with the development and maintenance of a sensory-response system for altered performance (Dewitt et al. 1998; Lessells and Kate 2008). For most animals, the neuroendocrine system already exists as a complex sensory-response system and does not require the *de novo* creation or maintenance. The prior existence (for other functions) and co-option of the neuroendocrine system to new regulatory pathways will make it difficult to separate the energetic costs of neuroendocrine signaling.

Environmental cues and developmental signaling

In many, and perhaps in most, cases of phenotypic plasticity, ''the environmental variable that induces the alternative phenotype is a token stimulus that serves as a predictor of, but is not itself, the environment to which the polyphenism is an adaptation'' (Nijhout 2003). Development of predator-evading spines or chloride cells that secrete salt may take days or even weeks, but their need in the face of environmental challenge may be immediate. The use of a ''surrogate'' cue likely evolved as a result of increased fitness resulting from the removal of lag time between exposure to potentially lethal environmental conditions and the time required to make or alter structures (proteins, cells, and tissues) responsible for increased performance. This lag effect between the time to develop an adaptation and ''need'' in the face of changing environmental conditions may, in fact, be an impediment to phenotypic plasticity in general (Dewitt et al. 1998), but may also explain why surrogates such as photoperiod and other reliable cues are widely involved in preparatory phenotypic plasticity. Thus, many phenotypic changes may be induced by reliable cues for the presence of altered environmental conditions, predators, food, or mates, such as changes in daylength, temperature, crowding, and pheromones. These cues must be both reliable and provide sufficient advanced notice of altered conditions to be effective. In most cases, the detection of these cues requires sensory input from outside the body and communication to the interior (via a neuroendocrine system) where phenotypic response takes place. As noted above, in salmonids with a facultative form of anadromy salinity exposure itself is the primary cue for development of the mechanisms for salt secretion, whereas in salmon in which anadromy is the predominant life-history strategy preparatory phenotypic response using environmental and/or developmental cues is the norm. The shift from phenotypic plasticity to preparatory plasticity involving predictive cues in more advanced lineages may be a common feature of the hormonal control of performance (Nijhout 2003); understanding the evolution of these altered regulatory pathways will be an important area of research.

In some cases, environmental factors that are the focus of an adaptation can themselves act as a cue for controlling performance. Exposure to increased temperature may itself be a signal for changes in membrane composition, and protein isoforms and abundance that confer increased thermal tolerance and muscle performance at high or low temperatures (Willmer et al. 2005). This is a reliable cue, especially in most ectotherms, whereby the entire body is exposed to ambient temperature conditions and thus is a reliable signal for exposure. Availability of food is another important environmental factor that can control performance. In previously fasted snakes availability of food, or more specifically the amount of food in the gut, can induce hyperplasia and elevate digestive capacity of the gut (Arnold 1983).

As noted above for the case of smolt development of salmon, altered performance is associated with a life-history event that occurs at a particular stage of development. One of the most important life-history events is the development of reproductive maturation (puberty), which varies among species and is at least in part regulated by size, age, and developmental state. Thus, a system for determining and signaling the developmental and energetic state of an animal exists for many types of endocrine control of performance. But what are the mechanisms of this system? How does an individual know how big or old or fat it is, and how is this translated to a physiological response? Puberty is induced by increases in pulsatile secretion of gonadotropin releasing hormone from the hypothalamus, which itself is controlled by excitatory factors (primarily glutamate and kisspeptin) and inhibitory factors (primarily GABAergic and opiatergic neurons) (Ojeda et al. 2006). This control system is in turn impacted by hormones involved in growth and metabolism such as IGF-I (Ojeda et al. 2006). Many details of these internal signals and their integration are still lacking, and few have been subjected to comparative approaches (Ketterson and Nolan 1992; Ebling 2005). Thus, understanding the developmental signals involved in life history decisions, their underlying neuroendocrine pathways, and how they have been shaped by evolution will be an important area for future research.

Coordination of complex traits underlying performance

Irschick et al. (2008) have argued that the strength of selection will be greater for animal performance than their underlying phenotypic traits because the former is more directly related to fitness. Regulatory and dynamic performances are often controlled by a number of phenotypic traits in different organs, tissues, and types of cells (Husak et al. 2009). In the case of salt secretory capacity necessary for the survival of teleosts in seawater, the intestine first absorbs water and ions, the gill then secretes excess sodium and chloride (the bulk of the ionic load), and the kidney excretes excess divalent ions. There are several cell types within the gill, but only chloride cells are the site of sodium and chloride secretion, and these cells have numerous number of receptors that are responsiveness to growth hormone and cortisol (McCormick 2001). Muscle, nerve, tendon and bone may all be involved in altering complex dynamic performances such as jumping, running, and swimming. Exercise in humans is a strong stimulator of circulating levels of growth hormone which, along with endocrine and paracrine IGF-I, increases erythropoiesis by the bone marrow, cardiac contractility, lipolysis in adipose tissue, and hypertrophy of muscles that combine to increase strength and endurance (Gibney et al. 2007). Thus, the capacity to coordinate multiple tissue systems throughout the body may have resulted in selection for endocrine control of performance plasticity.

It has long been recognized that through their ability to control and coordinate complex responses, hormones are a strong target of selection and may be involved in many evolutionary innovations (Gould 1977; West-Eberhard 2003). The large number of genes involved in the sensory-response capacities of the neuroendocrine system present a number of targets for evolution to finely tune developmental and environmental responses. That is not to say, however, that optimal performance is achieved. Because hormones move throughout the body and control a variety of responses, selection for one trait may cause the promotion of another trait that can reduce fitness, i.e., a negative or antagonistic pleiotropy. Hau (2007) presented a framework for understanding and testing whether hormones control responses in several tissues that are always linked (evolutionary constraint hypothesis), or alternatively can evolve tissue-specific responses (evolutionary potential hypothesis). Although specifically applied to male traits and testosterone, it seems that this approach may also apply to many hormones (such as cortisol) that have broad regulatory capacities with apparent benefits under some conditions but potentially negative long-term consequences. This, and other developmental constraints, may limit the capacity of selection to alter endocrine control of performance.

Perspectives

The need for detecting changes in the internal and external environment and bringing about coordinated responses are reasons to predict that the endocrine system is involved in controlling performance when performance changes over the lifetime of an individual. If these are not necessary attributes, altered performance under discontinuous selection may nonetheless exist, but control by hormones may be absent. Individual cells have a substantial capacity for controlling their own homeostasis and responding to their local environment. Temperature can induce the production of heat-shock proteins that can increase the capacity of tissues and organisms to withstand lethal

temperatures without the involvement of the neuroendocrine system (Feder and Hofmann 1999a). Thus, discontinuous selection may result in plasticity in animal performance, but not all of them will be controlled by hormones.

Migratory and metamorphic species provide solid examples of how hormones can control performance and survival in a new habitat. In more subtle examples of phenotypic plasticity, it will be important to connect endocrine mechanisms to the multiple traits they control, determine how these influence performance, and in turn determine the relationship of performance to survival and reproductive success (Arnold 1983). This is a component that is critical for demonstrating the adaptive value of the traits discussed here, and which have been proposed and discussed largely through an adaptationist program. Many aspects of this framework are open to modeling and testing. Manipulation of hormone levels or inhibition of receptors followed by measurement of performance and survival in the wild, especially under different environmental conditions, should provide an important tool (John-Alder HB, Cox RM, Haenel GJ, Smith LC, submitted for publication). Determining the mechanisms of developmental and environmental control of performance using a comparative approach should provide information on where endocrine mechanisms are involved in performance (Harvey and Purvis 1991). By examining the mechanisms involved in controlling performance, endocrinologists have an opportunity to contribute to the understanding of how evolutionary forces have shaped endocrine responses, and how future environmental change will affect the survival, growth, and reproduction of animals.

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