Journal of Mammalogy, 86(2):225–235, 2005

STRESS IN FREE-RANGING MAMMALS: INTEGRATING PHYSIOLOGY, ECOLOGY, AND NATURAL HISTORY

DEEANN M. REEDER* AND KRISTIN M. KRAMER

Department of Biology, Boston University, 5 Cummington Street, Boston, MA 02215, USA (DMR)
The Brain–Body Center, Department of Psychiatry (MC 912), University of Illinois at Chicago, 1601 W Taylor Street, Chicago, IL 60612, USA (KMK)

We review developments in the study of stress in free-ranging mammals and summarize the physiological and behavioral components of the stress response. Both the sympathetic nervous system response and the regulation and reactivity of the hypothalamic–pituitary–adrenal (HPA) axis are discussed. In particular, we describe how the activity of the HPA axis at baseline levels follows circadian and circannual rhythms in ways that allow animals to respond to predictable environmental changes, focusing largely on the endpoint of this axis, the glucocorticoid hormones cortisol and corticosterone. Superimposed upon these rhythms are the elevated glucocorticoid levels characteristic of the stress response, which allow an animal to respond to unpredictable social, physical, or environmental challenges. Methods used to explore the stress response in free-ranging mammals are described. Both inter- and intraspecific variation in the stress response as they relate to the environment are discussed. Finally, how the regulation and reactivity of the HPA axis varies by life-history stage and sex in mammals is reviewed, focusing on reproduction and development.

Key words: corticosterone, cortisol, ecology, glucocorticoid, hypothalamic–pituitary–adrenal axis, natural history, physiology, mammals, stress

Although the behavioral and physiological components of stress are well studied in a handful of laboratory mammals (especially muroid rodents and primates), our understanding of stress and its relevancy for an animal in its natural environment is rudimentary at best, and completely unknown at worst for the majority of the 5,416 species of mammals currently recognized (Wilson and Reeder, in press). Nevertheless, recent studies have begun to explore stress in free-ranging mammals. These studies often must incorporate and are in fact interested in the very factors that laboratory studies control for, such as environmental variation, variable reproductive condition and life history, and social influences. The emergence of these studies has been permitted by the development of techniques that are feasible in field settings and by the advent of new methods of quantifying stress, including techniques for noninvasive sampling of hormonal indicators of stress.

Because of the growing interest in stress as it relates to the natural history and ecology of mammals, we (Reeder and Kramer) organized a symposium, ''Stress in Nature: Impact on Physiology, Ecology, and Natural History of Mammals'' for the 83rd Annual Meeting of the American Society of Mammalogists, held in Lubbock, Texas, in June 2003. Specific objectives of the symposium were to increase the attendees' understanding of physiological changes inherent in and associated with a stress response; adaptive and nonadaptive consequences of stress; the interaction between stress and ecology, social environment, and natural history of the animal in question; and methods available for assessing stress and their strengths and weaknesses. This paper and the 3 that follow highlight the results of that symposium. This paper will serve as a general introduction to the emerging field of stress biology in free-ranging mammals and will briefly review mammalian stress physiology, the role that stress plays in the way animals adjust to their ever-changing environment, and the interrelationship between stress and the natural history and life history of mammals.

PHYSIOLOGY OF THE STRESS RESPONSE

Stress is a problematic concept in biology, with the term ''stress'' being somewhat overly used, poorly defined, and generally considered undesirable. Modern stress theory defines stress simply as a state in which homeostasis is lost. The event or force that causes this disruption in equilibrium is a stressor, which can be physical, psychological, or both. The distinction between stress as a state of being and a stressor as that thing that causes stress is often muddled in the literature, with the term stress being used for both. Examples of physical stressors

* *Correspondent: dreeder@bu.edu*

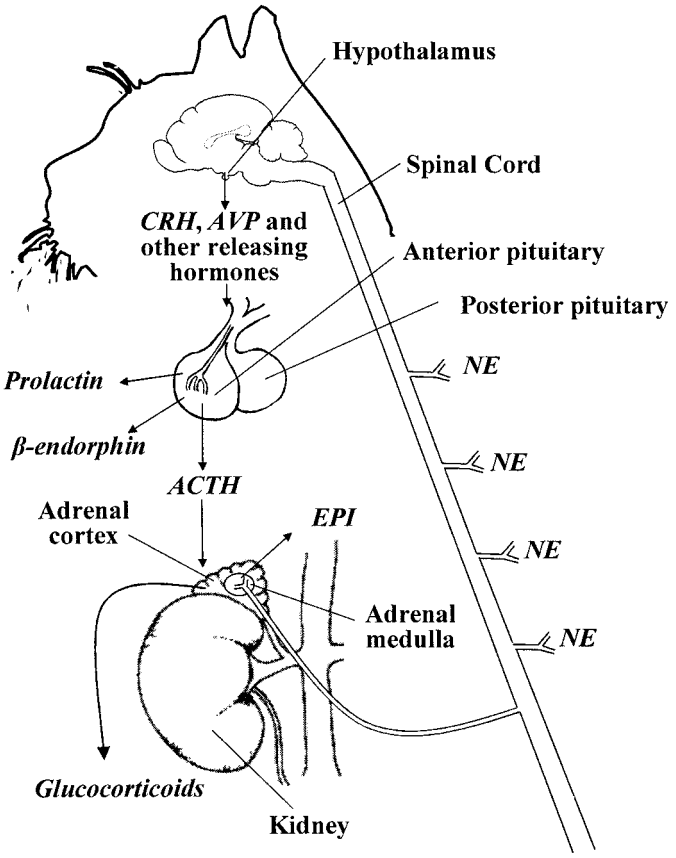

Fig. 1.—The hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system release hormones in response to a stressor. At the initiation of a stress response, the sympathetic nervous system releases norepinephrine (NE) from spinal nerves and epinephrine (EPI, also known as adrenaline) from the adrenal medulla. The HPA stress response begins at the same time, with the release of corticotrophin-releasing hormone (CRH) and other releasing hormones (including arginine vasopressin [AVP]) from the paraventricular nucleus of the hypothalamus. These hormones travel through a closed circulatory system to the anterior pituitary (the hypothalamus and pituitary are physically connected), where they cause the release of adrenocorticotropic-releasing hormone (ACTH) and also β-endorphin (an analgesic) into the blood stream. Prolactin also is released from the anterior pituitary in response to stress (and plays a role in suppressing reproduction). ACTH travels to the adrenal cortex to cause the release of the glucocorticoid hormones, cortisol, corticosterone, or a combination of these. See text for an explanation of the behavioral and physiological effects of the stress response, and also for a discussion of how the stress response is regulated and terminated (negative feedback).

include those internal to the animal, such as anoxia and hypoglycemia, as well as those external to the animal, such as heat or cold, exercise or injury, and other noxious stimuli. Psychological stressors, which have been well studied in the laboratory but are equally applicable to free-ranging animals, include stimuli that affect emotions, for example, eliciting fear, anger, anxiety, or frustration. In response to a stressor, an animal mounts a stress response, which is a suite of physiological and behavioral responses that serve to neutralize the effects of the stressor and to reestablish homeostasis. Responding to a stressor requires an animal to expend energy, which has important implications for understanding how the stress response in free-ranging mammals sometimes varies by environmental conditions and by the life-history stage of the animal.

The stress response is a cascade of events, mediated by an integrated network of neuroanatomical structures and peripheral organs that produce the behavioral and physiological changes necessary for reestablishing equilibrium. This cascade of events is initiated when a stressor is perceived as such by the brain of an animal. Whether a force or event is a stressor is subject to individual variation, and can even vary over time within an individual. That is, what initiates a stress response in one animal may not do so in another, and also may depend on factors such as an animal's life-history stage, developmental history, or reproductive condition. Behavioral responses to a stressor can include escape or avoidance behaviors, altered cognition and attention span, increased awareness, altered sensory threshold, sharpened memory, stress-induced analgesia, suppression of feeding behavior, and suppression of reproductive behavior. This suite of behavioral responses serves to redirect an animal's attention from those behaviors that can be resumed later (eating and sex) to those necessary to deal with the stressor immediately at hand (for a review of stress physiology and its interaction with behavior, see von Holst [1998]). Attendant to and underlying these behavioral responses is the simultaneous stimulation of a number of physiological processes. The 2 most important physiological responses to stress are the stimulation of the sympathetic nervous system (SNS) and the hypothalamic–pituitary–adrenal (HPA) axis; both systems are activated in the central nervous system and result in altered physiological processes in the periphery and central nervous system (see Fig. 1). When activated above basal functioning, these systems mobilize energy and combat the source of stress in a presumably adaptive fashion.

The response of the SNS to a stressor is almost instantaneous. The paraventricular nucleus of the hypothalamus projects to the hindbrain and hence to the spinal cord to activate the SNS, resulting in the secretion of the catecholamine neurohormones norepinephrine and epinephrine (also known as adrenaline). The SNS innervates multiple organs, including the medulla of the adrenal gland, which is essentially a modified sympathetic ganglion. In response to a stressor, norepinephrine is secreted from peripheral nerves and epinephrine is secreted from the adrenal medulla. Norepinephrine and epinephrine increase arousal, elevate heart rate, and provide energy to deal with the stressor by promoting glycogenolysis (the release of glucose from stored glycogen) and lipolysis (the breakdown of fat). Each organ that is innervated by the SNS is dually innervated by the parasympathetic nervous system. Activation of the parasympathetic nervous system serves to down-regulate the SNS (and vice versa), achieving a dynamic balance between these opposing and complimentary systems.

The HPA axis is activated in response to stress simultaneously with the SNS. The paraventricular nucleus projects not only to the hindbrain and spinal cord to activate the SNS, but also projects to the pituitary and activates the HPA axis. Activation of the HPA axis above baseline levels occurs when

the paraventricular nucleus is stimulated by input from a number of other brain areas, such as the amygdala (a part of the limbic system, where some emotions are processed) and the medulla oblongata, which processes, among other things, blood pressure information (central control of HPA response is reviewed by Herman and Cullinan [1997]). Activation of the paraventricular nucleus causes these neurons to synthesize and release corticotrophin-releasing hormone and other secretagogs such as arginine vasopressin. Corticotrophin-releasing hormone then travels through the hypophyseal portal system, a closed circulatory system connecting the hypothalamus with the anterior pituitary, to release adrenocorticotropic hormone (ACTH) from the anterior pituitary into the blood stream. ACTH is cleaved from the precursor protein, pro-opiomelanocortin, from which β-endorphin (which is important for stress-induced analgesia) also is made. ACTH then acts at the cortex of the adrenal gland, to release glucocorticoid steroid hormones. Whether the primary glucocorticoid produced is cortisol or corticosterone varies among species, and some species produce both in significant proportions. The amount by which glucocorticoids are elevated may reflect the severity of the stressor (Hennessy et al. 1979).

Although each component of the stress response operates in concert with the other components, the timescale for the actions of the various hormones is highly variable. The release of corticotrophin-releasing hormone, norepinephrine, and epinephrine occurs nearly instantaneously, whereas ACTH and glucocorticoid levels can take minutes to rise and may remain elevated for long periods of time. This variation in timing ensures that an animal can redirect its behavior and its energy balance to deal with an immediate stressor (within seconds) and its ramifications (within minutes) as well as with challenges that become stressors only after a prolonged period of time.

The measurement of hormones that rise nearly instantaneously (corticotrophin-releasing hormone, norepinephrine, and epinephrine) is not yet feasible in free-ranging mammals, and these hormones are very difficult to assess in captive mammals as well because they are released within the central nervous system (corticotrophin-releasing hormone) or have a short half-life in the periphery. However, SNS activity can be assessed indirectly in the field by monitoring heart rate or body temperature fluctuations, by means of implanted or attached microloggers (e.g., Harms et al. 1997; Moe and Bakken 1997; United States Geological Survey 1997, http://www.npwrc.usgs.gov/resource/tools/telemtry/telemtry.htm [accessed 8 December 2004]; van Acker et al. 2002; Zervanos and Salsbury 2001). In contrast, HPA output, glucocorticoids, and to a lesser degree ACTH, are relatively easy to assess. Blood samples for glucocorticoid analysis can be collected in the field and plasma or serum separated immediately with a manual or battery-operated field centrifuge (Reeder et al. 2004) or separated up to several hours later in the laboratory. Because glucocorticoids are steroid hormones, they are relatively stable and do not easily break down. In contrast, ACTH is a relatively small protein hormone, and is subject to rapid degradation. Samples for ACTH analysis must be collected with the anticoagulant ethylenediaminetetraacetic acid (rather than heparin) and immediately cooled, centrifuged, and frozen. Glucocorticoids in either plasma or serum samples can be stored at −20°C for months before measurement by radioimmunoassay or enzyme immunoassay. The remainder of this paper will focus on HPA, rather than SNS, activity because of its greater role in metabolic processes and behavior and its ease of measurement in the field compared to SNS activation.

Like other steroids, glucocorticoids are bound in the bloodstream by a binding or carrier protein, in this case corticosteroid-binding globulin, which protects them from degradation. Traditional thinking holds that only the free (unbound) portion of glucocorticoids is biologically active (Rosner 1990), hence many researchers (e.g., Boonstra et al. 2002) differentiate between the free and the bound portions of these hormones in order to interpret their actions. That corticosteroid-binding globulin serves to bind excess glucocorticoids and hence protect tissues from excessive levels of glucocorticoids has been referred to as the ''buffer hypothesis'' (Romero 2002) and is contrary to the alternative ''carrier hypothesis.'' Under the carrier hypothesis, corticosteroid-binding globulin is thought to act as a transport molecule that facilitates the movement of glucocorticoids to their target tissues and that potentially mediates their actions (see Breuner and Orchinik 2002). Uncovering which of these hypotheses is correct is critical for understanding the actions of glucocorticoids and deserves future study. In some cases it is clear that, at baseline levels, the total plasma glucocorticoid levels are proportionate to the amount of free glucocorticoids; thus, comparisons between groups without detailed analysis of corticosteroid-binding globulin may be possible (D'Agostino et al. 1982). However, comparisons between baseline and stress glucocorticoid levels should include levels of corticosteroid-binding globulin if possible, because glucocorticoids rise much more quickly than does corticosteroid-binding globulin (Lynn et al. 2003), rapidly altering the level of unbound glucocorticoids in circulation.

Glucocorticoids serve a number of important roles in metabolism at both basal and stress-induced levels, generally increasing available energy through increased gluconeogenesis, decreased glucose use, decreased sensitivity to insulin, and protein and fat metabolism. Glucocorticoid hormones also interact in complex ways with the immune system and the hypothalamic–pituitary–gonadal axis. Despite the generally adaptive function of acute rises in glucocorticoids in response to a stressor, prolonged exposure to high levels of glucocorticoids, as occurs with repeated exposure to stress, is deleterious. Selye (1956) characterized the stress response as consisting of 3 phases in what is now termed the general adaptation syndrome; the alarm phase (activation of the SNS), the resistance phase (activation of the HPA axis), and the exhaustion phase during which elevated glucocorticoids begin to have deleterious effects. For example, prolonged exposure to glucocorticoids results in neuronal cell death, hyperglycemia, insulin resistance, muscle and bone atrophy, poor wound healing, hypertension and growth inhibition, and even collapse of the immune system to the point of death (e.g., as occurs in some semelparous marsupials—Boonstra 2005; McDonald et al. 1981). For this reason, the ability to regulate HPA activation (i.e., to turn off

this component of the stress response) is as important as the ability to mount the stress response in the 1st place. A number of feedback mechanisms normally serve this function (reviewed by Whitnall [1993]). For example, high circulating levels of cortisol negatively feed back at multiple points on the HPA axis to down-regulate their own production. Glucocorticoid receptors are found in the anterior pituitary as well as in multiple sites in the brain including the hypothalamus, hippocampus, and amygdala; binding of glucocorticoids at these sites serves to lower levels of corticotrophin-releasing hormone and ACTH, resulting in lowered glucocorticoids. Similarly, ACTH feeds back negatively on the hippocampus to down-regulate production of corticotrophin-releasing hormone. There are 2 types of glucocorticoid receptors, type I (mineralocorticoid receptors), which are normally occupied at basal levels of glucocorticoids, and type II (glucocorticoid receptors), which have slightly lower affinity for glucocorticoids than type I and are occupied primarily when glucocorticoid levels are higher because of stress (Munck and Náray-Fejes-Tóth 1992; Sapolsky et al. 2000). Type II receptors, found in the paraventricular nucleus of the hypothalamus, the hippocampus, and the amygdala, play a role in the negative feedback of glucocorticoids in the brain. Negative feedback on the HPA axis through type II receptors helps regulate the HPA axis, but other mechanisms also may contribute, including roles for gamma-aminobutyric acid, β-endorphin, and oxytocin (reviewed by Jessop [1999]).

Stress and Ecology: Coping with Environmental Change

The HPA axis is not dormant, resting at some fixed baseline level before stress activation. Rather, it is dynamic, shifting in response to environmental changes. For example, glucocorticoids exhibit profound circadian and circannual rhythms that are essential for regulating energy balance in relation to the environment. The elevated levels of glucocorticoids found at the peak of the circadian rhythm (e.g., Coe and Levine 1995; D'Agostino et al. 1982), the period just before arousal from sleep, provide the high levels of energy needed for the behaviors that occur after awakening, such as increased locomotor, exploratory, and food-seeking behavior (McEwen et al. 1988). Elevated glucocorticoid levels not only provide the energy needed for engaging in behavior, but, in many cases, influence (directly or indirectly) the expression of behavior through central mechanisms (McEwen et al. 1988; Romero 2002; von Holst 1998).

Seasonal cycles in HPA function have evolved in response to predictable changes in abiotic (e.g., seasonal changes in weather) and biotic (e.g., annual search for mates) environmental conditions. These rhythms are especially marked for species in the farthest northern and southern latitudes, where seasonal changes are extreme and resources often limited (e.g., little brown myotis [*Myotis lucifugus*]—Gustafson and Belt 1981). Seasonal cycles in HPA function also exist in tropical vertebrate species (Romero 2002), which also experience seasonal differences in environmental conditions and resource availability. However, we know of no studies of glucocorticoids in tropical mammals. Seasonal cycles in HPA function have presumably evolved to allow animals to balance their energetic needs in each seasonal state, for example, by changing metabolic rate. Metabolic rate shifts seasonally in red deer (*Cervus elaphus*—Arnold et al. 2004), and in sugar gliders (*Petaurus breviceps*—Holloway and Geiser 2001); but Peacock et al. (2004) found no differences in metabolic rate in response to changing photoperiod in bank voles (*Clethrionomys glareolus*). In addition, the HPA mediates other seasonal changes in physiology, including changes in water metabolism (Deavers and Musacchia 1980), gonadal function (Viau 2002), and immune competence (Cancedda et al. 2002; Nelson and Demas 1996); see also reviews by McEwen and Wingfield (2003) and Sapolsky et al. (2000). In his recent review of seasonal and stress-induced variations in glucocorticoid output in free-living vertebrates, Romero (2002) concluded that the majority of species studied in all 4 classes of terrestrial vertebrates seasonally modulate both baseline glucocorticoid concentrations and stress-induced glucocorticoid secretion. Most species studied show a peak in baseline glucocorticoid secretion in the breeding season relative to pre- and postbreeding periods.

Despite this generalization, the relationship between any given season and the regulation of the HPA axis is somewhat species- and sex-specific and likely depends on the relative energetic costs of the different seasons for each species and on life-history patterns. For example, some mammals conserve energy in resource-limited and extreme environments by hibernating. Most hibernators prepare for hibernation by laying down fat (Mrosovsky 1976; Young 1976), and prehibernatory hyperphagia and weight gain have been associated with elevated glucocorticoids. For example, elevations in plasma glucocorticoids are associated with prehibernatory fattening in little brown myotis (males sampled up to 24 h after capture—Gustafson and Belt 1981; and free-ranging males and females—Reeder et al. 2004), free-ranging yellow-bellied marmots (*Marmota flaviventris*—Armitage 1991), free-ranging golden-mantled ground squirrels (*Spermophilus saturatus*—Boswell et al. 1994), captive garden dormice (*Eliomys quercinus*—Boulouard 1971), and captive European hedgehogs (*Erinaceus europaeus*—Saboureau et al. 1980). In contrast, prehibernatory glucocorticoid levels are low relative to other times of the year in the yellow-pine chipmunk (*Tamias amoenus*), which prepares for hibernation by caching food and does not gain weight before hibernation (Kenagy and Place 2000; Place and Kenagy 2000; Stebbins and Orich 1977). With the exception of the study by Reeder et al. (2004) on little brown myotis, the samples collected in these studies were either not true baseline samples (not collected within 3 min of capture) or not from free-ranging animals.

Endogenous circadian rhythms and seasonal cycles in HPA function have evolved to cope with predictable environmental change. However, not all change can be predicted. To survive and reproduce, animals also must have mechanisms to cope with unexpected stressors. Unpredictable environmental changes may come in the form of severe weather events or climatic conditions (Wingfield 2005), and unpredictable changes in the

social environment, such as intruders in a territory (see Mendoza and Mason 1986), changes in dominance status (see Creel 2005; Lyons et al. 1994), or loss of an attachment figure (e.g., a mother or a mate in pair-bonded species—see Hennessy 1997; Mason and Mendoza 1998; Mendoza and Mason 1986). The stress response to unpredictable changes is superimposed upon circadian rhythms and seasonal cycles discussed above. For example, a stress-induced increase in glucocorticoids is larger if it occurs at the nadir of the circadian rhythm (Pfister and King 1976).

As with baseline patterns, seasonal rhythms are apparent in stress-induced glucocorticoid levels in many species. Because baseline glucocorticoid values are difficult to assess in free-ranging mammals, seasonal variation in stress-induced glucocorticoid levels has been more adequately described than baseline HPA function. In contrast to the robust trend across taxa toward higher baseline glucocorticoid levels during breeding, the effect of seasonal cycles on the stress response is highly species-specific. Two different species living in the same environment can have profoundly different responses to stressors, which are likely related to differences in their life histories and their phylogenetic histories. For example, arctic ground squirrels (*Spermophilus parryii*) typically hibernate, whereas red squirrels (*Tamiasciurus hudsonicus*) survive winter by defending individual territories and their resources. These 2 species often live in proximity in the same boreal environment, but arctic ground squirrels exhibit a much greater response to stimulation with ACTH (Boonstra and McColl 2000). HPA activity also varies within a species. For example, arctic ground squirrels are more chronically stressed in boreal forests than in alpine meadows, which Hik et al. (2001) suggested was related to differences in predation risk between the 2 environments.

Although it seems maladaptive not to respond maximally to stressors at all times, other physiological and behavioral needs of the animal (such as lactation, sexual behavior, or immune challenges) may place constraints on the ability of an animal to mount a stress response or reduce the importance of doing so. Scenarios in which animals should be resistant to the effects of stressors because they have limited opportunity for mating and thus trade off potential survival for reproductive success include when aged animals have limited future reproductive potential, when seasonal breeders have a very short time in which to breed, when there is only a single breeding season in the life of an individual (i.e., semelparous species), and when subordinate individuals have only a short opportunity for mating (Wingfield and Sapolsky 2003).

Stress and the Natural History of Mammals—Complications and Methods

Compared to the number of studies that have examined baseline and stress-induced glucocorticoid levels in reptiles, amphibians, and especially in birds, data for free-living mammals are sparse (Romero 2002). In addition, some studies of variation in glucocorticoid levels in mammals did not report sampling times or exceeded 3 min, making the interpretation of these data as baseline values questionable. The scarcity of data on baseline HPA function in mammals is largely due to difficulties in obtaining samples within the 3-min window necessary to avoid measuring the response to capture and sampling itself, further complicated by the fact that most mammals are nocturnal and solitary. However, baseline samples have been successfully collected from free-living mammals by constantly monitoring traps (e.g., yellow-pine chipmunks—Kenagy and Place 2000; Place and Kenagy 2000; and little brown myotis—Reeder et al. 2004). Baseline samples also have been collected by terminal sampling (e.g., gun shot—Boonstra and Singleton 1993). Nonbaseline (presumably ''stress-induced'') levels of glucocorticoid secretion are easier to measure in free-living mammals than are baseline samples, because most mammals spend >3 min in a trap before being sampled (Romero 2002). For example, seasonal changes in glucocorticoid levels have been described for animals that have either been in a trap ≥ 1 h (e.g., Boswell et al. 1994; Kenagy and Place 2000; Kenagy et al. 1999; Place and Kenagy 2000) or that were collected in the field and sampled later in the laboratory (e.g., Gustafson and Belt 1981; Krishna et al. 1998). Place and Kenagy (2000) and Kenagy and Place (2000) compared this standard protocol with one that assessed both baseline and stress-induced levels in the same individuals and found that both methodologies told roughly the same story regarding seasonal variation in glucocorticoid levels in yellow-pine chipmunks.

Comparison of baseline glucocorticoids with glucocorticoid levels reached some time after the application of a stressor is one of the primary methods used to assess the stress response in mammals and other vertebrates. Some also have used a hormone-challenge protocol (see Boonstra 2005). In this instance, animals held in traps for unknown periods of time are brought to roughly equivalent glucocorticoid levels through administration of the synthetic glucocorticoid dexamethasone, which feeds back negatively on the HPA axis and thus returns glucocorticoids to ''baseline'' levels. ACTH is then administered, stimulating glucocorticoid production, and glucocorticoid levels at subsequent time points can be assessed. Variation in the level of glucocorticoid suppression in response to dexamethasone (the dexamethasone suppression test) and in the response of glucocorticoids to ACTH administration can be used to compare HPA activity levels both across species and within species across different life-history stages or environments. Animals in which glucocorticoid levels remain high after dexamethasone administration are often thought to be under chronic stress (e.g., arctic ground squirrels in some environments—Hik et al. 2001). Another method to assess the response of the HPA axis is to collect adrenal glands from individuals, superfuse them with ACTH, and measure resultant glucocorticoid production. This technique was used to show that meadow voles (*Microtus pennyslvanicus*) have higher adrenal responsiveness in the spring (Seabloom et al. 1978).

Hypothalamic–pituitary–adrenal function in free-ranging mammals also has been assessed by measuring glucocorticoid metabolites in urine or feces (e.g., Carlstead et al. 1992; Möstl et al. 1999; Zav'yalov et al. 2003). This avoids the necessity of collecting samples within 3 min but the results represent total

glucocorticoid output over an unknown period of time rather than acute or immediate values (Boonstra 2005). For these data to be interpretable, the individual that produced the sample and the time the sample was produced must be known. In some cases, this cumulative glucocorticoid level may in fact be of greater interest than acute or immediate glucocorticoid levels. In many species (especially larger species and those that are difficult to trap), this noninvasive monitoring is the only currently feasible way to collect samples.

Mammalian Life-History Stages and the HPA Axis

The HPA axis has such an important influence on mammalian physiology and behavior that understanding HPA function is critical to understanding a mammal's life history, especially from a comparative perspective. For example, male mammals employ life-history strategies ranging from iteroparity to semelparity. Boonstra (2005) demonstrates that differences in HPA function between semelparous, semisemelparous, and iteroparous species explain variation in their survival, and how they balance survival with reproduction. As with all comparative work, we must keep phylogenetic constraints in mind. For example, true semelparity in mammals has apparently only evolved in some marsupials, which may differ from other mammals in physiological ways that facilitate the evolution of semelparity. Only by adding data for a variety of mammalian species in different life-history stages and environmental conditions will a broader and more complete understanding of baseline and stress-induced HPA activity in mammals emerge.

Differences between the sexes further make studying HPA function in mammals both interesting and difficult. Because of the paucity of field data, once again we must gain insight from the study of captive mammals. Glucocorticoid resistance and circadian rhythms of glucocorticoid secretion have been studied in laboratory populations of prairie voles (*Microtus ochrogaster*—Taymans et al. 1997), and circadian as well as ultradian rhythms in glucocorticoid secretion have been described in red-backed voles (*Clethrionomys gapperi*—Kramer and Sothern 2001). In both species, basal glucocorticoid levels are higher in females than in males. Females having higher basal glucocorticoids is a general trend that appears to hold for most mammalian species. A notable exception to this rule is found in variable flying foxes (*Pteropus hypomelanus*), in which males have significantly higher baseline glucocorticoid levels than females (Reeder et al. 2004). In addition to higher baseline glucocorticoid levels, females generally have a more robust stress response (e.g., Brett et al. 1983; Handa et al. 1994), likely because of the central actions of estrogen and androgens (Handa et al. 1994). For example, female arctic ground squirrels responded to a stressor with a 12-fold increase whereas plasma cortisol increased only 4-fold in males (Boonstra et al. 2001).

From an energetic perspective, gestation and lactation are the most metabolically expensive periods of a female's life history (Gittleman and Thompson 1988; Wade and Schneider 1992). Not surprisingly, this burden is reflected in dramatic shifts in glucocorticoid regulation. Unfortunately, the complications that arise in understanding HPA function and other physiological processes during pregnancy and lactation in free-ranging mammals have been dealt with largely by ignoring females and focusing exclusively on males. Rather than being a complication, however, this variation in energetic demands and life-history strategies of males compared to females provides an excellent opportunity to understand the interrelationship between reproduction, life-history traits, and glucocorticoid physiology all within 1 species.

Just as the HPA axis has a role in physiological changes associated with environmental change, the HPA axis is intimately involved in reproduction. In a variety of female mammals, glucocorticoid levels increase during middle and late gestation and decline at parturition to levels that are still somewhat elevated relative to males and cycling or nonreproductive females (Atkinson and Waddell 1995). Plasma glucocorticoids were much higher in pregnant and lactating yellow-pine chipmunks than in females at emergence from hibernation or during the prehibernatory period (Kenagy and Place 2000). In little brown myotis, baseline glucocorticoids were elevated in females during mid to late pregnancy relative to early pregnancy and lactation and relative to glucocorticoid levels in males (Reeder et al. 2004). One role of these elevated glucocorticoids is to prepare for and maintain lactation (Voogt et al. 1969; Walker et al. 1992). Despite the similarity across species in HPA function during pregnancy, some interspecific variation exists in HPA function during lactation. In contrast to laboratory rats, which show slightly reduced levels of glucocorticoid secretion during lactation at the peak of the circadian rhythm compared to males and cycling females (Stern et al. 1973), glucocorticoid levels in lactating little brown myotis females at the peak of their rhythm were not distinguishable from those of males or from females in early pregnancy. It is possible, however, that glucocorticoid levels are elevated during other parts of the circadian rhythm that would result in the higher total daily output of glucocorticoids seen in rodents (Stern et al. 1973).

Despite the fact that baseline glucocorticoids are increased in late pregnancy, stress-induced glucocorticoid levels are markedly decreased during pregnancy, as well as during lactation in laboratory rats and other mammals (Lightman et al. 2001; Stern et al. 1973). For example, adrenal response to ACTH in meadow voles is lower in pregnant females than in nonpregnant females (Seabloom et al. 1978). In addition to lower sensitivity of the adrenal gland to ACTH, a difference in HPA function between males and females during reproduction can result from differences in corticosteroid binding capacity. Female arctic ground squirrels sampled after trapping (nonbaseline) during pregnancy and lactation had total cortisol levels similar to those of males, but significantly lower levels of free cortisol and higher levels of maximum corticosteroid-binding capacity than did males (Boonstra et al. 2001). Assuming that corticosteroid-binding globulin makes glucocorticoids unavailable (Rosner 1990; but see discussion of the role of corticosteroid-binding globulin above), the increased corticosteroid-binding capacity at this time likely buffers females from elevated glucocorticoids.

This may reflect the need to minimize large fluctuations in glucocorticoids in the fetus during pregnancy and in the neonate during lactation (glucocorticoids can enter via maternal milk—Lightman et al. 2001) because high levels of glucocorticoids can adversely affect developmental processes and subsequent health and survival (Wadhwa et al. 2001).

Although reproduction is clearly costly for female mammals, a variety of energetically expensive behaviors are associated with reproduction in male mammals as well. The quintessential example of this occurs in semelparous didelphid and dasyurid marsupials (Boonstra 2005), where breeding males show high glucocorticoids, failure of negative feedback, and immunosuppression. Even in iteroparous species such as arctic ground squirrels, basal and stress-induced total and free cortisol can be higher in males than in females during the breeding season (Boonstra et al. 2001). Breeding males often engage in energetically expensive activities, such as territorial aggression, male–male competition and dominance interactions (Creel 2001, 2005), and courtship. They may suffer from increased predation and wounding and immunosuppression, and, for some species, expend energy providing parental care. In the highly social Malayan flying fox (*Pteropus vampyrus*), but not in the relatively solitary little golden-mantled flying fox (*P. pumilus*), males housed in breeding groups have significantly higher glucocorticoid levels during periods of high breeding activity than males living in all-male groups (D. M. Reeder, T. H. Kunz, and E. P. Widmaier, in litt.). The levels of testosterone and glucocorticoids measured in male mammals during breeding periods and the period of parental care (if applicable) often represent a compromise between the costs and benefits of each hormone (Wingfield et al. 1997).

The HPA axis also modulates social behaviors necessary for reproduction. In monogamous prairie voles, increased corticosterone levels stimulate pair-bonding in males, whereas females have the opposite response to elevated glucocorticoids (DeVries et al. 1996). Glucocorticoids may play a role in modulating both maternal and paternal behavior as well (e.g., Bardi et al. 2004; review by Wynne-Edwards [2001]). Seasonal shifts in glucocorticoid levels (at least in birds—Romero 2002) may occur not only to affect metabolic processes, but also to promote (or suppress) the expression of certain glucocorticoid-mediated social behaviors.

Although we have focused primarily on the role of the HPA axis in reproduction, the function of the HPA axis also varies with age (reviewed by de Kloet et al. [1988]). In laboratory rats and mice, from approximately postnatal days 2 to 12, basal glucocorticoid levels are relatively low and there is little glucocorticoid response to stressors (Sapolsky and Meaney 1986; Schmidt et al. 2003). This period has been termed the stress hyporesponsive period. Sheep appear to have a similar stress hyporesponsive period (Challis and Brooks 1989). The stress hyporesponsive period appears to result from adrenal insensitivity to ACTH because stressors during this period elicit increases in corticotrophin-releasing hormone. As with low stress-responsiveness in lactating females, the stress hyporesponsive period might serve to buffer the developing HPA axis from perturbations with permanent physiological and behavioral consequences. Stressors (and elevated glucocorticoids) encountered during the prenatal development of the HPA axis permanently affect central distribution of hormone receptors as well as subsequent physiology and behavior (Koehl et al. 1999; Weinstock 1997). These alterations typically last into adulthood.

Most efforts at describing the HPA axis as a function of age have focused on either the early postnatal period or senescence. However, a few have examined glucocorticoid levels in juveniles. For example, the adrenal glands from juvenile meadow voles are less responsive to ACTH than are those from adults (Seabloom et al. 1978). The HPA axis may play an important role during sexual maturation, particularly in social species such as prairie voles, in which corticosterone secretion has a clear role in regulating social behaviors such as pair-bonding (DeVries et al. 1996).

Deregulation of the HPA axis occurs with aging; however, the nature of the deregulation appears to vary between and within species. Different results also might be an artifact of experimental design. For example, many have documented increases in basal glucocorticoid levels with age (Dellu et al. 1996; Meaney et al. 1988; Sapolsky et al. 1983) but others have found no change (Goncharova and Lapin 2002; Sonntag et al. 1987). One finding that seems to be fairly consistent is an effect of age on the stress response and, in particular, an impairment of the negative feedback system regulating the glucocorticoid response to stress. In species ranging from laboratory rats to nonhuman primates, the recovery time following a stressor, in terms of time to return to basal glucocorticoid levels, is significantly greater in older than in younger animals (e.g., Bizon et al. 2001; Dellu et al. 1996; Goncharova and Lapin 2002; Sapolsky et al. 1983). In addition, the impairment of the negative feedback loop for the HPA axis is associated with cognitive impairment (Issa et al. 1990; Meaney et al. 1988). In a comparison of young rats and aged rats subdivided into those showing cognitive impairment or those that were unimpaired, only the aged rats with cognitive impairment also showed an increased recovery time of the HPA axis (Bizon et al. 2001). This was associated with a reduction in glucocorticoid receptor mRNA in the hippocampus but without a reduction in neurons (Bizon et al. 2001). The connection between stress, aging, and cognitive impairment led to the ''glucocorticoid cascade hypothesis'' (Sapolsky et al. 1986), which suggests that repeated stress results in increased glucocorticoid levels that in turn cause hippocampal cell death and a reduction in glucocorticoid receptors, leading to elevated glucocorticoid levels and cognitive impairment. This theory has motivated much work on the mechanisms underlying aging and fits well within the framework of allostatic load (McEwen 2002; McEwen and Wingfield 2003; Wingfield 2005). However, this theory is based largely on data from cross-sectional studies rather than longitudinal studies; thus interindividual differences in HPA function could be a confounding factor (Sabatino et al. 1991). A recent review by McEwen (2002) discusses individual differences in vulnerability to allostatic load, stress, and their role in aging.

Most of our knowledge about the HPA axis and senescence comes from captive populations and primarily from domesticated

species. For free-living populations of mammals, the functioning of the HPA axis during ''middle age'' might be more relevant than the HPA axis in aged animals because it is questionable in how many species a significant portion of a free-living population survives to a point where physiological senescence occurs. Unfortunately, studies of the HPA axis as a function of age have focused on the 2 extremes—either very young or very old. The limited data available for middle age suggest that the HPA does function differently during this life stage. For example, laboratory rats that respond to stress with a relatively high plasma glucocorticoid level show an elevated response to stress at 16 months of age but this hyperresponsiveness disappears by the age of 21 months (Dellu et al. 1996). Increasing our understanding of variation in stress reactivity by developmental stage will help us better understand variation in survival, reproductive stress, and even extinction risk among species.

Conclusion and Future Directions

Knowing how the sympathetic nervous system operates under stressful conditions and how the HPA axis functions under both baseline and stressful conditions is critical to understanding mammalian biology. In particular, studying these systems helps explain how a free-ranging mammal is able to respond to its ever-changing environment.

Technological advances continue to make the exploration of both the SNS and the HPA axis in a field setting easier. The field of stress biology in general is evolving in a more holistic manner on several fronts. For example, there is a growing recognition of the interrelationships between the nervous system, the endocrine system (collectively called the neuroendocrine system), the immune system (hence the term neuroimmunology), and behavior (hence the fields of behavioral neuroendocrinology, psychoneuroimmunology, and others). These systems and their regulatory mechanisms are being increasingly studied in the real world, especially in terms of understanding how they relate to energy balance over the life of the animal (see McEwen and Wingfield 2003; Wingfield 2005). Finally, a growing number of studies of stress are organismically oriented and less reductionistic. Placement of the whole organism in its natural setting is an active and exciting focus of current research on stress, as we integrate our understanding of physiological responses with what is known about the ecology and natural history of mammals.

Acknowledgments

Our thanks are extended to the American Society of Mammalogists for funding and hosting the symposium from which this paper emerged. DMR and KMK are funded by National Research Service Awards from the National Institute of Child Health and Human Develpoment (award F32 HD41305 to DMR and award F32 HD41293 to KMK).

Literature Cited

Armitage, K. B. 1991. Factors affecting corticosteroid concentrations in yellow-bellied marmots. Comparative Biochemistry and Physiology, A. Comparative Physiology 98:47–54.

Arnold, W., T. Ruf, S. Reimoser, F. Tataruch, K. Onderscheke, and F. Schober. 2004. Nocturnal hypometabolism as an overwintering strategy of red deer (*Cervus elaphus*). American Journal of Physiology. Regulatory, Integrative and Comparative Physiology 286:R174–R181.

Atkinson, H. C., and B. J. Waddell. 1995. The hypothalamic–pituitary–adrenal axis in rat pregnancy and lactation: circadian variation and interrelationship of plasma adrenocorticotropin and corticosterone. Endocrinology 136:512–520.

Bardi, M., J. A. French, S. M. Ramirez, and L. Brent. 2004. The role of the endocrine system in baboon maternal behavior. Biological Psychiatry 55:724–732.

Bizon, J. L., et al. 2001. Hypothalamic–pituitary–adrenal axis function and corticosterone receptor expression in behaviourally characterized young and aged Long-Evans rats. European Journal of Neuroscience 14:1739–1751.

Boonstra, R. 2005. Equipped for life: the adaptive role of the stress axis in male mammals. Journal of Mammalogy 86:236–247.

Boonstra, R., A. H. Hubbs, E. A. Lacey, and C. J. McColl. 2001. Seasonal changes in glucocorticoid and testosterone concentrations in free-living arctic ground squirrels from the boreal forest of the Yukon. Canadian Journal of Zoology 79:49–58.

Boonstra, R., and C. J. McColl. 2000. Contrasting stress response of male arctic ground squirrels and red squirrels. Journal of Experimental Zoology 286:390–404.

Boonstra, R., and G. R. Singleton. 1993. Population declines in the snowshoe hare and the role of stress. General and Comparative Endocrinology 91:126–143.

Boonstra, R., N. Takagi, N. Bissoon, S. Vij, and J. W. Gurd. 2002. Trapping-induced changes in expression of the *N*-methyl-D-aspartate receptor in the hippocampus of snowshoe hares. Neuroscience Letters 324:173–176.

Boswell, T., S. C. Woods, and G. J. Kenagy. 1994. Seasonal changes in body mass, insulin, and glucocorticoids of free-living golden-mantled ground squirrels. General and Comparative Endocrinology 96:339–346.

Boulouard, R. 1971. Étude de la function corticosurrénalienne au cours du cycle annuel chez un hibernant: le lérot (*Eliomys quercinus* L.). II. Activité durant l'automne: période de preparation à l'hibernation. [Study of adrenocortical function during the annual cycle in a hibernant: the garden dormouse (*Eliomys quercinus* L.). II. Activity during autumn: period of hibernation preparation.] Journal of Physiology (Paris) 63:77–86 (in French, English summary).

Brett, L. P., G. S. Chong, S. Coyle, and S. Levine. 1983. The pituitary adrenal response to novel stimulation and ether stress in young adult and aged rats. Neurobiology of Aging 4:133–138.

Breuner, C. W., and M. Orchinik. 2002. Beyond carrier proteins. Plasma binding proteins as mediators of corticosteroid action in vertebrates. Journal of Endocrinology 175:99–112.

Cancedda, C., G. Filaci, F. Puppo, M. Ghio, P. Contini, and F. Indiveri. 2002. Immune homeostasis requires several biologic factors including glucocorticoid hormones. Annals of the New York Academy of Sciences 966:49–63.

Carlstead, K., J. L. Brown, S. L. Monfort, R. Killens, and D. E. Wildt. 1992. Urinary monitoring of adrenal responses to psychological stressors in domestic and nondomestic felids. Zoo Biology 11:165–176.

Challis, J. R. G., and A. N. Brooks. 1989. Maturation and activation of hypothalamic–pituitary–adrenal function in fetal sheep. Endocrine Reviews 10:182–204.

COE, C. L., AND S. LEVINE. 1995. Diurnal and annual variation of adrenocortical activity in the squirrel monkey. American Journal of Primatology 35:283–292.

CREEL, S. 2001. Social dominance and stress hormones. Trends in Ecology and Evolution 16:491–497.

CREEL, S. 2005. Dominance, aggression, and glucocorticoid levels in social carnivores. Journal of Mammalogy 86:255–264.

D'AGOSTINO, J., G. F. VAETH, AND S. J. HENNING. 1982. Diurnal rhythm of total and free concentrations of serum corticosterone in the rat. Acta Endocrinologica 100:85–90.

DEAVERS, D. R., AND X. J. MUSACCHIA. 1980. Water metabolism and renal function during hibernation and hypothermia. Federation Proceedings 39:2969–2973.

DE KLOET, E. R., P. ROSENFELD, J. A. M. VAN EEKELEN, W. SUTANTO, AND S. LEVINE. 1988. Stress, glucocorticoids and development. Progress in Brain Research 73:101–119.

DELLU, F., ET AL. 1996. Behavioral reactivity to novelty during youth as a predictive factor of stress-induced corticosterone secretion in the elderly—a life-span study in rats. Psychoneuroendocrinology 21:441–453.

DEVRIES, A. C., M. B. DEVRIES, S. E. TAYMANS, AND C. S. CARTER. 1996. The effects of stress on social preferences are sexually dimorphic in prairie voles. Proceedings of the National Academy of Sciences USA 93:11980–11984.

GITTLEMAN, J. L., AND S. D. THOMPSON. 1988. Energy allocation in mammalian reproduction. American Zoologist 28:863–875.

GONCHAROVA, N. D., AND B. A. LAPIN. 2002. Effects of aging on hypothalamic–pituitary–adrenal system function in non-human primates. Mechanisms of Ageing and Development 123: 1191–1201.

GUSTAFSON, A. W., AND W. D. BELT. 1981. The adrenal cortex during activity and hibernation in the male little brown bat, *Myotis lucifugus lucifugus*: annual rhythm of plasma cortisol levels. General and Comparative Endocrinology 44:269–278.

HANDA, R. J., L. H. BURGESS, J. E. KERR, AND J. A. O'KEEFE. 1994. Gonadal steroid hormone receptors and sex differences in the hypothalamo–pituitary–adrenal axis. Hormones and Behavior 28: 464–476.

HARMS, C. A., W. J. FLEMING, AND M. K. STOSKOPF. 1997. A technique for dorsal subcutaneous implantation of heart rate biotelemetry transmitters in black ducks: application in an aircraft noise response study. Condor 99:231–237.

HENNESSY, M. B. 1997. Hypothalamic–pituitary–adrenal responses to brief social separation. Neuroscience and Biobehavioral Reviews 21:11–29.

HENNESSY, M. B., J. P. HEYBACH, J. VERNIKOS, AND S. LEVINE. 1979. Plasma corticosterone concentrations sensitively reflect levels of stimulus intensity in the rat. Physiology and Behavior 22:821–825.

HERMAN, J. P., AND W. E. CULLINAN. 1997. Neurocircuitry of stress: central control of the hypothalamo–pituitary–adrenocortical axis. Trends in Neuroscience 20:78–84.

HIK, D. S., C. J. MCCOLL, AND R. BOONSTRA. 2001. Why are arctic ground squirrels more stressed in the boreal forest than in alpine meadows? Ecoscience 8:275–288.

HOLLOWAY, J. C., AND F. GEISER. 2001. Seasonal changes in the thermoenergetics of the marsupial sugar glider, *Petaurus breviceps*. Journal of Comparative Physiology, B. Biochemical, Systemic, and Environmental Physiology 171:643–650.

ISSA, A. M., W. ROWE, S. GAUTHIER, AND M. J. MEANEY. 1990. Hypothalamic–pituitary–adrenal activity in aged, cognitively impaired and cognitively unimpaired rats. Journal of Neuroscience 10: 3247–3254.

JESSOP, D. S. 1999. Central non-glucocorticoid inhibitors of the hypothalamo–pituitary–adrenal axis. Journal of Endocrinology 160: 169–180.

KENAGY, G. J., AND N. J. PLACE. 2000. Seasonal changes in plasma glucocorticosteroids of free-living female yellow-pine chipmunks: effects of reproduction and capture and handling. General and Comparative Endocrinology 117:189–199.

KENAGY, G. J., N. J. PLACE, AND C. VELOSO. 1999. Relation of glucocorticosteroids and testosterone to the annual cycle of free-living degus in semiarid central Chile. General and Comparative Endocrinology 115:236–243.

KOEHL, M., M. DARNAUDÉRY, J. DULLUC, O. VAN REETH, M. LE MOAL, AND S. MACCARI. 1999. Prenatal stress alters circadian activity of hypothalamo–pituitary–adrenal axis and hippocampal corticosteroid receptors in adult rats of both gender. Journal of Neurobiology 40:302–315.

KRAMER, K. M., AND R. B. SOTHERN. 2001. Circadian characteristics of corticosterone secretion in red-backed voles (*Clethrionomys gapperi*). Chronobiology International 18:933–945.

KRISHNA, A., K. SINGH, J. DOVAL, AND D. CHANDA. 1998. Changes in circulating insulin and corticosterone concentrations during different reproductive phases and their relationships to body weight and androstenedione concentration of male *Scotophilus heathi*. Journal of Experimental Zoology 281:201–206.

LIGHTMAN, S. L., R. J. WINDLE, S. A. WOOD, Y. M. KERSHAW, N. SHANKS, AND C. D. INGRAM. 2001. Peripartum plasticity within the hypothalamo–pituitary–adrenal axis. Progress in Brain Research 133:111–129.

LYNN, S. E., C. W. BREUNER, AND J. C. WINGFIELD. 2003. Short-term fasting affects locomotor activity, corticosterone, and corticosterone binding globulin in a migratory songbird. Hormones and Behavior 43:150–157.

LYONS, D. M., S. P. MENDOZA, AND W. A. MASON. 1994. Psychosocial and hormonal aspects of hierarchy formation in groups of male squirrel monkeys. American Journal of Primatology 32:109–122.

MASON, W. A., AND S. P. MENDOZA. 1998. Generic aspects of primate attachments: Parents, offspring and mates. Psychoneuroendocrinology 23:765–778.

MCDONALD, I. R., A. K. LEE, A. J. BRADLEY, AND K. A. THAN. 1981. Endocrine changes in dasyurid marsupials with differing mortality patterns. General and Comparative Endocrinology 44:292–301.

MCEWEN, B. S. 2002. Sex, stress and the hippocampus: allostasis, allostatic load and the aging process. Neurobiology of Aging 23: 921–939.

MCEWEN, B. S., R. W. BRINTON, AND R. M. SAPOLSKY. 1988. Glucocorticoid receptors and behavior: implications for the stress response. Advances in Experimental Medicine and Biology 245: 35–45.

MCEWEN, B. S., AND J. C. WINGFIELD. 2003. The concept of allostasis in biology and biomedicine. Hormones and Behavior 43:2–15.

MEANEY, M., D. AITKEN, C. V. BERKEL, S. BHATNAGAR, AND R. SAPOLSKY. 1988. Effect of neonatal handling on age-related impairments associated with the hippocampus. Science 239: 766–768.

MENDOZA, S. P., AND W. A. MASON. 1986. Contrasting responses to intruders and to involuntary separation by monogamous and polygynous New World monkeys. Physiology and Behavior 38: 795–801.

MOE, R. O., AND M. BAKKEN. 1997. Effects of handling and physical restraint on rectal temperature, cortisol, glucose and leucocyte counts in the silver fox (*Vulpes vulpes*). Acta Veterinaria Scandinavica 38:29–39.

MÖSTL, E., S. MESSMANN, E. BAGU, C. ROBIA, AND R. PALME. 1999. Measurement of glucocorticoid metabolite concentrations in faeces of domestic livestock. Zentralblatt für Veterinärmedizin Reihe A 46:621–631.

MROSOVSKY, N. 1976. Lipid programmes and life strategies in hibernators. American Zoologist 16:685–697.

MUNCK, A., AND A. NÁRAY-FEJES-TÓTH. 1992. The ups and downs of glucocorticoid physiology. Permissive and suppressive effects revisited. Molecular and Cellular Endocrinology 90:C1–C4.

NELSON, R. J., AND G. E. DEMAS. 1996. Seasonal changes in immune function. Quarterly Review of Biology 71:511–548.

PEACOCK, W. L., E. KROL, K. M. MOAR, J. S. MCLAREN, J. G. MERCER, AND J. R. SPEAKMAN. 2004. Photoperiodic effects on body mass, energy balance and hypothalamic gene expression in the bank vole. Journal of Experimental Biology 207:165–177.

PFISTER, H. P., AND M. G. KING. 1976. Adaptation of the glucocorticosterone response to novelty. Physiology and Behavior 17:43–46.

PLACE, N. J., AND G. J. KENAGY. 2000. Seasonal changes in plasma testosterone and glucocorticoids in free-living male yellow-pine chipmunks and the response to capture and handling. Journal of Comparative Physiology, B. Biochemical, Systemic, and Environmental Physiology 170:245–251.

REEDER, D. M., N. S. KOSTECZKO, T. H. KUNZ, AND E. P. WIDMAIER. 2004. Changes in baseline and stress-induced glucocorticoid levels during the active period in free-ranging male and female little brown myotis, *Myotis lucifugus* (Chiroptera: Vespertilionidae). General and Comparative Endocrinology 136:260–269.

REEDER, D. M., T. H. KUNZ, AND E. P. WIDMAIER. 2004. Baseline and stress-induced glucocorticoids during reproduction in the variable flying fox, *Pteropus hypomelanus* (Chiroptera: Pteropodidae). Journal of Experimental Zoology. Part A, Comparative Experimental Biology 301:682–690.

ROMERO, L. M. 2002. Seasonal changes in plasma glucocorticoid concentrations in free-living vertebrates. General and Comparative Endocrinology 128:1–24.

ROSNER, W. 1990. The functions of corticosteroid-binding globulin and sex hormone–binding globulin: recent advances. Endocrine Reviews 11:80–91.

SABATINO, F., E. MASORO, C. MCMAHAN, AND R. KUHN. 1991. Assessment of the role of the glucocorticoid system in aging processes and in the action of food-restriction. Journals of Gerontology. Series B, Psychological Sciences and Social Sciences 46:171–197.

SABOUREAU, M., J. P. BOBET, AND J. BOISSIN. 1980. Activité cyclique de la function corticosurrénalienne et variations saisonnières du métabolisme périphérique du cortisol chez un mammifère hibernant, le hérisson (*Erinaceus europaeus* L.). [Cyclic activity of adrenal function and seasonal variations of cortisol peripheral metabolism in a hibernating mammal, the hedgehog (*Erinaceus europaeus* L.).] Journal of Physiology (Paris) 76:617–629 (in French, English summary).

SAPOLSKY, R. M., L. KREY, AND B. S. MCEWEN. 1983. The adrenocortical stress-response in the aged male rat: impairment of recovery from stress. Experimental Gerontology 18:55–64.

SAPOLSKY, R. M., L. C. KREY, AND B. S. MCEWEN. 1986. The neuroendocrinology of stress and aging: the glucocorticoids cascade hypothesis. Endocrine Reviews 7:284–301.

SAPOLSKY, R. M., AND M. J. MEANEY. 1986. Maturation of the adrenocortical stress response: neuroendocrine control mechanisms and the stress hyporesponsive period. Brain Research Reviews 11: 65–76.

SAPOLSKY, R. M., L. M. ROMERO, AND A. U. MUNCK. 2000. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocrine Reviews 21:55–89.

SCHMIDT, M., L. ENTHOVEN, M. VAN DER MARK, S. LEVINE, E. R. DE KLOET, AND M. S. OITZL. 2003. The postnatal development of the hypothalamic–pituitary–adrenal axis in the mouse. International Journal of Developmental Neuroscience 21:125–132.

SEABLOOM, R. W., S. L. IVERSON, AND B. N. TURNER. 1978. Adrenal response in a wild *Microtus* population: seasonal aspects. Canadian Journal of Zoology 56:1433–1440.

SELYE, H. 1956. The stress of life. McGraw-Hill, New York.

SONNTAG, W., A. GOLISZEK, A. BRODISH, AND J. ELDRIDGE. 1987. Diminished diurnal secretion of adrenocorticotropin but not corticosterone in old male rats: possible relation to increased adrenal sensitivity to ACTH in vivo. Endocrinology 120:2308–2315.

STEBBINS, L. L., AND R. ORICH. 1977. Some aspects of overwintering in the chipmunk *Eutamias amoenus*. Canadian Journal of Zoology 55:1139–1146.

STERN, J. M., L. GOLDMAN, AND S. LEVINE. 1973. Pituitary–adrenal responsiveness during lactation in rats. Neuroendocrinology 12: 179–191.

TAYMANS, S. E., ET AL. 1997. The hypothalamic–pituitary–adrenal axis of prairie voles (*Microtus ochrogaster*): evidence for target tissue glucocorticoid resistance. General and Comparative Endocrinology 106:48–61.

VAN ACKER, S. A., M. S. OITZL, M. F. FLUTTERT, AND E. R. DE KLOET. 2002. Centrally regulated blood pressure response to vasoactive peptides is modulated by corticosterone. Journal of Neuroendocrinology 17:56–63.

VIAU, V. 2002. Functional cross-talk between the hypothalamic–pituitary–gonadal and –adrenal axes. Journal of Neuroendocrinology 14:506–513.

VON HOLST, D. 1998. The concept of stress and its relevance for animal behavior. Advances in the Study of Behavior 27:1–131.

VOOGT, J. L., M. SAR, AND J. MEITES. 1969. Influence of cycling, pregnancy, labor and suckling on corticosterone-ACTH levels. American Journal of Physiology 216:655–658.

WADE, G. N., AND J. E. SCHNEIDER. 1992. Metabolic fuels and reproduction in female mammals. Neuroscience and Biobehavioral Reviews 16:235–272.

WADHWA, P. D., C. A. SANDMAN, AND T. J. GARITE. 2001. The neurobiology of stress and human pregnancy: implications for prematurity and development of the fetal central nervous system. Progress in Brain Research 133:131–142.

WALKER, C. L., S. L. LIGHTMAN, M. K. STEELE, AND M. F. DALLMAN. 1992. Suckling is a persistent stimulus to the adrenocortical system of the rat. Endocrinology 130:115–125.

WEINSTOCK, M. 1997. Does prenatal stress impair coping and regulation of hypothalamic–pituitary–adrenal axis? Neuroscience and Biobehavioral Reviews 21:1–10.

WHITNALL, M. H. 1993. Regulation of the hypothalamic corticotropin-releasing hormone neurosecretory system. Progress in Neurobiology 40:573–629.

WILSON, D. E., AND D. M. REEDER (EDS.). In press. Mammal species of the world. A taxonomic and geographic reference. 3rd ed. Johns Hopkins University Press, Baltimore, Maryland.

WINGFIELD, J. C. 2005. The concept of allostatis: coping with a capricious environment. Journal of Mammalogy 86:248–254.

WINGFIELD, J. C., J. JACOBS, AND N. HILLGARTH. 1997. Ecological constraints and the evolution of hormone–behavior interrelationships. Annals of the New York Academy of Sciences 807:22–41.

WINGFIELD, J. C., AND R. M. SAPOLSKY. 2003. Reproduction and resistance to stress: when and how. Journal of Neuroendocrinology 15:711–724.

WYNNE-EDWARDS, K. E. 2001. Hormonal changes in mammalian fathers. Hormones and Behavior 40:139–145.

YOUNG, R. A. 1976. Fat, energy, and mammalian survival. American Zoologist 16:699–710.

ZAV'YALOV, E. L., L. A. GERLINSKAYA, AND V. L. EVSIKOV. 2003. Estimation of stress level in the bank vole *Clethrionomys glareolus* (Rodentidae, Rodentia) by fecal corticosterone. Zoologicheskii Zhurnal 82:508–513.

ZERVANOS, S. M., AND C. M. SALSBURY. 2001. Telemetric monitoring of free-ranging animals. Bulletin of the Ecological Society of America 82:189–191.

Special Feature Editor was Edward J. Heske.