



SYMPOSIUM

Cellular Respiration: The Nexus of Stress, Condition, and Ornamentation

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From the symposium “Stress, Condition and Ornamentation” presented at the annual meeting of the Society for Integrative and Comparative Biology, January 3–7, 2014 at Austin, Texas.

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Synopsis A fundamental hypothesis for the evolution and maintenance of ornamental traits is that ornaments convey information to choosing females about the quality of prospective mates. A diverse array of ornaments (e.g., colors, morphological features, and behaviors) has been associated with a wide range of measures of individual quality, but decades of study of such indicator traits have failed to produce general mechanisms of honest signaling. Here, I propose that efficiency of cellular respiration, as a product of mitochondrial function, underlies the associations between ornamentation and performance for a broad range of traits across taxa. A large biomedical literature documents the fundamental biochemical links between oxidative phosphorylation (OXPHOS) and the production of reactive oxygen species (ROS), the process of metabolism, the function of the immune system, the synthesis of proteins, and the development and function of the nervous system. The production of virtually all ornaments whose expressions have been demonstrated to be condition-dependent is directly affected by the efficiency of cellular respiration, suggesting that the signaling of respiratory efficiency may be the primary function of such traits. Furthermore, the production of ornaments links to stress-response systems, including particularly the neuroendocrine system, through mitochondrial function, thereby makes ornamental traits effective signals of the capacity to withstand environmental perturbations. The identification of a unifying mechanism of honest signaling holds the potential to connect many heretofore-disparate fields of study related to stress and ornamentation, including neuroendocrinology, respiratory physiology, metabolic physiology, and immunology.

Introduction

For more than three decades, behavioral, evolutionary, and physiological ecologists have been fascinated by the idea that the quality of an ornamental display might signal key information about an individual's condition (Zahavi 1975; Kodric-Brown and Brown 1984; Andersson 1994; Møller 1994; Hill 2002; Warren et al. 2013). Many studies have shown links between ornamentation and various measures of condition, including recovery from, and resistance to, parasites (Møller 1994; Lindström and Lundström 2000; Roulin et al. 2001; Hill and Farmer 2005), immunocompetence (Reid et al. 2005; Mougeot 2008), oxidative state (Pérez-Rodríguez et al. 2010), capacity to survive an epidemic (Nolan et al. 1998; Van Oort and Dawson 2005), moderation of stress-response (Douglas et al. 2009; Almasi et al. 2010), cognition

and problem-solving (Keagy et al. 2011; Mateos-Gonzalez et al. 2011), and quality of sperm (Peters et al. 2004; Helfenstein et al. 2010; Navara et al. 2012). Despite this focused interest, studies of condition-dependent signaling lack coherency (Warren et al. 2013).

The failure to uncover general mechanisms linking ornamentation to individual condition is at least in part a consequence of the lack of a clear and comprehensive definition of the concept of condition. In a recent essay, I proposed condition to be “the functionality of vital cellular processes” such that “A condition-dependent display trait is a conspicuous feature of an organism that varies in expression depending on the capacity to withstand environmental challenges” (Hill 2011). These definitions help to clarify what is meant by the concept of condition

and how ornamentation can serve as a signal of condition, but they retain significant ambiguities regarding which of many vital cellular pathways potentially underlie the execution of ornamentation. Here, I further clarify the concept of condition by proposing that the core cellular process that determines the condition of animals is cellular respiration. I propose that most condition-dependent ornaments are signals of the efficiency of cellular respiration and that cellular respiration links stress-response systems, particularly the neuroendocrine system, to the production of ornamental traits.

Testable assumptions

The hypothesis that cellular respiration is the fundamental biochemical process signaled by ornaments provides a testable hypothesis for the mechanistic basis for condition-dependency and honest signaling. For this hypothesis to be an accurate description of natural systems, three key assumptions must be met: First, within populations, individuals must vary in their efficiency of cellular respiration. Mitochondrial functionality, which dictates respiratory efficiency, is a result both of intrinsic and of extrinsic factors (Burton et al. 2013; Pereira et al. 2014). Intrinsic effects on cellular respiration arise from genetic interactions that are independent of the extra-organismal environment. In contrast, extrinsic effects on cellular respiration arise from impacts of the environment on mitochondrial function. There is abundant evidence from model systems studied in laboratory environments that intrinsic effects, and especially mitochondrial–nuclear genetic interactions, can generate within-population variation in mitochondrial function (Frank and Hurst 1996; Gemmell et al. 2004) including the functionality of cellular respiration (McKenzie et al. 2003; Smith et al. 2010; Pereira et al. 2014). The few studies that have examined cellular respiration in wild animals indicate that there is also substantial variation in natural populations, with important effects on organisms' performance (Salin et al. 2010, 2012).

A second key assumption is that mitochondrial function can be affected by environmental perturbations. In other words, extrinsic effects on mitochondrial function can lead to variation in respiratory efficiency (Pereira et al. 2014). The effects of a wide range of stressors on mitochondrial function and the central role that mitochondria play in stress–responsiveness are focal topics in the biomedical literature (e.g., Manoli et al. 2007) but have been largely unexplored within the realm of wild animals responding to environmental challenges. Much of

this article will focus on reviewing the mechanisms that link environmental stressors to mitochondrial function.

Finally, the third critical assumption is that efficiency of cellular respiration affects the production of condition-dependent ornaments. The central premise of this hypothesis is that a choosing female cannot directly assess the cellular respiration of a prospective mate. Ornaments evolve as conspicuous, easily perceived, and assessed signals of the efficiency of cellular respiration. I spend the last sections of this article reviewing available evidence that ornamentation signals the efficiency of cellular respiration.

The hypothesis that I propose is that a vital life-process underlies honest signaling in a diversity of ornaments. The identification of such a unifying mechanism holds the potential to connect fields of study related to stress and ornamentation, including neuroendocrinology, respiratory physiology, metabolic physiology, and immunology.

Cellular respiration—the core life-process in animals

Life persists by capturing energy from the environment and using energy to organize molecules into more copies of itself (Lane 2010). Energy both enables and constrains life. For animals, energy is made available for life-processes via respiration—the slow combustion of carbohydrates, fats, and proteins through which the chemical energy in food is captured in ATP (adenosine triphosphate) or released as heat (Shutt and McBride 2013). Aerobic respiration involves three metabolic steps: glycolysis, the Krebs cycle, and oxidative phosphorylation (OXPHOS). Glycolysis occurs in the cytosol; the Krebs cycle takes place in the matrix of the mitochondria; OXPHOS occurs via the electron-transport chain and is carried out on the inner mitochondrial membrane. The efficiency of cellular respiration determines the number of ATP molecules derived from each unit of food, as well as the number of harmful free radicals that are created by the respiratory process (Brand 2005; Lane 2011a; Shutt and McBride 2013).

In this article, I focus primarily on the final stage in the respiratory process, the production of ATP by OXPHOS via the electron-transport system. OXPHOS is of special interest with regard to stress, condition, and ornamentation because: (1) it is the part of the respiratory process in which 90% of oxygen is consumed and from which most ATP is produced (Lane 2005; Wallace 2008), (2) it is the source of most of the free radicals that create the

oxidative state of an animal (Barja 2007; Lane 2011a; 2011b; Murphy 2009), (3) it is under regulatory control by retinoids (Hill and Johnson 2012) and glucocorticoids (Lee et al. 2013; Scheller and Sekeris 2013), (4) it is intimately linked to the synthesis of proteins (Lane and Martin 2010) and to the folding and maintenance of proteins (Simmen et al. 2010), and (5) it is dependent on the compatibility of products from mitochondrial and nuclear genes (Lane 2011a; Bar-Yaacov et al. 2012).

Approximately 90% of ATP is produced from OXPHOS via the transfer of electrons along the electron transport chain from a donor such as NADH to oxygen as the terminal acceptor (Lane 2005). This flow of electrons powers the pumping of protons across the inner mitochondrial membrane, establishing the membrane potential that ultimately leads to production of ATP from ADP. Efficient production of ATP depends on availability of oxygen and on an unimpeded flow of electrons along the electron transport chain (Lane 2011a). If there are structural problems with the complexes of the electron transport chain then the flow of electrons along the chain is impeded, leading to decreased output of ATP and increased leakage of free radicals (Murphy 2009). The release of cytochrome C under such conditions of poor OXPHOS performance can trigger apoptosis and the removal of cells that have compromised respiration (Hengartner 1998). Efficient respiration depends critically not only on the functional integrity of electron transport complexes, but also on the match between respiratory capacity, electron donors, and electron receivers (Brand and Nicholls 2011; Lane 2011a). If capacity is too low for the electron donors, the result is wasted energy and an increased production of free radicals (Barja 2007). In this case, free radicals play a critical role as signaling molecules (Dröge 2002), initiating the up-regulation of genes that code for respiratory capacity (Lane 2011a). Efficiency of cellular respiration is not simply a maximization of ATP production; rather, efficiency describes the matching of the output of energy to the need for energy, with minimal production of free radicals (Brand and Nicholls 2011; Lane 2011a).

The proposition that indicator traits signal the functionality of OXPHOS is inherently attractive because the fundamental premise of indicator traits has always been that they signal core aspects of an individual's quality (Kodric-Brown and Brown 1984; Zahavi 1975). Cellular respiration via OXPHOS lies at the very heart of eukaryotic function (Lane and Martin 2010; Wallace and Fan 2010). Numerous, apparently unrelated components of condition such as immunocompetence, oxidative state, energy reserves,

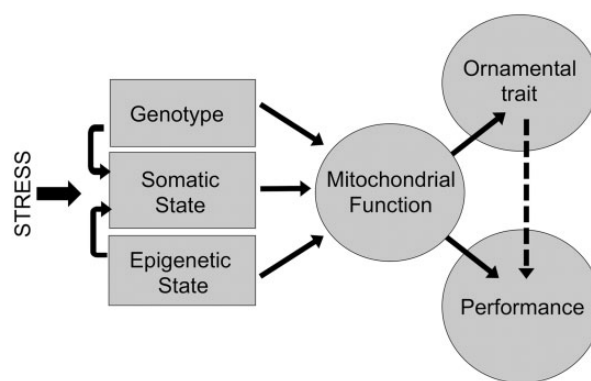


Fig. 1 A conceptual framework for the mechanistic connections between stress, condition, and ornamentation. Cellular respiration/mitochondrial function determine the condition of an individual. The efficiency of cellular respiration is a product of the somatic state of an animal as influenced by genotype and epigenotype. Stressors can also have a significant impact on somatic state and, in turn, on cellular respiration. The outcome of the efficiency of cellular respiration is the performance of the animal and the ability to produce ornaments. A choosing female can predict future performance by assessing the ornamentation of a prospective mate. Adapted from Hill (2011).

the neuroendocrine stress axis, and cognition are united in their close association with the process of OXPHOS and mitochondrial function. In this article I review the evidence for links between conventional measures of condition and mitochondrial function and discuss the implications of the hypothesis that cellular respiration is the nexus of condition, stress, and ornamentation (Fig. 1).

Mitochondrial function, efficiency of OXPHOS, and mitonuclear compatibility

The emergence and evolution of eukaryotes involved the chimeric union of two genomes now recognized as the nuclear and mitochondrial genomes (Dyall et al. 2004; Lane 2005). Even though these genomes likely began with approximately equal numbers of genes, the great majority of mitochondrial genes (mt genes) migrated to the nuclear genome, leaving only 34 mt genes in vertebrate animals (Lane 2005; Wallace 2007). Mitochondrial processes, however, are extremely complex and multifarious and involve the products of more than 1500 genes (Lopez et al. 2000). Thus, many nuclear genes produce proteins that are expressed in the mitochondria (N-mt genes). Proper functioning of the mitochondria, including efficient OXPHOS, requires both the appropriate production and function of N-mt genes and the appropriate production and function of mt genes (Calvo and Mootha 2010). In addition, the products

of some N-mt genes form complexes with, or interact in important ways with, the products of mt genes, and there must be close coordination of these interacting genetic systems (hereafter called mitonuclear compatibility) for full functionality of mitochondrial systems (Blier et al. 2001). Mitochondrial and nuclear components of these protein complexes not only must fit and function together, they must also be produced in stoichiometric proportions (i.e., there must be mitonuclear protein balance) (Woodson and Chory 2008; Hootkooper et al. 2013). Mitonuclear protein imbalance leads to reduced cellular respiration and triggers an unfolded protein response, a classic stress-response mechanism (Wu and Kaufman 2006; Mandl et al. 2013).

In this article, when I refer to poor mitochondrial function (mitochondrial dysfunction), I mean poor performance of the cellular and biochemical processes that are known to take place within mitochondria (Manoli et al. 2007). Mitochondrial dysfunction will include poor performance of OXPHOS, because this is a core mitochondrial process, but it will also include other biochemical processes carried out by mitochondria. Mitochondrial dysfunction can also relate to the number, size, and distribution of mitochondria within cells and across regions of the body (Duchen 2004). When there are specific ties to OXPHOS, I will refer to OXPHOS function rather than to mitochondrial function.

Stress, condition, and cellular respiration

Cellular respiration and oxidative stress

Along with ATP, the primary product of OXPHOS is reactive oxygen species (ROS). In general, production of less ROS is indicative of a well functioning electron transport chain (Murphy 2009; Lane 2011a). However, production of some ROS is critical for proper system function because ROS serve as key signaling molecules, regulating mitochondrial function (Mittler et al. 2011). Mitochondria also are primarily responsible for oxidative stress-responses that enable increased release of free radicals for defense against invaders and for signaling (Apel and Hirt 2004), or that lead to reduced release of free radicals, thereby protecting vital tissues (Foyer and Noctor 2005).

The molecular structure of cells, including proteins, nucleic acids, and lipids, can be damaged by the redox reactions that are initiated by ROS. The body neutralizes free radicals by employing a host of antioxidants that are both endogenously produced or derived from diet that can either donate or receive

electrons without becoming reactive molecules themselves (Radak et al. 2013). von Schantz et al. (1999) first articulated the hypothesis that ornamentation is a signal of individual condition because production of ornaments is sensitive to oxidative stress. Although von Schantz et al. did not focus on trade-offs, other biologists interested in honest signaling related to oxidative stress have proposed that production of ornaments diverts antioxidants away from the body's protective mechanisms (Aguilera and Amat 2007; Alonso-Alvarez et al. 2007; Costantini 2008). Hence, it is proposed that individuals subject to lower oxidative stress have more resources of antioxidant to use for production of ornaments, whereas individuals with higher oxidative stress have fewer resources (McGraw et al. 2010).

An alternative to the resource-allocation hypothesis is the shared-pathway hypothesis whereby the mechanisms of production of ornaments share functional pathways with core life-supporting pathways, such that ornamentation cannot be fully produced unless core life-supporting pathways are fully functional (Hill 2011). By this hypothesis, the link between the oxidative state of an animal and ornamentation is the functionality of cellular respiration. Mitochondrial dysfunction leading to increased release of free radicals also leads to reduced capacity for production of ornaments because ornament production depends on efficient mitochondrial function (Hill and Johnson 2013; Johnson and Hill 2013). I propose that it is not a tradeoff of resources—be they antioxidants, ATP molecules, lipids, or any other currency—but rather the pathways shared between ornament production and cellular respiration that is the basis for the persistent associations between oxidative state and ornamentation.

Stressors and the stress-response

In the physiological literature, there is a variable and somewhat inconsistent use of the terms “stress” and “stressor” (Buchanan 2000; Romero et al. 2009). Biologists commonly use the term “stress” to describe both the physiological response to a stressor as well as the stress-response itself (Romero et al. 2009). In this review, I will generally avoid the term “stress” except in general contexts when ambiguity is acceptable, and instead use the less ambiguous terms “stressor” and “stress-response”. I consider a stressor to be an environmental perturbation that disrupts the functionality of the organism (*sensu* Badyaev 2005; Hill 2011), whereas a

stress-response refers to the physiological responses brought about by a stressor (Buchanan 2000).

The overarching concept of stress is intimately linked to condition. Indeed, the signaling function of indicator traits is proposed to be “the capacity to withstand environmental challenges” (Hill 2011). Stressors are proposed to impact an individual’s condition and hence its ornamentation, while condition mediates the effects of an environmental stressor on system function (Fig. 1). Thus, two inter-related aspects of an individual are potentially signaled via condition-dependent ornamentation: (1) functionality under normal, non-stressful conditions and (2) functionality under duress caused by a stressor. The most useful ornaments will be those in which expression under optimal conditions indicates functionality under duress.

To make the point of the value of condition-dependent ornaments that signal integrity of systems under duress, an analogy can be drawn between financial systems and biological systems. Both are highly complex with inputs of resources, pathways through which resources are modified and repackaged, and end-products that contribute to the fitness (biological or economic) of the entity. The recent financial crisis that beset banks, in which a drop in the value of real estate acted as a powerful stressor on financial systems, could be thought of as analogous to the environmental perturbations that sometimes beset organisms. In the face of a poor market environment some banks failed, some survived in a seriously compromised state, and a few flourished. In other words, some had a higher capacity to maintain functionality of their system while under duress, while others did not. How useful would it have been for investors to have had honest signals of the quality of the internal systems of these financial institutions? If banks and investment firms had published uncheatable and easily perceived signals of the system’s integrity, such signals would obviously have been closely monitored by individuals choosing a bank in which to invest. Indicator traits are proposed to evolve as just such uncheatable and easily perceived signals of system-integrity (Kodric-Brown and Brown 1984), and I propose that they do so because ornamentation is intimately linked to cellular respiration (Fig. 1).

The stress axis, immune-response, and mitochondrial function

Hormonal control of mitochondrial function

The stress-response of vertebrates commonly is discussed within the context of the neuroendocrine

mechanisms involved in extra-cellular signaling (Wingfield et al. 1998; Buchanan 2000; Husak and Moore 2008). Indeed, the hypothalamic–pituitary–adrenal (HPA) axis is termed “the stress axis” (Herman and Cullinan 1997; Romero 2004). One of the primary outcomes of vertebrates’ stress-response is a change in immune responsiveness (Segerstrom and Miller 2004), and it has been proposed and widely discussed that condition-dependent ornamental traits are signals of immunocompetence (Hamilton and Zuk 1982; Folstad and Karter 1992; Westneat and Birkhead 1998). Hence, the honesty of ornamental signals often is proposed to emerge either from the cost of immune suppression that arises when testosterone is increased to stimulate the production of ornaments (Folstad and Karter 1992) or from tradeoffs in the use of immune-enhancing elements for ornamentation versus maintenance (Alonso-Alvarez et al. 2007, 2009). In such discussions of stress, condition, immunocompetence, and ornamentation, the missing linchpin is cellular respiration and mitochondrial function.

Mitochondria are among the primary sites of action of the steroid and thyroid hormones (Koufali et al. 2003; Psarra et al. 2006; Du et al. 2009; Lee et al. 2013). They primarily are responsible for meeting the energy demands of a stress-response by oxidizing energy-storing molecules that are mobilized from energy stores. Thus, stress hormones might be viewed as regulators of mitochondrial processes (Psarra and Sekeris 2009) and particularly OXPHOS (Scheller and Sekeris 2013); such that the links between stress hormones and system function play out through mitochondrial processes (Fig. 2). Stressors can have a direct effect on mitochondrial function and hence on cellular respiration. Indeed, a stress-response is largely a mitochondrial response (Manoli et al. 2007; Shutt and McBride 2013), and mitochondria employ a range of mechanisms, often under regulation of stress hormones, in response to stress (Manoli et al. 2007) including: (1) modifying the production of energy, (2) making more mitochondria in targeted tissue thereby providing greater respiratory capacity (Jornayvaz and Shulman 2010), (3) mediating rate of transcription–regulation both of mitochondrial and nuclear subunits of electron-transport complexes that control respiratory capacity (Psarra et al. 2006), (4) fever response (Mackowiak 1998), (5) controlling signal transduction to the nucleus and other organelles that coordinate whole-cell responses (Hamanaka and Chandel 2010), (6) generating ROS for signaling and defense (Underhill and Ozinsky 2002; Lambeth 2004), (7) regulating innate immune-responses (Arnoult et al. 2011; West et al.

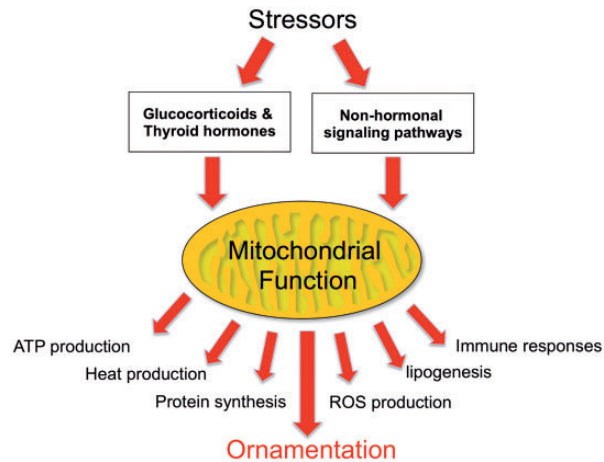


Fig. 2 A conceptual framework for the connections between the stress-response system, mitochondrial function, and key aspects of individual performance. Stressors affect various aspects of mitochondrial function via hormonal and non-hormonal signaling molecules, especially glucocorticoids via the HPA axis. Changes in mitochondrial function in turn affect a host of key aspects of the performance of individuals, including ATP production, heat production via uncoupling of the inner membrane, metabolic rate, lipogenesis, immune responsiveness, and oxidative state. Conventional views of the connections between ornamentation and the stress axis have focused on the effects of hormones *per se*, but moving the focus to the effects of mitochondria, under regulation of hormones, holds promise of clarifying the links between stress, condition, and ornamentation.

2011), and (8) regulating apoptosis of cells in affected tissues (Arnoult et al. 2009; Ohta and Nishiyama 2011). Each of these stress-responses is intimately related to cellular respiration.

Hormones affect mitochondrial function through action on nuclear and mitochondrial gene transcription (Psarra et al. 2006; Scheller and Sekeris 2013). Glucocorticoid receptors are present in mitochondria and the mitochondrial genome has elements of glucocorticoid response, suggesting that mitochondrial genes are under direct glucocorticoid control (Lee et al. 2013). Thus, it appears that mitochondrial function can be regulated by glucocorticoids either via direct action on mitochondrial OXPHOS genes or by indirect effects through interaction with nuclear genes that code for OXPHOS complexes (Lee et al. 2013).

Innate immunity and mitochondrial function

There are also direct connections between cellular respiration and immune-system response, and the metabolic control of immunity is a fast-growing field (Moore et al. 2008; West et al. 2011; Strowig et al. 2012). Mitochondrial bioenergetics is tightly linked to innate immunity and to the overall

immune-response (Lartigue and Faustin 2013). Mitochondria first gained attention as key regulators of innate immunity with the discovery of mitochondrial antiviral signaling protein (MAVS) (Seth et al. 2005), which plays a key role in recognition of viruses and activates a cascade of innate-response mechanisms. Subsequently, mitochondria were shown also to play a key role in bacterial defense (West et al. 2011). It is now well established that mitochondria sit at the core of innate immune signaling and are the primary effectors of immune-responses (Arnoult et al. 2011; West et al. 2011; Cloonan and Choi 2012).

Arnoult et al. (2011) proposed that by serving as the center of multiple pathways for innate immunity as well as for production both of ATP and ROS, mitochondria could coordinate tight functional integration of host-defense and metabolic processes. Moreover, functional coupling of innate immunity and mitochondria would ensure that efficient cell-intrinsic defense pathways involving release of ROS would only be activated in cells with appropriate mitochondrial membrane potential and oxidative state. These recent studies linking immune defense to mitochondrial function and cellular respiration provide an intriguing explanation for the often-observed associations between ornamentation, immunocompetence, and the oxidative state of wild animals (reviewed by Simons et al. 2012).

Mitochondrial function and metabolism

In many papers that focus on the condition of animals in natural environments, condition is defined as the amount of body fat—usually mass-corrected for body size but sometimes actual amount of fat in the body [discussed by Hill (2011)]. This conceptualization of condition is flawed for most animals in most environments because it assumes that animals are selected to maximize their amount of body fat, an assumption that often is not true (Rogers 1987; Witter and Cuthill 1993). However, there does seem to be a fundamental connection between condition and metabolism. Not coincidentally, mitochondrial dysfunction and, in particular, dysfunction of mitochondrial bioenergetics, has taken center stage in biomedical research on metabolic disorders (Koene and Smeitink 2011), including diabetes (Lane 2006), and in studies focused on diet and aging (Keagy et al. 2011; Shutt and McBride 2013). Cellular respiration in mitochondria provides the link between stress-response systems and metabolic regulation and function (Metallo and Vander

Heiden 2013; Morava and Kozicz 2013; Scarpulla 2012).

One especially interesting link between environmental stress and the production of ATP and ROS via OXPHOS is the metabolic intermediate nicotinamide adenine dinucleotide (NAD⁺). NAD⁺ is a central regulator of cellular energy homeostasis (Karpac and Jasper 2013) and the maintenance of an optimal NAD⁺/NADH ratio is essential for a fully functional electron-transport system and high output of ATP associated with low production of ROS. The synthesis and catabolism of NAD⁺ is sensitive to environmental conditions, especially nutrition and pathogens, thereby linking environmental stressors to metabolic activity (Hootkooper et al. 2013; Houtkooper et al. 2010). At present, metabolic studies of wild animals in ecological contexts are limited to measures of body-composition, oxygen consumption, and basal metabolic rates (Speakman et al. 2003). New insights into the mechanistic links between cellular respiration, fat stores, and ornamentation should emerge as studies begin to include specific pathways related to the control of mitochondrial processes.

Stress, condition, and ornamentation

I propose that the widely discussed associations between glucocorticoids, stress, ornamentation, and immune responses (e.g., Buchanan 2000; Bortolotti et al. 2009) arise as stressors affect mitochondrial function and hence affect ornamentation and performance, with hormones mediating these responses (Fig. 1). If this hypothesis is correct, then fundamental advances in understanding of responsiveness to stress will come not through studies of the mediators of metabolic responses but through studies of mitochondrial function.

Linking ornamentation to cellular respiration

Behavioral displays

The simplest links between cellular respiration and ornamentation involve ATP. If production of an ornament demands so much energy that high levels of ATP are required, then necessarily there is a direct connection between ornamentation and cellular respiration. Such a link between ornamentation and capacity for production of ATP is best demonstrated in the classic work on sexual selection in *Colias* butterflies. These insects were studied under variable thermal conditions, and different allelic variants of phosphoglucose isomerase (PGI) were favored in

different environments (Watt et al. 1983). PGI is responsible for the second step of glycolysis and thus plays a key role in production of ATP. Whether or not males had the correct PGI type for their thermal environment influenced their flight-display and females used flight-display as an important criterion for choosing a mate (Watt et al. 1986). Thus, the ornament (flight-display) served as an honest signal of functionality of the glycolytic system of a male under thermal stress, which has direct consequences for fitness (Watt et al. 1983). In this example it is efficiency of glycolysis rather than OXPHOS that is signaled by the behavioral display, but OXPHOS efficiency was not investigated. OXPHOS efficiency would also affect output of ATP and hence flight-display within this same *Colias* system.

Note that in this *Colias* butterfly system, it is the capacity to produce ATP rather than the size of the pool of previously produced energy that is signaled by flight displays. There is a need for in-time production of energy at a high rate for maximal flight-displays. Thus, in the *Colias* example there is no need to invoke tradeoffs between the use of energy for body maintenance versus its use for ornamentation (reviewed by Hill 2011). Indeed, there is little empirical support for tradeoffs in the use of stored energy as the basis for honest signaling in any system, and the shared-pathways hypothesis invokes no such tradeoffs. If the production of ornaments is dependent on immediate production of ATP and ATP-production is derived from the functionality of cellular respiration, then ornamental traits can serve as direct windows into the functionality of cellular respiration. The sorts of links between capacity for energy-production, system-performance, mate-choice, and cellular respiration that were observed for *Colias* butterflies seem likely to exist for many energy-demanding behavioral displays in a wide range of species.

Given that all functions of the body require energy, there is potential for competing energy demands to restrict production of ornaments, as proposed by Rowe and Houle (1996). However, a healthy system can respond to an increased demand for energy by increasing output (Barja 2007; Lane 2011b). I propose that it is not the availability of energy *per se* that is likely to be signaled by ornamentation but the capacity to produce energy. I predict that many of the behavioral displays of animals serve as uncheatable signals of the capacity for efficient energy production via cellular respiration.

Carotenoid pigmentation

Carotenoid coloration is among the classes of ornaments that are most frequently studied within the context of condition-dependent signaling (Cotton et al. 2006; Hill 2007; Garratt and Brooks 2012). Carotenoids were first proposed to be honest signals of the quality of a male because carotenoid pigments were viewed as scarce resources that were difficult to accrue such that only high-quality males could display bright coloration (Endler 1980; Hill 1992). More recently, the focus has been on the resource-tradeoff hypothesis, wherein carotenoids are proposed to be essential, but limited, resources needed for immune-defense and protection against free radicals (Møller et al. 2000; Alonso-Alvarez et al. 2007, 2009). By this hypothesis, only high-condition males can sacrifice carotenoid resources for ornamentation. However, even when access to carotenoid resources is not limiting, individuals often display significant variation in carotenoid coloration (Bortolotti et al. 1996; Karu et al. 2008).

The hypothesis that ornamental coloration is a signal of the functionality of cellular respiration (Hill and Johnson 2012) presents a novel explanation for the associations between carotenoid coloration and measures of performance such as the production of protein structures (Hill and Montgomerie 1994), oxidative stress (Cote et al. 2010; Pérez-Rodríguez et al. 2010), immunocompetence (Blount et al. 2003; McGraw and Ardia 2003), body fat (Pérez-Rodríguez and Viñuela 2008), and aerobic capacity (Kelly et al. 2012; Mateos-Gonzalez et al. 2014). The key assumption of this shared-pathway hypothesis as it applies to carotenoids is that the mechanisms of carotenoid pigmentation are closely tied to mitochondrial function (Hill and Johnson 2012, 2013; Johnson and Hill 2013).

With few exceptions, animals attain carotenoid-based red coloration by oxidizing dietary yellow carotenoid pigments into ketolated products with a red hue (Goodwin 1984; McGraw 2006). This process of carotenoid ketolation is sensitive to oxidative conditions in cells and is thus inherently tied to OXPHOS (Hill and Johnson 2012). Moreover, it has been proposed that ketolation of dietary carotenoids takes place on the inner mitochondrial membrane in close association with electron-transport complexes, such that respiratory efficiency dictates the production of color (Johnson and Hill 2013). For displays of non-ketolated carotenoids, different mechanisms have been proposed to link the production of color to mitochondrial function (Hill and Johnson 2012). In support of the hypothesis that yellow xanthophylls

can signal respiratory efficiency, a recent study found that the brightness of yellow coloration in American Goldfinches (*Carduelis tristis*) was significantly positively correlated with resting metabolic rate (Kelly et al. 2012). Carotenoid signaling systems are prime arenas for testing the hypothesis that ornamental traits signal cellular respiration.

Other forms of pigmentation might also be linked to mitochondrial function but the connections to cellular respiration are not as clear as with carotenoids. Recent studies have shown that basic patterns of light/dark coloration among species of animals, as well as between color morphs within species, are under control of melanocortin-1-receptor (MC1R) (Mundy et al. 2004). Ducrest et al. (2008) highlighted the connections between proopiomelanocortins (POMC), which bind MC1R and which in turn control the darkness of plumage and pelage, and a host of cellular pathways including mitochondrial pathways that are linked to POMC through melanocortin. The same POMC that binds MC1R also binds melanocortin receptors, which in turn play roles in the control of immune-function and regulation of energy, and are linked to the HPA axis (Ducrest et al. 2008). At this point, links between cellular respiration and individual variation in melanin pigmentation are indirect, and weak connections between mitochondrial function and melanin systems may be the reason that between-individual variation in melanin ornamentation tends not to be as closely linked to individual performance as is carotenoid pigmentation (Hill and Brawner 1998; McGraw and Hill 2000); but see Griffith et al. (2006).

Displays of cognitive and motor ability

Some ornamental traits—such as the production of multifarious songs, the rendering of intricate and complicated dances, the creation of complex nests and bowers—are founded on cognitive ability. The production and maintenance of the central nervous system are among the most energy-demanding of all system-processes (Wallace 2008; Vannuvel et al. 2013; Wang et al. 2013), so cognitive function could simply relate to OXPHOS through a high demand for ATP (Federico et al. 2012), as described above. However, the links between mitochondrial function and neurological function are far more complex than simply the production of ATP (Dröge 2002; Lin and Beal 2006).

Associations between cellular respiration and neurological function have been studied primarily within the realm of human neurological disorders. Mitochondrial dysfunction has been linked to several

prominent neurological diseases in humans, especially Alzheimer's and Parkinson's diseases (Fukui and Moraes 2008; Filosto et al. 2011). In neurons, the ability of mitochondria to modulate the flux of calcium is essential for controlling neurogenesis, neuronal plasticity, and release of neurotransmitters (Chinopoulos and Adam-Vizi 2006; Kann and Kovács 2007; Wojda et al. 2008), thereby placing mitochondria at the center of pathways related to nervous-system function. Growing evidence suggests that mitochondrial respiratory pathways play central roles in neurogenesis, maintenance of an effective nervous system, motor coordination, and cognitive function that results from nervous-system function (Lin and Beal 2006; Bishop et al. 2010).

It is intriguing to speculate that the many courtship displays of animals, including complex songs; long, complicated, and challenging movements; and products of cognitive performance such as complex weaving in nests, or decoration of bowers, are the objects of female-choice because they reflect highly functioning nervous systems (Nowicki et al. 1998). Proficient nervous function, in turn, may be one of the best indicators of a fully functional system of cellular respiration because of the links between mitochondrial function and nervous-system function. At present, there is virtually no direct observation by which to assess the idea that better cognitive and motor-neural performance by individuals in a population reflects better mitochondrial function. Studies of the links between cognitive performance and mitochondrial function should yield fascinating results.

Conclusions

Current theory proposes that stress, condition, and ornamentation are linked through energy stores, with condition reflecting the pool of available energy that is needed for both ornamentation and body maintenance. This resource-tradeoff view of the associations between stress, condition, and ornamentation, however, is not supported by many studies of either model or non-model organisms in which resources are provided *ad libitum* and stress-responsiveness and ornamentation still vary among individuals. Indeed, the resource-tradeoff hypothesis is a conceptual framework that is contradicted by every-day experiences. We provide our pets, our livestock, and ourselves with unlimited access to energy, yet we still observe substantial differences in all manner of performances from running-endurance to disease resistance to longevity. I propose that stress, condition, and ornamentation are connected not by energy

reserves, but through the capacity to efficiently produce energy, which is a product of the genotype, epigenotype, and somatic state (Hill 2011; Fig. 1). I further propose that condition-dependent ornamental traits evolved specifically as signals of cellular respiration and the capacity to resist the disruptive effects of stressors. Efficiency of cellular respiration is the core aspect of a prospective mate about which a choosing female should most desire information (Hill and Johnson 2013), and ornamentation gives females essential and otherwise imperceptible information about the cellular respiration of prospective mates.

Acknowledgments

Wendy Hood, Haruka Wada, Amy Skibiell, and the Hill/Hood/Wada laboratory groups provided valuable feedback on the manuscript.

Funding

IOS0923600. The symposium "Stress, condition, and ornamentation" at the 2014 meeting at the Society of Integrative and Comparative Biology was supported by NSF grant DEB1359537 to W. R. Hood and by SICB Divisions: Animal Behavior, Comparative Endocrinology, Ecology & Evolution, and Comparative Physiology & Biochemistry.

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