Trends in Ecology & Evolution

CellPress

Review

Endocrine Flexibility: Optimizing Phenotypes in a Dynamic World?

Conor C. Taff[1,*] and Maren N. Vitousek[2]

Responding appropriately to changing conditions is crucial in dynamic environments. Individual variation in the flexibility of physiological mediators of phenotype may influence the capacity to mount an integrated response to unpredictable changes in social or ecological context. We propose here a conceptual framework of rapid endocrine flexibility that integrates ecological endocrinology with theoretical and empirical studies of phenotypic plasticity and behavioral syndromes. We highlight the need for research addressing variation in the scope and speed of flexibility, and provide suggestions for future studies of these potentially evolving traits. Elucidating the causes and consequences of variation in endocrine flexibility may have important implications for the evolution of behavior, and for predicting the response of individuals and populations to rapidly changing environments.

Trends

There is growing recognition that within-individual variation in endocrine traits has been understudied. An increased ability to repeatedly sample individual endocrine parameters coupled with methodological developments allowing estimation of within-individual reaction norms has enhanced interest in understanding within-individual endocrine variation.

Rapid endocrine flexibility is a crucial component of an appropriate response to dynamic environments, especially when environmental changes that demand an endocrine response are stochastic.

Individual differences in endocrine flexibility can be analyzed in the same way as any potentially evolving trait. Studies of endocrine flexibility have the potential to reveal how and why some individuals and populations are able to survive in dynamic environments while others fail.

Endocrine Flexibility in Dynamic Environments

Surviving and reproducing in dynamic environments often requires the ability to alter phenotype to match the current environment. A fundamental unanswered question in biology, however, is how selection shapes rapid flexibility in coordinated suites of traits. Adaptive behavioral responses to rapidly changing conditions have been documented in several systems [1] and understanding the scope and implications of these responses currently represents a major area of research [2–4]. Yet, while these behavioral shifts are often assumed to have a physiological basis [5,6], surprisingly little is known about whether individual variation in rapid physiological flexibility influences the expression and evolvability of flexibility in other traits. Determining the causes and consequences of variation in physiological flexibility may help to elucidate why some individuals – and some populations – are able to survive and thrive in conditions that prove fatal to others. Rapid physiological flexibility, and its costs and benefits, may also have important implications for the evolution of behavior, and for predicting responses to human-induced rapid environmental changes [1,3,7].

Because endocrine systems mediate the flexible expression of a diversity of phenotypic traits, these systems are likely to play a central role in facilitating rapid phenotypic changes [8,9]. While we focus here on **endocrine flexibility** (see Glossary), note that the conceptual framework that we develop applies to any physiological response to dynamic environments where individuals vary in flexibility, such as phytohormone-induced rapid defense against herbivory in plants [10]. In animals, individual variation in the degree of endocrine flexibility may be an important determinant of fitness. We define two aspects of endocrine flexibility. First, individuals may vary in the magnitude of the endocrine response when conditions change (Box 1). Variation in the scope of response can be assessed using a within-individual **reaction norm** approach in which endocrine traits – or their response to a stimulus – are measured across a relevant environmental gradient [11–13]. Second, individuals may vary in the speed of the endocrine response when

[1]Cornell Laboratory of Ornithology, Cornell University, Ithaca, NY 14850, USA
[2]Department of Ecology and Evolutionary Biology, Cornell University, Ithaca, NY 14850, USA

*Correspondence: cct63@cornell.edu (C.C. Taff).

 http://dx.doi.org/10.1016/j.tree.2016.03.005

conditions change (Box 2), which can be measured using a time-series of samples following an environmental change [14–16].

Despite the potential importance of flexibility in these key mediators of phenotype, few empirical studies have addressed individual variation in endocrine flexibility or its functional significance, even when appropriate data are available (but see [13,17]). Recent conceptual reviews have drawn attention to the need for a better understanding of within-individual endocrine variation, and to the utility of adopting a reaction norm approach [18–21], but none have focused explicitly on **rapid endocrine flexibility** as a trait of particular interest. We argue here that this important component of the response to dynamic environments can be studied using the same techniques that are applied to any potentially evolving trait. The conceptual framework that we propose integrates classic endocrinology (e.g., [22–25]) with the well-developed literatures on phenotypic plasticity [26,27] and behavioral syndromes [4,5]. Adapting the approaches developed in these

Box 1. The Scope of Endocrine Flexibility: A Reaction Norm Approach

Individuals may differ in both their maximum potential endocrine response and in their realized endocrine response to changing conditions. We propose that these magnitudes represent the 'potential scope' and 'realized scope' of endocrine flexibility, respectively. Potential scope can be measured by physiological manipulations with repeated sampling [e.g., challenges with **adrenocorticotropic hormone** (ACTH), **dexamethasone** (DEX), or **gonadotropin-releasing hormone** (GnRH)], while realized scope can be measured by repeatedly sampling under experimentally manipulated or naturally varying conditions (e.g., over a temperature gradient). In both cases, testing for between-individual differences in within-individual endocrine scope can be accomplished using a reaction norm approach (Figure IA–D). This concept was originally developed as a way to describe the full range of phenotypes that can be produced by a single genotype experiencing different conditions [27]. Recently, the reaction norm approach has been extended to repeated observations of labile behavioral phenotypes without replicated genotypes by using random regression modeling [82]. This analytical approach is equally applicable to repeated physiological measures [18]. The scope of endocrine flexibility can be measured as the slope of the reaction norm (Figure IIA). The technique can also be extended to non-linear reaction norms and to discrete environmental variation [4,82]. Note that in behavioral studies the statistical 'slope' is usually interpreted biologically as behavioral plasticity or flexibility [82]. For endocrine reaction norms, we prefer the term 'scope' [89] rather than endocrine flexibility because it allows clear differentiation of scope and speed.

If the scope of endocrine flexibility does not vary between individuals (Figure IA,B), then there is no opportunity for selection to act on flexibility. Note, however, that researchers should carefully consider the power of their experimental design before concluding that there is no variation in the scope of flexibility [78]. Assuming that variation in scope has been detected (Figure IC,D), and has a heritable component (heritability can be estimated using the animal model in natural populations with known relatedness [60]), selection on the scope of flexibility may contribute to the evolution of adaptive endocrine responses to rapidly changing conditions. If individuals with greater scope of flexibility are better able to match the optimal endocrine phenotype over a wide range of environmental conditions, they will achieve higher fitness (Figure IIA,B). However, it is important to note that even in variable environments flexibility might not be favored when costs or limits constrain endocrine responses.

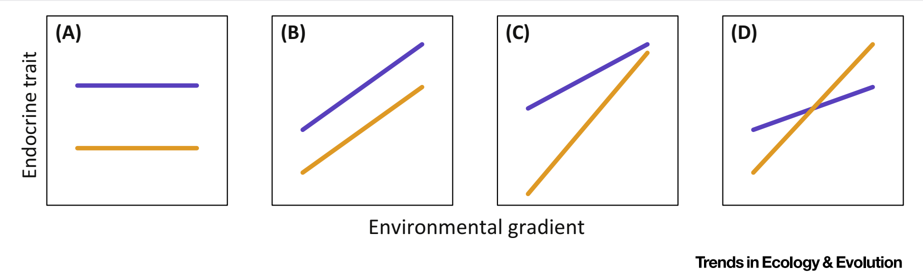

Figure I. Possible Patterns of Linear Reaction Norms for the Scope of Endocrine Flexibility. Each line represents one hypothetical individual sampled across an environmental gradient. In all four panels, individuals vary in the absolute levels of endocrine traits expressed, and differ in patterns of the scope of endocrine flexibility. (A) No endocrine flexibility. (B) Endocrine flexibility exists, but there is no between-individual variation in the scope of flexibility. (C) Individuals vary in the scope of flexibility, but the scope is correlated with the absolute level of endocrine traits, such that the rank order of endocrine expression is stable across conditions. (D) Individuals vary in the scope of endocrine flexibility independently of the absolute value of endocrine traits.

Glossary

Adrenocorticotropic hormone (ACTH): hormone produced by the pituitary that stimulates the adrenal glands to secrete glucocorticoids.
Androgens: steroid hormones that include testosterone, dihydrotestosterone, and 11-ketotestosterone. Involved in mediating many phenotypic traits including sexual, aggressive, and parental behavior, as well as secondary sexual traits and sperm production.
Dexamethasone (DEX): a synthetic glucocorticoid agonist. Experimental administration can be used to assess how rapidly and effectively the production of glucocorticoids is downregulated by negative feedback.
Endocrine flexibility: phenotypic plasticity in endocrine traits that is reversible, takes place within an individual, and occurs in response to non cyclical changes in stimuli (i.e., in response to stochastic changes rather than predictable circadian or circannual variations [65]). Measured as the extent to which the endocrine expression of an individual varies in scope or speed in response to a change in stimuli.
Endocrine reaction norm: the pattern of endocrine expression within a single individual across an environmental gradient or following exposure to a stimulus. Individual endocrine reaction norms can be estimated using random regression modeling [82].
Glucocorticoids: steroid hormones that include corticosterone and cortisol. At low levels glucocorticoids bind to mineralocorticoid receptors and function as metabolic regulators. Stress-induced increases in glucocorticoids, which saturate mineralocorticoid receptors and begin binding predominantly with glucocorticoid receptors, mediate organismal responses to challenges.
Gonadotropin-releasing hormone (GnRH): stimulates the pituitary to secrete luteinizing hormone, which induces gonadal androgen production.
Potential endocrine flexibility: an estimate of the maximum flexibility of endocrine traits. The potential scope of flexibility is often assessed using pharmacological manipulations that stimulate or inhibit downstream components of neuroendocrine pathways.