CHAPTER 13

Role of Stress in Evolution: From Individual Adaptability to Evolutionary Adaptation

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INTRODUCTION

Environments outside the range normally experienced by a population, and the associated changes in organisms' morphological, physiological, or behavioral homeostasis (stress), accompany most evolutionary changes (Bijlsma and Loeschcke, 1997; Hoffmann and Parsons, 1997; Hoffmann and Hercus, 2000). Depending on the intensity, predictability, and recurrence of stress, responses might range from stress tolerance and avoidance at organismal level to the rapid

Variation

appearance of novel traits or extinction at population level. Yet, moderate stress is essential for normal growth and differentiation of metabolic, physiological, neurological, and anatomical systems of an organism (Huether, 1996; Clark and Fucito, 1998; Muller, 2003). For example, a large part of skeletal development is directed by exposure to tension and mechanical overloads in excess of those normally experienced by the organism (Hall, 1986; Carter 1987). Stress plays an important role in facilitating local adaptation by enabling better adjustments, synchronization, and functioning of many organismal systems (Simons and Johnston, 1997; Emlen *et al.*, 2003; Wingfield, 2003). Anyone who has experienced the invigorating effects of diving into icy-cold water after a sauna (both of which are extreme environments), the health benefits of rigorous exercise (which by definition exceeds the range of everyday environments), or analgesic and attention-sharpening effects accompanying stressful encounters (McEwen and Sapolsky, 1995; Shors and Servatious, 1997) will testify to these effects of stress. On the other hand, response to an acute and unfamiliar stressor precludes normal organismal functions (Sibly and Calow, 1989), and the high cost of stress tolerance or lack of evolved stress response strategies can lead to evolutionary stasis (Parsons, 1994).

Extreme environments not only disrupt normal development and induce large phenotypic changes in novel directions, but they also simultaneously exert strong phenotypic selection that favors changes in these directions (Waddington, 1941; Schmalhausen, 1949; Bradshaw and Hardwick, 1989; Jablonka *et al.*, 1995; Eshel and Matessi, 1998). Not surprisingly, evolutionary diversification, the appearance of phenotypic novelties, and mass extinction are all closely associated with extreme environmental changes (Howarth, 1993; Guex, 2001; Nicolakakis *et al.*, 2003). Yet, there exists a remarkable gap in our understanding of the mechanisms behind the evolutionary importance of stress. Whereas it is widely recognized, especially in physiological and neurological studies, that stress plays an important role in directing and organizing the adaptive adjustment of an organism to ever-changing environments, very little is known about the mechanisms that enable the organismal accommodation of stress-induced effects and the evolution of a response to stress.

Lack of a developmental perspective in evolutionary studies of stress has left us with several unresolved questions. First, how can organisms *prepare* for novel and extreme environmental change? The organismal ability to mount an appropriate reaction to a stressor requires recognition and evaluation of the extreme environment. How can this ability evolve in relation to stressors that are short and rare in relation to a species generation time? Second, numerous studies have documented an increase in phenotypic and genotypic variance under stress, and it is suggested that this variance is a source of novel adaptations under changed environments. Yet, for stress-induced modifications to have evolutionary importance they have to be inherited and persist in a sufficient number of individuals within a population. This requires an organism to survive stress and reproduce at least once; thus stress-induced variation has to be accommodated by an organism without reducing its functionality. How is such accommodation accomplished? Moreover, could existing organismal systems channel accumulation of stress-induced variance in some directions, but not others and thus direct evolutionary change in response to stress? The perspective outlined here, with specific focus on the effect of stress during development in animals, suggests that these questions are resolved by considering (1) the organization of developmental systems that enable accommodation and channeling of stress-induced variation without compromising organismal functionality; (2) the significance of phenotypic and genetic assimilation of neurological, physiological, morphological, and behavioral responses to stressors; as well as (3) multiple inheritance systems that transfer the wide array or developmental resources and conditions between the generations enabling long-term persistence and evolution of stress-induced adaptations.

I. EVOLUTION OF RESPONSE TO STRESS

A. Detection and Avoidance

Stress occurs when changes in the external or internal environment are interpreted by an organism as a threat to its homeostasis (e.g., Greenberg *et al.*, 2001; McEwen and Wingfield, 2003). The ability of an organism to mount an appropriate response to potentially stressful environmental changes requires correct recognition of environmental change and the activation of a stress response (e.g., Johnson *et al.*, 1992). The costs and benefits of stress detection and stress response implementation and the costs and benefits of maintaining stress resistance strategies vary among environments and individuals, favoring multiple solutions of dealing with stress. Crucial to these solutions is an organism's familiarity with the strength and types of stressors. This familiarity is determined, in turn, by the recurrence of a particular stressor in relation to a species' generation time (Lively, 1986; Lachmann and Jablonka, 1996; Meaney, 2001; Piersma and Drent, 2003). Yet, it is unclear how the ability to recognize and assess potentially stressful environments can evolve. How can organisms judge the appropriate reaction to a stressor, such as is required to select between stressor avoidance and stress tolerance? Are the mechanisms of assessment and avoidance specific to a particular stressor?

1. Familiarity with Stressor: Cognitive and Physiological Assimilation of a Rare Event

The response to stress depends crucially on prior experience and a "memory" of response to a stressor. Generally, repeated exposure to a particular stressor favors the evolution of mechanisms that suppress an organism-wide stress reaction and, instead, activate stress-specific responses (Johnson *et al.*, 1992; Veenema *et al.*, 2003).

For example, in higher vertebrates, stress-induced activation of the neuroendocrinological system increases its reactivity to internal and external stimuli, facilitates the processing of sensory information, and ultimately enables the formation of a behavioral or physiological strategy for dealing with a stressor. Furthermore, stress-induced activation of neuroendocrinological systems facilitates long-term retention of information about a stressful event and corresponding organismal response after the stressor is gone. Interestingly, once formed, the maintenance of such "memory" can be accomplished by periodic exposure to different stressors. For example, hormones associated with stress detection and avoidance also play a major role in modifications of neural circuits (Gold and McGaugh, 1978); once the stress-avoidance strategy is formed, exposure to even low concentration of these hormones maintains the strategy (McGaugh *et al.*, 1982).

Physiological studies of animals show that the repeated experience of successfully overcoming social stresses during ontogeny is a prerequisite for the acquisition of a normal repertoire of behavioral strategies (Huether, 1996; see also Gans, 1979). An insightful example comes from experiments that show that individuals exposed to repeatable but consistently unfamiliar (and thus "uncontrollable" by an animal) stressors develop "stressful helplessness"; i.e., they lose their ability to react to any stressor (Katz *et al.*, 1981; Johnson *et al.*, 1992; Avitsur *et al.*, 2001).* On the contrary, individuals that were allowed to develop a stress-avoidance strategy by exposure to a previously encountered stressor not only developed stress tolerance to a particular stressor but also actively sought out other mild stressors. In the absence of other stressors, their stress-avoidance abilities diminished (Katz *et al.*, 1981; Johnson *et al.*, 1992; Avitsur *et al.*, 2001). These results suggest that, once originated, a stress-response strategy can be maintained by other environments and that adaptation to one type of stressor, at least in "social" stresses, may facilitate adaptation to other stressors.

Phenotypic assimilation of the appropriate stress response is facilitated when neural circuits and hormones related to the stress response are also involved in other organismal functions (Aston-Jones *et al.*, 1986; Greenberg *et al.*, 2001). In such cases, even a single stressful experience during development is often enough to induce changes that, in the future, will prevent organism-wide stressful reactions and activate stress-specific behavioral and physiological responses (Levine *et al.*, 1967; 1989). Generally, stress-induced reorganization of developmental pathways and organismal function rather than the production of novel stress-specific pathways is thought to account for the ease with which individuals and populations lose and gain the ability to resist stress in laboratory populations (Chapin *et al.*, 1993).

*Organisms' "stress helplessness" from lack of opportunity to develop stress-specific avoidance strategy is conceptually analogous to "morphological stasis" of lineages that occur in environments with frequent acute and diverse stresses that prevent the evolution of stress-specific adaptations.

B. Stress-Avoidance Strategies

The ability to remove a stressor *actively* by either relocation or avoidance requires an evolved ability to detect or anticipate stressful changes and the "knowledge" or "memory" of stress-avoidance strategies or adjustments (Bradshaw and Hardwick, 1989; Jablonka *et al.*, 1995; Denver, 1999). Therefore, the evolution of stress avoidance is more likely when stressful events are predictable, prolonged, and frequent in relation to generation time (Ancel Meyers and Bull, 2002; Figure 13-1). Alternatively, the short-term avoidance of a frequent and mild stressor might be accommodated by behavioral or physiological plasticity of an organism (Figure 13-1; Schlichting and Smith, 2002; Nicolakakis *et al.*, 2003; Piersma and Drent, 2003; Wingfield and Sapolsky, 2003). For example, repeated challenges of an organism's immune system enable a more precise reaction to a specific pathogen, frequent and diverse stressors facilitate the formation of complex and robust metabolic

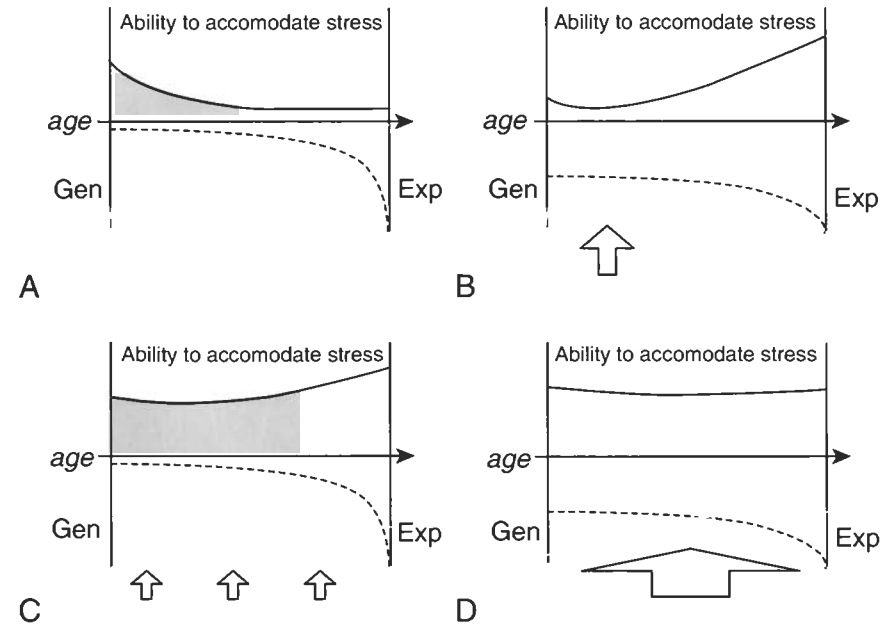

FIGURE 13-1. Conceptual outline of the acquisition of ability to accommodate stress (solid black line and gray area) across a life span of an individual under (A) normal (i.e., not stressful) environment; (B) novel strong stressor (examples: stress-enhanced learning, behavioral avoidance of a stressor, social stressors), (C) frequent mild stressor (examples: weather-induced migrations of arctic passerines, periodic torpor), (D) frequent, novel, and strong stressors (e.g., "living fossils," "stressful helplessness"). "Gen" (solid gray line) indicates genetic effects on acquisition of ability to accommodate stress; "exp" (dotted black line) indicates the effects of individual experience with stressor over the generation time; "age" is a duration of a single generation; gray arrows show the timing and strength of a stressor.

networks (Clark and Fucito, 1998), and challenges to skeletal tissues caused by mechanical overload during growth lower developmental errors (see also Simons and Johnston, 1997; Graham *et al.*, 2000). Wingfield (2003; Wingfield and Sapolsky, 2003) reviews the cases when selection favors stress avoidance and where suppression of organism-wide stress response is accomplished by a blockage of either neural system perceiving a stressor or sensitivity of individual organismal systems to stress-induced increase in circulating glucocorticosteroids. Generally, when the environment during growth is a good predictor of the environment to be experienced as an adult, developmental plasticity in morphology and behavior can enable the accommodation of internal and external environmental fluctuations (Levine *et al.*, 1967). Consequently, organisms activate stress reactions when there is a discordance between environments during their development and their current external and internal environments (Meaney, 2001; Bateson *et al.*, 2004, Weaver *et al.*, 2004).

On the longer time scale, avoidance of a predictable stressor can be accomplished by changes in an organism's life history, especially by altering the timing of reproduction or duration of development. Common cases include stress-induced modification of the timing of metamorphism in amphibians, changes in the duration of gestation in mammals, and the timing of flowering and seeding in plants (e.g., Bradshaw and Hardwick, 1989; Stanton *et al.*, 2000). For example, tadpoles of several species accelerate metamorphosis when environmental changes indicate a greater probability of desiccation; this sensitivity to stressor cues is regulated by the corticotropin-releasing hormone signaling system (Denver, 1999). Heil *et al.* (2004) describe evolutionary establishment of environmentally induced stress avoidance in *Acacia* plants.

In sum, initial behavioral accommodations of stress (e.g., hiding, relocation, lowering metabolism) may set the stage for the evolution of adaptive stress-avoidance strategies (e.g., periodic hibernation, migration, torpor). When a stressor is reliably preceded by other environmental changes, their mutual recurrence facilitates the establishment of stressor recognition, assessment and avoidance strategies, such that an evolved stress-specific strategy does not involve an activation of an organism-wide stress response. When individuals vary in their reaction to stress and when stress-induced strategies are favored by natural selection during and after stressful events, these strategies can become phenotypically and genetically assimilated in a population (Baldwin, 1896; Hinton and Nolan, 1980; Oyama, 2000; West-Eberhard, 2003; Figure 13-1).

II. EVOLUTIONARY CONSEQUENCES OF STRESS

A. Stress-Induced Variation

A stress-induced increase of phenotypic and genetic variance in a population has three main sources. First, directional selection imposed by a stressor can result in faster rates of mutation and recombination. Second, stress challenges to regulatory

mechanisms can release and amplify previously accumulated, but unexpressed, genetic and phenotypic variation. Third, stressful environments can facilitate developmental expression of genetic variance that had accumulated, but was phenotypically neutral, under normal range of environments. These sources of variation can be adaptive under stressful conditions when they facilitate the population's persistence through a stressful event by the development of novel adaptations to changed environments.

1. Generated Variance

Organismal reaction to a stressor is often associated with generation of variation in a directional and locally adaptive manner (Jablonka and Lamb, 1995; West-Eberhard, 2003). In some cases, such directionality is attributed to the channeling effects of complex developmental networks (e.g., Walker, 1979; Roth and Wake, 1985). In other cases, it is associated directly with a stressful environment (e.g., Wills, 1983) or with stress effects on organismal fitness (Hadany and Beker, 2003). Some studies documented that an extreme environment increases genetic variation because of the increase in mutation and recombination rates (Imasheva, 1999, reviewed in Hoffmann and Parsons, 1997). When such mutations are directional (or "focused", *sensu* Caropale, 1999) in relation to a stressor—that is when the stressful environment both causes a mutation and favors phenotypic change associated with this mutation—such an increase in mutation rate results in greater similarity among individuals in response to a stressor facilitating evolutionary adaptation to novel environments (Shapiro, 1992; Jablonka and Lamb, 1995; Wright, 2000). For example, exposing *Chlamydomonadas* to a stressful ultraviolet irradiation increased mutation rates in traits affecting fitness (Goho and Bell, 2000). Similarly, stress induced directional and locally appropriate mutations in bacteria (Cairns *et al.*, 1988; Sniegowski *et al.*, 2000; Wright, 2000; Bjedov *et al.*, 2003). Exposure to acute stress was associated with rapid adaptive evolution of a gene family, primarily because of gene duplication, in cyanobacteria (Dvornyk *et al.*, 2002), with rapid amplification of a gene in humans (Prody *et al.*, 1989), and with greater frequency of sexual recombination in *Volvox* (Nedelcu and Michod, 2003). Other examples include long-term effects of stress on gene expression and DNA sequence, activation of previously unexpressed genes by stressful events, and stress-induced transposition in plants (Belyaev and Borodin, 1982; Ruvinsky *et al.*, 1983; McClintock, 1984; Wessler, 1996). At the level of phenotype, induction of a phenotypic trait by a stressor and concurrent selection on the induced trait are common (Jablonka *et al.*, 1995; Oyama, 2000; Nicolakakis *et al.*, 2003; Price *et al.*, 2003; West-Eberhard, 2003).

2. Hidden Variance

Stressful environments often reveal greater phenotypic and genetic variability than is seen under normal environments. It is commonly suggested that such hidden variation results from stress-induced challenge of preexisting genetic and developmental

architecture of organismal homeostasis (Scharloo, 1991). In turn, an increase in variation in individual organismal systems and their subsequent reorganization is thought to enable the formation of novel adaptations (Bradshaw and Hardwick, 1989; Eshel and Matessi, 1998; Gibson and Wagner, 2000; Lipson *et al.*, 2002; Schlichting and Smith, 2002; Badyaev, 2004c). The idea that the extreme environment's challenge to previously canalized system is the source of such hidden variation is collaborated by observations of the stress-induced sudden appearance of primitive, ancestorlike forms in some lineages (Guex, 2001), by studies of phenotypic responses to stress that mimic the expression of mutation (Goldschmidt, 1940; Chow and Chan, 1999; Schlichting and Smith, 2002), by documentation that phenotypically neutral genetic variance in ancestral forms of cultivated plants becomes highly adaptive in the hybrid backgrounds of domesticated forms (Lauter and Doebley, 2002; Rieseberg *et al.*, 2003), and by numerous examples of environment dependency in expression of genetic variation (Kondrashov and Houle, 1994; Leips and MacKay, 2000; Badyaev and Qvarnström, 2002; Keller *et al.*, 2002; Badyaev, 2004b).

Yet, despite these examples, it is not clear how genetic and developmental systems accumulate and store phenotypically neutral genetic variance while not expressing it (Eshel and Matessi, 1998; Wagner and Mezey, 2000; Hermission *et al.*, 2003; Masel and Bergman, 2003). Specifically, the discussion has focused on the existence of "evolutionary capacitors" (Rutherford, 2000) and "adaptively inducible canalizers" (Meiklejohn and Hartl, 2002) which are *specific* mechanisms that buffer and accumulate developmental variation, producing "hidden reaction norms" of a phenotype. A debated question is whether "evolutionary capacitors" are stressor-specific regulatory systems or whether evolutionary capacity is a property of any complex and locally adapted organismal system. Rutherford and Lindquist (1998) described that mutations at the gene for the stress-induced chaperone proteins (Hsp90) harbor abundant but normally unexpressed genetic variation that when selected leads to the appearance and assimilation of novel phenotypes in the population (Ruden *et al.*, 2003). Thus Hsp90 might be a specialized evolutionary capacitor that buffers developmental variation but under stressful conditions facilitates adaptation (Meiklejohn and Hartl, 2002). However, recent studies suggested that "evolutionary capacity" is a property of most adapted developmental systems that when challenged by a novel environment (external or internal) reveal large genetic variation (Kirschner and Gerhart, 1998; Rutherford, 2000; Bergman and Siegal, 2003; Badyaev, 2004a). For example, Milton *et al.* (2003) showed experimentally that Hsp90 is involved in buffering of only some developmental pathways and not others. Similarly, Szafraniec *et al.* (2001) found that as long as mutant effects are not expressed, many complex and redundant developmental systems enable accumulation of mutational variance. Thus complex developmental processes and genetic networks can constrain variation in individual traits (Rice, 2004), and phenotypically neutral genetic variation can accumulate in such systems given sufficient time and population size (Hermission and Wagner, 2005).

Interestingly, in many complex social networks, a stress-induced decrease in integration accelerates acquisition of a new optimum phenotype. An interesting example is the stress-induced modification of foraging and nest site searches in social insects. In some ant species, a destruction of the nest site leads to the breaking of the strict hierarchical social structure and rapid proliferation of random individual nest search routes and patterns. When a few individuals find a new suitable site, their recruitment of other individuals to follow them to the site rapidly leads to crystallization of the relocation route and movement patterns and reinstatement of the social integration of the colony (Britton *et al.*, 1998; Couzin and Franks, 2003).

In sum, stress resistance might be a by-product of an organism's complexity, and accumulation of unexpressed variation by genetic and phenotypic developmental systems facilitate evolutionary change under extreme environments. Organismal homeostasis can be compromised by either novel directional selection on some organismal systems but not others, or by organism-wide effects of a stressor, resulting in weaker organismal homeostasis and greater phenotypic plasticity (Schlichting and Pigliucci, 1998; Newman and Muller, 2000). Under the former scenario, a more directional and faster response to a stressor at the population level is expected because stress-induced variation will be channeled and amplified by existing functional complexes. The latter scenario should produce a greater opportunity for the evolution of morphological novelty. Overall, the weakening of complex phenotypic regulatory systems and accumulation of neutral genetic variance provides a link between diversification, evolutionary change, and extreme environments.

B. Buffering, Accommodating, and Directing Stress-Induced Variation

Organisms can maintain functionality in stressful environments by channeling and accommodating stress-induced variation. This is accomplished by buffering some organismal functions while increasing the flexibility of others (Alberch, 1980; Nijhout, 2002). How can such organization evolve?

1. Stress Buffering: A By-Product of Complexity in Development or an Evolved Strategy?

Organismal functions most closely related to fitness are thought to be the most buffered against internal and external stressors (Waddington, 1941; Schmalhausen, 1949; Stearns and Kawecki, 1994). Yet, an organism's functioning in changing environments requires the ability to track and respond to these environments. Consequently, evolved systems that shield an organism from stressors restrict an organism's ability and capacity to adapt continuously to changing environments (Wagner *et al.*, 1997; Eshel and Matessi, 1998; Ancel, 1999; Schlichting

and Smith, 2002). For example, suppression of stress-induced activation of the sensory systems limits an organism's ability to acquire and retain the sensory cues and behavioral strategies necessary for stress avoidance (see preceding text; Huether, 1996). On the one hand, a lack of phenotypic plasticity results in population extinction under stress (Gavrilets and Scheiner, 1993; Ancel, 1999). On the other hand, extensive phenotypic variability in organismal functions weakens the effects of directional selection imposed by stressful environments and thus lessens the opportunity for genetic assimilation and evolution of adaptations to stress (Fear and Price, 1998; Ancel, 2000; Huey *et al.*, 2003). Thus, for functioning of organismal systems that are most closely related to fitness, intermediate levels of phenotypic plasticity and environmental sensitivity should be the most optimal (Behera and Nanjundiah, 1995; Wagner *et al.*, 1997; Ancel, 2000; Price *et al.*, 2003). Yet, it is unclear how an optimal level of stress buffering can evolve. Specifically, is it shaped by natural selection exerted by extreme environments or by internal stabilizing selection for the cohesiveness of an organism?

Recent studies suggest that buffering is an emerging property of developmental complexity rather than an evolved stress-resistance mechanism (see preceding text); the increasing complexity of developmental pathways and networks leads directly to environmental and genetic stability and canalization (Baatz and Wagner, 1997; Clark and Fucito, 1998; Rice, 1998; Waxman and Peck, 1998; Meiklejohn and Hartl, 2002; Siegal and Bergman, 2002; Ruden *et al.*, 2003; Rice, 2004). Complex genetic and developmental networks can accommodate the effects of stressful perturbations without the loss of function or structure, while building up neutral genetic variation (Rutherford, 2000; Bergman and Siegal, 2003; Masel, 2004).

An organism's resistance to extreme environments depends on the historical recurrence of stressors as well as the ability of existing developmental processes to accommodate stress-induced changes (Gans, 1979; Lively, 1986; Jablonka and Lamb, 1995; Chipman, 2001; Arthur, 2002; Emlen *et al.*, 2003). Thus differences among organisms and organismal systems in response to stress may reflect different histories of past selection. Some traits (such as foraging or sexual traits) may experience recurrent and fluctuating directional selection that favors rapid transformations in response to changing environments, whereas other parts of a phenotype might be under concurrent stabilizing selection favoring canalization (Olson and Miller, 1958; Wagner, 2001). A combination of long-term stabilizing selection on the entire organism with strong and variable directional selection imposed by a stressor on a few organismal components should favor the evolution of modular organization where stress-induced modifications of traits can be accomplished with minimum interference with the rest of the phenotype (Simpson, 1953; Berg, 1960; Kirschner and Gerhart, 1998; Wagner and Mezey, 2004; Wagner *et al.*, 2005; Figures 13-2 and 13-3). Persistence of such modular organization under fluctuating selection pressures is enabled by developmental complexity of its components (Badyaev, 2004a,c); such organization channels stress-induced variation while buffering

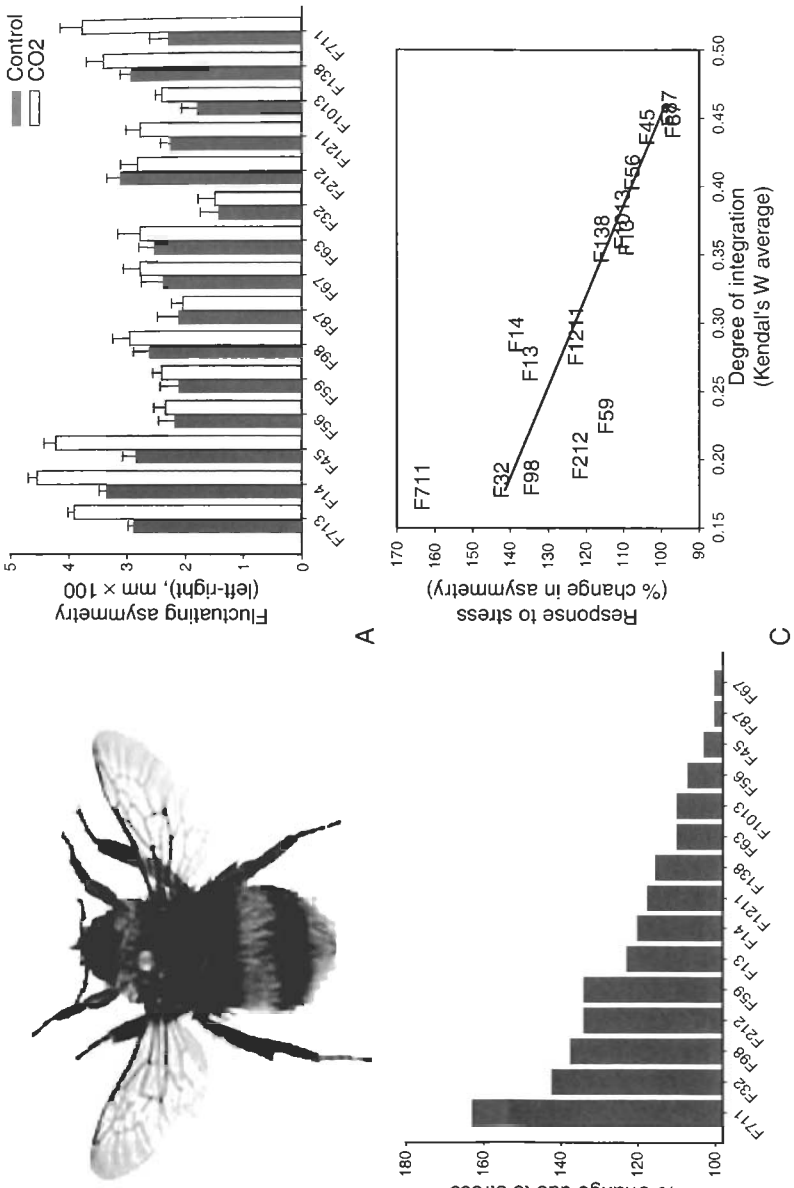

FIGURE 13-2. Degree of developmental integration in relation to accumulation of random developmental variation in bumblebees (*Bombus empatiens*). Bumblebees were raised under normal (control) and elevated (stress) concentration of CO_2. (A, B) Individual wing traits (intervein distances, shown on X axis) varied in reaction to the stressor, i.e., accumulated different amounts of developmental noise (measured as fluctuating asymmetry between left and right side). (C) Traits that were most closely developmentally integrated with other traits had lower response to the stressor and accumulated lower amount of random developmental variation (Sowry and Badyaev, 1999).

FIGURE 13-3. Degree of functional integration in relation to accumulation of random developmental variation in three species of soricid shrews (*Sorex*). Shrews were raised on plots where vegetation was not manipulated (control) and plots where vegetation was removed (stress). (A) Individual mandible traits (distances between muscle attachments) varied in response to the stressor as measured by an increase in fluctuating asymmetry (FA).

organismal components and thus enables a greater and more similar response to a stressful environment among individuals.

2. Stress Accommodation by Changes in an Organism's Integration

Organisms might accommodate stress-induced variation without the loss of function by lessening homeostasis of individual systems. Such a decrease in an organism's integration under stress allows exploration of new environmental niches and novel solutions to adapt to these environments (Holloway *et al.*, 1990, 1997; Raberg *et al.*, 1998; Badyaev and Foresman, 2000; Hoffmann and Woods, 2001). For example, individual hormonal systems have a greater potential range of performances and can remain functional under a wider range of environments than is allowed by homeostasis under normal range of environments (Dickinson, 1988; Johnson *et al.*, 1992; Greenberg *et al.*, 2001). In other words, organism-wide homeostasis is accomplished at the expense of the potential of individual systems and components (e.g., Smith-Gill, 1983), and organisms might react to a stressor by actively weakening homeostasis. For example, frequently documented suppression of immunocompetence under stressful conditions might facilitate novel adaptations to a stressor by realizing full capabilities of individual immune systems (Raberg *et al.*, 1998; Avitsur *et al.*, 2001). When stress is associated with damage of tissues and accumulation of heat shock proteins, as is the case with hypertension and greater activity, suppression of immunological functions enables individual organismal systems to respond to a stressor without activation of organism-wide autoimmunological response (Dickinson, 1988; Raberg *et al.*, 1998; Avitsur *et al.*, 2001).

However, there are examples of stress-induced increases in organismal integration and corresponding suppression of random genetic and developmental variation under stress (e.g., Siegel and Doyle, 1975; Bennington and McGraw, 1996; Badyaev and Foresman, 2004). For example, exposure to stress prevented the expression of deleterious mutations in *Escherichia coli* (Kishony and Leibler, 2003). Similarly, fluctuating asymmetries of developmentally independent forewings and hindwings became integrated in bumblebees raised under stressful, but not under control conditions, apparently as a result of a greater resource exchange between different tissues under stress (Klingenberg *et al.*, 2001). An increase in overall integration accounted for lesser phenotypic variation in the foraging structures of several mammalian species raised under stressful conditions (Badyaev, 1998; Badyaev *et al.*, 2000). Similarly, when breeding opportunities are limited or when the benefit of the current breeding attempt exceeds the costs of stress response, organisms can "buffer" reproductive systems by blocking or reducing their sensitivity to stress or by increasing compensatory interactions within reproductive systems to counteract the stress effects on the organism (Wingfield and Sapolsky, 2003).

When stressors are mild and occur during ontogeny, individual organismal systems often accommodate stress-induced variation without the reduction in functionality

(Bradshaw and Hardwick, 1989; Clarke and McKenzie, 1992; Huether, 1996; Schandorff, 1997). The degree of phenotypic plasticity is usually the highest, and ability to accommodate stress-induced variation (and to be shaped by stress) is the greatest during early stages of development (Figure 13-1). The importance of the timing of stress for directing the evolution of morphological traits is well documented. For example, when components of foraging structures differ in patterns of ossification, morphological variation in later ossified components is directed by stress-induced modifications of earlier ossified components (Figure 13-1; Badyaev, 1998; Mabee *et al.*, 2000; Badyaev and Foresman, 2004; Badyaev *et al.*, 2005). Neyfakh and Hartl (1993) documented that prior exposure to a stressor makes the ontogeny of morphological structures more amenable to subsequent modification. Moreover, when stress occurs early in ontogeny, accommodation and channeling of stress-induced variation by existing organismal structures causes similar reorganization in many individuals simultaneously (Roth and Wake, 1985; Chapin *et al.*, 1993; Figure 13-2), which facilitates adaptive evolution (Goldschmidt, 1940; West-Eberhard, 2003). Our studies of shrew mandibles (Fiumara and Badyaev, 1998; Badyaev and Foresman, 2000, 2004; Foresman and Badyaev, 2003; Badyaev *et al.*, 2005) and bumblebee wings (Sowry and Badyaev, 1999; Klingenberg *et al.*, 2001), as well as other studies (Leamy, 1993; Badyaev, 1998; Klingenberg and McIntyre, 1998; Klingenberg and Zaklan, 2000; Badyaev *et al.*, 2001; Juste *et al.*, 2001; Badyaev and Young, 2004), support these ideas; patterns of expression of stress-induced developmental variation were similar among individuals because of the similar effects of integration on channeling stress-induced variation and because variation from different sources is expressed by the same developmental pathways (Cheverud, 1982; Meiklejohn and Hartl, 2002, Figures 13-2 and 13-3).

Gans (1979) suggested that because extensive reorganization of the organismal phenotype is needed to deal with extreme environments, only a small portion of the population survives the stressful environment. This increases the probability of appearance of extreme phenotypes. Population size fluctuations under stress also affect the ability of genetic and developmental systems to accumulate and retain solutions to rare environmental events (Wagner, 2003; Hermission and Wagner, 2005). However, the effect of population size on the probability of establishing and retaining a novel phenotype differs between normal and extreme environments. Under normal conditions, modifications are likely to be established in larger populations that are more buffered from stochastic fluctuations and are able to accumulate larger amounts of neutral genetic variance (Gavrilets, 2004). Under stressful environments, that not only introduce greater variability, but also select toward a new phenotypic optimum, smaller populations should allow greater evolutionary change (Barton and Charlesworth, 1984; Gavrilets, 2004). Moreover, when a stressor is associated with abrupt changes in population composition—as is the case with extensive mortality or dispersal—it can lead to the modification of genetic and phenotypic interrelationships among the traits (Bryant and Meffert, 1988; Cheverud *et al.*, 1999; Badyaev and Foresman, 2000).

3. Accommodation of Stressor by Channeling Stress-Induced Variation

Natural selection favors organismal homeostasis that maintains some developmental variation for adjustment of the organism to its external and internal environments (Simons and Johnston, 1997; Wagner *et al.*, 1997; Eshel and Matessi, 1998; Emlen *et al.*, 2003; Nanjundiah, 2003). Stressful conditions can increase this variation and differences among organismal systems in their reaction to a stressor (and the corresponding channeling of stress-induced variation) might bias the introduction and expression of variation available for selection and thus bias evolutionary change (Bonner, 1965; Roth and Wake, 1985; Jablonka and Lamb, 1995; West-Eberhard, 2003).

Empirical studies show that the coordinated development of morphological traits leads to their similarity in expression of stress-induced developmental variation (Leamy, 1993; Smits *et al.*, 1996; Badyaev and Foresman, 2000; Klingenberg and Zaklan, 2000; Klingenberg *et al.*, 2001, 2004; Badyaev *et al.*, 2005). Our studies of four species of shrews showed that stress-induced variation was largely confined to the directions delimited by groups of traits involved in the same function (muscle attachments) (Badyaev *et al.*, 2000; Badyaev and Foresman, 2004). Interestingly, this channeling was concordant with the direction of species divergence—species differed most in the same traits that were most sensitive to stress within each species (Badyaev *et al.*, 2000). These results not only confirm a strong effect of functional complexes on directing and incorporating stress-induced variation during development, but also might explain the historical persistence of complex groups of traits despite the effects of stressful environments.

C. Inheritance

For a stress-induced modification to be preserved in a lineage, it needs to be accommodated by an organism, and if conditions favoring this modification recur, transmitted between generations, i.e., inherited. This presents two problems. First, can environmentally induced effects become inherited? Second, if each organism accommodates a stressor by different adjustments, then how can this diversity enable directional evolution of a stress-response strategy?

Stress-induced phenotypic changes commonly persist across several generations; such across-generations carry-over effects (*sensu* Jablonka *et al.*, 1995) can be caused by the transfer of physical substances, inheritance and developmental incorporation of a stressor, hormonal effects that influence expression of genetic variance in subsequent generations, epigenetic inheritance of stress-induced variation and structures, as well as behavioral effects (Jablonka and Lamb, 1995; Oyama, 2000; West-Eberhard, 2003). For example, inheritance of dominant-subdominant relationships in groups of many social mammals is accomplished by mechanisms different from original stressful encounters that established the dominance structure (Creel *et al.*, 1996; Goymann and Wingfield, 2004). Similarly, maternal care often

sets the stage for a lifelong reaction to stressors, by modifying the expression of genes that regulate behavioral, physiological and endocrinological responses to stressors (Mousseau and Fox, 1998; Meaney, 2001; Badyaev, 2002; Weaver *et al.*, 2004). Stress-induced changes in neuroendocrinological systems often occur with significant delay after the exposure to stress and persist for a long time. This led to the suggestion that the primary function of such delayed changes is integration of past stress-induced responses and sensitization of the organism to future occurrences of similar stressors (Huether, 1996). In turn, within-generation and between-generation maintenance of stress-induced changes in neural and physiological systems is accomplished by similar hormonal mechanisms (McGaugh *et al.*, 1982; Meaney, 2001). Poststress fluctuating environments are often different from both the environment before the stressor and the stressful environment itself and have few predictable cues to organisms that survived stressful event. Under such conditions, a short-term inheritance of developmental resources is highly advantageous (Jablonka *et al.*, 1995). More generally, short-term and nongenetic inheritance is beneficial when the frequency of stress recurrence is greater than the generation time, but shorter than is necessary for the spread and fixation of adaptive mutation (i.e., the evolution of genetic adaptation) (Levins, 1963; Ancel Meyers and Bull, 2002).

In sum, accommodation of stress-induced variance by an organism can be facilitated by recurrent developmental stressors; genetic assimilation replaces stress-induced developmental modification if this modification has a fitness advantage in both stressful and poststress environments (Schmalhausen, 1949; Waddington, 1952). Even when the short-term organismal responses to a stressor are not genetically heritable, differences among organisms in the ability to survive stress and the recurrence of stressful environments will canalize stress-induced responses developmentally (Baldwin, 1896; Schlichting and Pigliucci, 1998; Ancel, 1999; West-Eberhard, 2003).

III. EVOLUTIONARY ADAPTATION

Close association between extreme environments and the pattern and rate of adaptive evolution is one of the best-documented patterns in evolutionary biology; stressful environments uncover, generate, and amplify phenotypic and genetic variation among individuals in the population and facilitate population divergence (Hoffmann and Parsons, 1997). Unlike environmental fluctuations within a range normally experienced by a population, stressful environments modify and reorganize integrated developmental and genetic networks simultaneously in a large group of individuals; directional change produced by these networks in combination with strong and novel directional selection by stressful environment facilitates rapid evolution and diversification (Jablonka and Lamb, 1995; West-Eberhard, 2003). Moreover, when a stressor compromises an organismal trait, releasing accumulated

and unexpressed genetic variation associated with the trait's function, such variance enhances the organismal response to selection acting on this trait (Zakharov, 1993; Robinson and Dukas, 1999; Bergman and Siegal, 2003). Example include stress-induced cartilage changes during development of bird skeletons that lead to the formation of novel structures (Muller, 2003), and stress-induced modifications in integration of foraging structures that facilitate diversification of cichlid jaw morphology (Chapman *et al.*, 2000; Albertson *et al.*, 2003). Moreover, extreme environments cause evolutionary change by modifying population dynamic processes such as immigration, population size, inbreeding, and competition (Kawata, 2002; Gavrilets, 2004). For example, in shrews, periods of environmental stress are accompanied by increased food competition and extensive mortality (Zakharov *et al.*, 1991; Badyaev *et al.*, 2000). In turn, greater interspecific competition for food amplified and extended the effects of stress exposure on the ontogeny of morphological structures (Foresman and Badyaev, 2003).

A. Stress-Induced Evolution versus Stress-Induced Stasis

Stress specificity, intensity, and recurrence are of fundamental importance for its evolutionary consequences (Bradshaw and Hardwick, 1989; Parsons, 1994; Ancel Meyers and Bull, 2002). Parsons (1994) suggested that only some subsets of stressful environments—narrowly fluctuating and slowly changing in relation to generation time—are associated with a rapid evolutionary change, whereas extreme and rapidly changing environments promote morphological stasis because of the costs associated with stress tolerance (see also Hoffmann *et al.*, 2003). Furthermore, only stressors specific to an organismal system are expected to enable assimilation and evolutionary persistence of stress-induced adaptations, because more general stressors favor stress tolerance by increasing homeostasis, in turn leading to a reduction in organismal metabolism and fitness. Thus, among the array of organismal responses to stressful environments, only accommodation of stress-induced variation and stress avoidance leads to evolutionary change (Parsons, 1993). In turn, because of its association with lower metabolism and stronger regulatory systems, stress tolerance is unlikely to be associated with greater organismal plasticity, thus leading to stasis under extreme environments, which is observed in "living fossils" (Parsons, 1993, 1994; Figure 13-1).

IV. CONCLUSIONS

Several themes and approaches in recent studies significantly further our understanding of the relationship between stressful environments and evolution. First, stressful environments modify (most often reduce) the integration of neurological, endocrinological, morphological, and behavioral regulatory systems. Second, such

reduced integration and subsequent accommodation of stress-induced effects by complex developmental systems enables organismal "memory" of a stressful event as well as phenotypic and genetic assimilation of the response to a stressor. Third, the widely held assumption of randomly generated variance under stressful conditions is not correct. In complex functional systems, a stress-induced increase in phenotypic and genetic variance is often directional, channeled and amplified by the existing developmental system, which accounts for similarity among individuals in stress-induced change and thus significantly facilitates the rate of adaptive evolution. Fourth, accumulation of phenotypically neutral genetic variance might be a property of any locally adapted and complex developmental system; novel or extreme environments facilitate the phenotypic expression of this variance. Fifth, stress-induced effects and stress-resistance strategies can persist for several generations. In animals, such carry-over effects are enabled by hormonal effects on learning and gene expression and are facilitated by maternal inheritance of either a stressor or a stress-induced response. These transgenerational effects along with the complexity of developmental systems and stressor recurrence might lead to genetic assimilation of stress-induced effects. Accumulation of neutral genetic variance by developmental systems and phenotypic accommodation of stress-induced effects, together with the inheritance of stress-induced modifications, ensures the evolutionary persistence of stress-response strategies and provides a link between individual adaptability and evolutionary adaptation.

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