Journal of Neuroendocrinology, 2003, Vol. 15, 711–724

REVIEW ARTICLE

Reproduction and Resistance to Stress: When and How

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Key words: stress, reproduction, glucocorticoids, social stress, gonads, environment.

Abstract

Environmental and social stresses have deleterious effects on reproductive function in vertebrates. Global climate change, human disturbance and endocrine disruption from pollutants are increasingly likely to pose additional stresses that could have a major impact on human society. Nonetheless, some populations of vertebrates (from fish to mammals) are able to temporarily resist environmental and social stresses, and breed successfully. A classical trade-off of reproductive success for potential survival is involved. We define five examples. (i) Aged individuals with minimal future reproductive success that should attempt to breed despite potential acute stressors. (ii) Seasonal breeders when time for actual breeding is so short that acute stress should be resisted in favour of reproductive success. (iii) If both members of a breeding pair provide parental care, then loss of a mate should be compensated for by the remaining individual. (iv) Semelparous species in which there is only one breeding period followed by programmed death. (v) Species where, because of the transience of dominance status in a social group, individuals may only have a short window of opportunity for mating. We suggest four mechanisms underlying resistance of the gonadal axis to stress. (i) Blockade at the central nervous system level, i.e. an individual no longer perceives the perturbation as stressful. (ii) Blockade at the level of the hypothalamic-pituitary-adrenal axis (i.e. failure to increase secretion of glucocorticosteroids). (iii) Blockade at the level of the hypothalamic-pituitary-gonad axis (i.e. resistance of the reproductive system to the actions of glucocorticosteroids). (iv) Compensatory stimulation of the gonadal axis to counteract inhibitory glucocorticosteroid actions. Although these mechanisms are likely genetically determined, their expression may depend upon a complex interaction with environmental factors. Future research will provide valuable information on the biology of stress and how organisms cope. Such mechanisms would be particularly insightful as the spectre of global change continues to unfold.

The stress-response plays a key role in allowing an organism to survive the acute challenge to homeostasis that constitutes the typical stressor. Energy is mobilized from storage sites and diverted to exercising muscle, cardiovascular tone is enhanced, long-term and costly anabolism is suppressed until a more auspicious time, and cognition is sharpened. However, following the pioneering work of Hans Selye in the 1930s, it is clear that an excess of stress can have pathogenic effects on metabolism, vascular function, growth, tissue repair, immune defences, and even the health of some neurones.

Among the most consistently adverse consequences of prolonged stress is disruption of reproductive physiology and behaviour (Figs 1 and 2). Whether one is a clinician trying to understand a patient's loss of libido, a wildlife biologist grappling with how habitat degradation translates into decreased fertility of wild populations, or a conservationist faced with an endangered species refusing to mate in a zoo enclosure, stress must be considered in the equation. As a result of considerable research, a great deal is known about the neuroendocrine bases by which the stress-response can impair reproduction (Figs 1 and 2).

In this review, we consider the general mechanisms by which such suppression occurs. More importantly, we provide examples where this yoking of stress and reproductive impairment does not occur. Such exceptions to the broad physiological effects of stress are not restricted to the reproductive axis. As an interesting recent precedent, socially subordinate mice subject to numerous bite wounds during fighting become resistant to the immunosuppressive effects of stress and glucocorticosteroids. The authors

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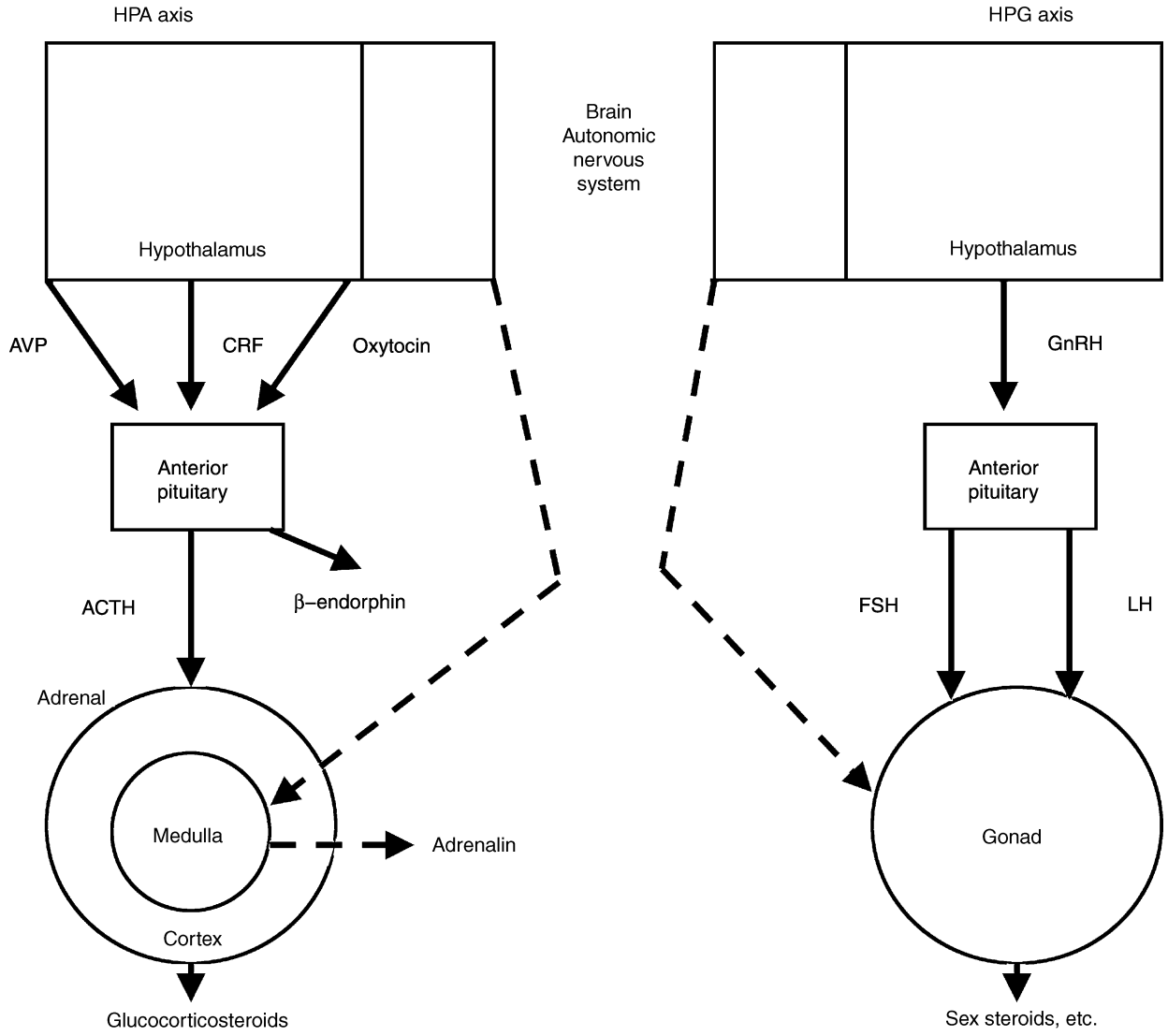

FIG. 1. A schematic of the hypothalamic-pituitary-adrenal (HPA) axis, and the hypothalamic-pituitary-gonadal (HPG) axis in many vertebrates. Note that the autonomic nervous system is also involved in both axes (see text). In the HPA axis, stimuli from the physical, social and internal environments are transduced through the hypothalamus resulting in the release of corticotropin-releasing factor (CRF) from the median eminence, This peptide regulates the release of adrenocorticotropic hormone (ACTH) and β-endorphin from the anterior pituitary. Release of hypothalamic peptides arginine vasopressin (AVP, arginine vastocin; AVT in nonmammalian tetrapods) and oxytocin (mesotocin in nonmammalian tetrapods) may be involved. ACTH acts on the adrenal cortex to release glucocorticosteroids: cortisol in some mammals and all teleosts; corticosterone in some mammals and all nonmammalian tetrapods. In the HPG axis, stimuli are transduced through the hypothalamus resulting in the release of gonadotropin-releasing hormone (GnRH) from the median eminence. This peptide regulates the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary. These gonadotropins regulate reproductive function in general, including the synthesis and release of sex steroid hormones. Many other peptides may be involved, but this scheme is applicable to many vertebrate taxa from mammals to fish. Possible sites where the HPG axis is vulnerable to stress hormones are indicated in Fig. 2.

speculate that this is adaptive, insofar as it is optimal to maintain immune defences in the face of numerous wounds (1). In a similar vein, we analyse instances of resistance of the reproductive axis to suppressive effects of stress from an adaptive/evolutionary standpoint. In addition, we consider the mechanisms underlying this resistance. Surprisingly, these mechanisms remain the least understood and we hope this review will stimulate research into the cell and molecular bases of the biology of stress.

Stress and reproduction, a generally negative relationship

The overwhelming impression of biologists is that stressful experiences of any kind inhibit reproductive function. Although we do not review this topic exhaustively, we give some classic general examples and then some specifically for males and females. We also acknowledge that metabolic 'challenges' (sometimes construed as stress) can also influence reproductive function via paracrine mechanisms at the level of the gonad. These are known to involve insulin, insulin-like growth factor and leptin but not glucocorticosteroids. Here, we restrict our discussion to specific interactions of the hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-pituitary-gonadal (HPG) axis (Figs 1 and 2). We also acknowledge that, under nonstress conditions, hormones of the HPA axis actually enhance reproduction and may play a critical role in managing energy income and use during the reproductive process (2, 3). It is the transition of activity

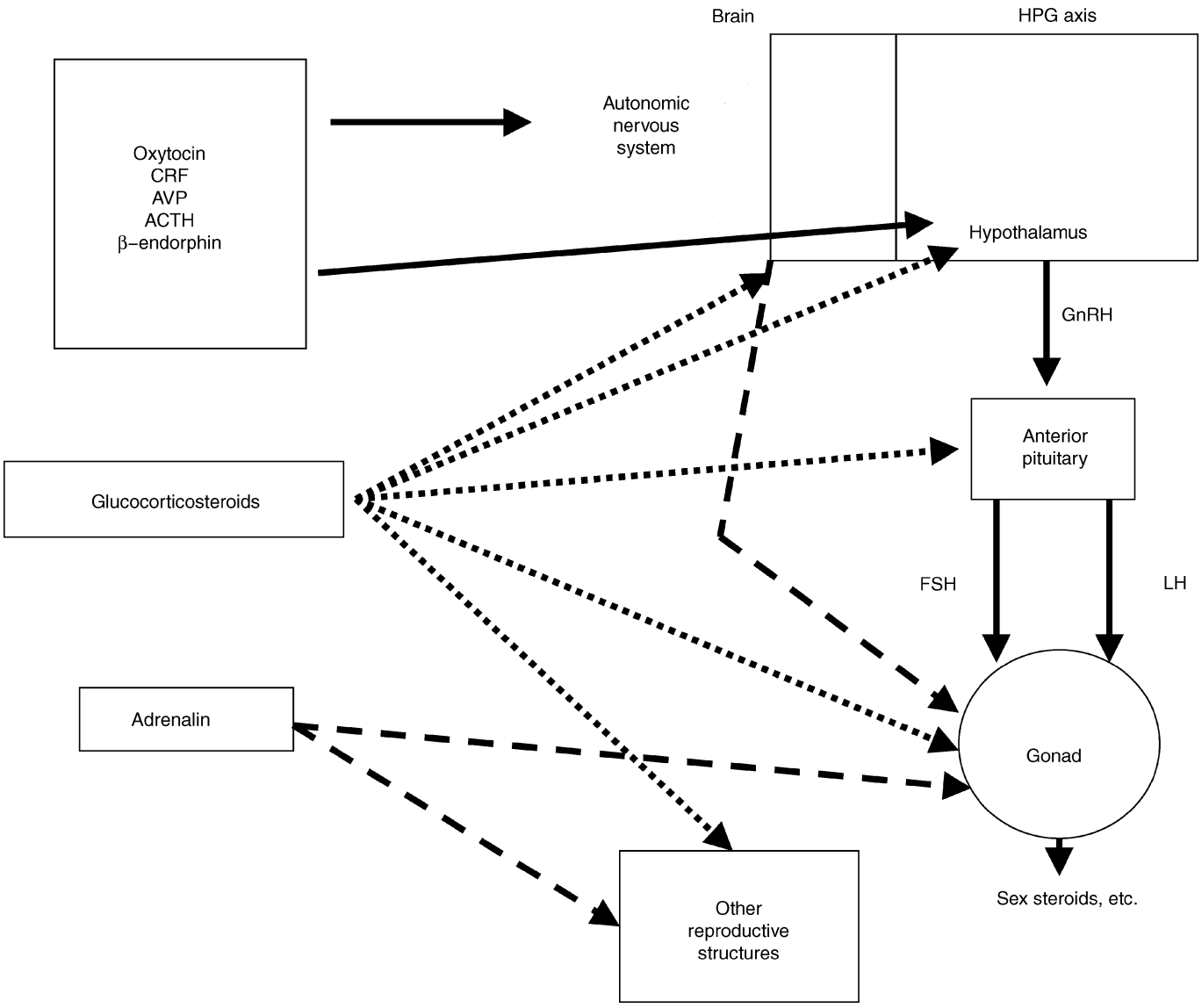

FIG. 2. The hypothalamic-pituitary-gonadal (HPG) axis, including other reproductive structures such as oviduct, uterus, vas deferens, penis, etc., is vulnerable to the actions of hormones associated with the hypothalamic-pituitary-adrenal (HPA) axis (Fig. 1). Hypothalamic and pituitary peptides such as arginine vasopressin (AVP, arginine vasotocin; AVT, in nonmammalian tetrapods), corticotropin-releasing factor (CRF), oxytocin (mesotocin in nonmammalian tetrapods), adrenocorticotropin (ACTH) and β-endorphin may act primarily at the central level (especially behavioural effects). Glucocorticosteroids may act at multiple levels (indicated by the dotted arrow lines). Dashed lines indicate possible sites of action of epinephrine.

of HPA axis hormones to an 'emergency mode' that triggers many behavioural and physiological effects that are potentially incompatible with successful reproduction (2–4). This transition, its boundaries, genetic basis and environmental control, represents a challenge to future research on the biology of the stress response.

A dramatic example of stress-induced suppression of reproduction in animals in their natural environment comes from the great boreal forests of the northern hemisphere: the 10-year cycle of abundance in snowshoe hares, *Lepus americanus*. In this cycle, hare populations expand followed by a similar increase in numbers of predators, particularly the lynx, *Lynx canadensis*, and then a population decline occurs. This 10-year cycle is apparently not a function of increasing population outstripping food supplies, nor is it caused by increased social interactions as the population peaks (5). Rather, it appears that the cycle is driven by predation risk. As the numbers of predators increase following the rise in hare numbers, risk of predation (by far the major cause of mortality) forces hares into habitat that provides shelter from predators but is poor in food. Hares must then move into open areas where predation increases dramatically. Thus the 10-year cycle appears to be driven by an interaction of food and predation (5).

Predation risk and hare behaviour have major consequences for population dynamics. During a decline in numbers of snowshoe hares in the Yukon, Canada, in the 1990s, hares appeared to be chronically stressed as indicated by higher levels of free cortisol and lower corticosteroid-binding protein (CBP) capacity. Circulating CBP is thought to play a role in maintaining high plasma levels of glucocorticosteroids and also influences the entry of these steroids into target tissues. There were no differences in baseline plasma testosterone levels, but they showed reduced

responsiveness to dexamethasone and adrenocorticotropic hormone (ACTH) treatment in the decline years (6). During the population collapse, hares also showed reduced leucocyte counts in blood, increased glucose mobilization and higher over-winter loss of body weight compared with hares already at a population low. High predation risk, not population density or poor nutrition, accounted for chronic stress and impaired reproductive function. The stress-response did not abate, and reproductive function did not improve until predation risk declined (6).

Stress and reproductive suppression in the female: a general overview

In mammals, the suppressive effects of stress on female reproductive physiology and behaviour typically have three broad components: (i) disruption of ovulation; (ii) impairment of the uterine maturation needed for implantation; and (iii) inhibition of proceptive and receptive behaviours.

At the endocrine level (Figs 1 and 2), stress-induced release of β-endorphin has inhibitory effects upon gonadotropin-releasing hormone (GnRH) release, such that there is a decline of GnRH concentrations in the hypophysial-pituitary portal system within seconds (7). In addition, there is decreased sensitivity of pituitary gonadotropes to stimulatory effects of GnRH, thus greatly reducing the amount of luteinizing hormone (LH) secreted. A number of studies suggest that stress-induced secretions of both prolactin and glucocorticosteroids mediate this (8). Finally, glucocorticosteroids act at the level of the ovaries to decrease responsiveness to LH (9). This has been reported in a variety of species, and is likely due, at least in part, to glucocorticosteroid-induced decreases in LH receptor number. The result is an extended follicular stage, making overall reproductive cycle length longer and more irregular. There is obviously considerable variability in the effects of stress, given the heterogeneity of female reproductive systems among mammals, including seasonal ovulators, reflex ovulators, and so on. As noted, the endocrine mechanisms discussed here represent a broad overview of the suppressive effects of stress.

Impairment of uterine maturation is brought about during stress by at least two mechanisms. First, in some species, stress is associated with a decline in levels of progesterone, which normally mediates preparation of the uterine wall for implantation during the luteal phase. As a more consistent mechanism across different species, stress-induced secretion of prolactin antagonizes the anabolic effects of progesterone in the uterus (9).

In numerous species, stress decreases proactive female behaviours designed to increase the likelihood of sex (i.e. proceptivity), as well as responsiveness to proceptive behaviours on the part of a male (i.e. receptivity) (10, 11). Some of this probably reflects central mechanisms, such as activation of neural systems relevant to anxiety and vigilance during stress. In addition, oestrogen promotes both proceptive and receptive behaviour, both through central mechanisms (predominately in the ventromedial hypothalamus) and by sensitizing tactile receptors in genitalia and elsewhere in the body to stimulation. In rodents, such oestrogenic effects are a prerequisite for normal sexual behaviour, whereas in primates, the relationship is weaker but still demonstrable. As such, stress-induced declines in oestrogen levels may contribute to loss of libido as well. Finally, adrenal androgens enhance proceptive and receptive behaviours in female primates, and there is some evidence of stress-induced suppression of secretion of such androgens.

In females, the specialized stressor of infection and consequent immune activation also suppresses reproductive behaviour, including attractivity. This is partially mediated by glucocorticosteroid secretion that is triggered by immune activation, secondary to the corticotropin-releasing hormone (CRH)-releasing actions of interleukin (IL)-1 in brain (12, 13). In addition, chemokines such as IL-1 and tumour necrosis factor-α appear to decrease sexual behaviour through direct actions in brain (14, 15).

Stress and reproductive suppression in the male: a general overview

In mammals, stress disrupts male reproductive physiology and behaviour in three broad ways: (i) inhibition of hormones of the gonadal axis; (ii) impairment of erectile function; and (iii) damping of proceptive and receptive behaviours.

At the endocrine level, the mechanisms mediating inhibition are quite similar to those in the female (Figs 1 and 2). As in the female, stress-induced release of β-endorphin has inhibitory effects upon GnRH release, such that there is a decline of GnRH concentrations in the hypophysial-pituitary portal system within seconds (16). In addition, there is decreased sensitivity of pituitary gonadotropes to GnRH, thus greatly reducing the amount of LH secreted. A number of studies suggest that stress-induced secretion of prolactin is most responsible for this (17). Finally, as in the female, glucocorticosteroids act at the level of the gonads to decrease responsiveness to LH (18). The result of this is a decline in testosterone levels over the course of minutes to hours in response to a variety of physical and psychological stressors.

Surprisingly, the decrease in testosterone levels is rarely sufficient to have markedly adverse effects on male fertility. Far more disruptive is stress-induced impairment of erectile function in mammals. This is rooted in the complex interplay between parasympathetic and sympathetic activation of the autonomic nervous system, with parasympathetic tone being a prerequisite for an erection in most species, and the transition to sympathetic tone mediating ejaculation. Consequently, stress can block the capacity for an erection in the first place (inability to establish parasympathetic tone), or can cause premature ejaculation (accelerating the transition to sympathetic tone) (Fig. 2).

While the capacity of stress to disrupt libido in males is well documented, the mechanisms underlying it are poorly understood, beyond the finding that it is probably not mediated by suppression of testosterone levels. Finally, by contrast to the female, there is little evidence that the specialized stressor of infection and immune activation alters libido in males (15).

The evolutionary logic of the occasional maintenance of reproductive function during stress

Despite the commonly held opinion that stress is always inhibitory to reproductive function, exceptions to this rule suggest that we should revisit our view of the biology of stress. There is no question that stress is potentially disruptive for reproduction. Nonetheless, in some cases, we might expect selection for individuals that are able to continue breeding in the face of at least acute stressors. For this reason, we focus on those examples in which environmental and social stresses do not appear to be detrimental to successful reproduction.

TABLE 1. Evolutionary Logic Behind Instances of Maintaining Reproduction During Stress.

Logic	Examples
A: Aged individuals with minimal future reproductive success	Leach's petrels
B: Seasonal breeder when environmental conditions are severe and'or time for actual reproduction is so short, there is only one breeding event	Arctic ground squirrels, many avian species, sea turtles, garter snakes
C: When both members of a breeding pair provide parental care, if the male is lost, the remaining individual must work 'double-time' to raise young succesfully	Pied flycatcher
D: 'Semelparous' species in which there is only a single round of breeding, followed by programmed death	Pacific salmon, lamprey, eels, Australian marsupial insectivores
E: Species where, because of the transience of dominance, indivduals may have only a short window of opportunity for mating	Males of numerous tournament species
F: Alternate male reproductive morphs modulate effects of glucocorticisteroids on behaviour according to dominance	Tree lizards

Sources include references (3, 19, 21, 45, 49, 75, 76, 87, 96–98, 101, 103, 104).

From a teleological standpoint, suppression of reproduction during major stressors can generally be viewed as adaptive. The hallmark of the stress-response is mobilizing considerable amounts of energy to the immediate fueling of muscle and cardiovascular physiology. By contrast, the hallmark of reproduction (particularly in females) is committing considerable amounts of energy to the optimistic and prolonged process of enhancing future reproductive success. As such, the suppression of reproduction during stress is readily framed as yet another example of triaging anabolism for a more auspicious time.

Despite that logic, there are circumstances where it would be evolutionarily advantageous for stress to not suppress reproductive physiology (Table 1). Some examples of this would occur when an individual's future reproductive potential is low. In effect, this is a case where it does not make sense to defer reproduction until a more auspicious, less stressful future opportunity to reproduce, if there are likely to be few such opportunities. Examples include species in which reproductive potential declines towards zero as it ages (case A, Table 1). Thus, one might predict an unyoking of the linkage between stress and reproductive suppression in aged individuals. This logic would also apply to the numerous species that are seasonal breeders, with only a single opportunity to breed per year (case B, Table 1). In such circumstances, continued fertility, even in the face of severe and stressful environments, would be selected for. Examples of this, and other cases will be reviewed from several taxa of vertebrates.

Some examples of resistance of the gonadal axis to the suppressive effects of stress

Biparental care and loss of mate

In avian species in which both sexes of a pair provide parental care, loss of a mate to, for example, a predator, would require the remaining parent to compensate to raise young (case C, Table 1). In a European songbird, the pied flycatcher *Ficedula hypoleuca*, females that have lost a mate increase provisioning rate for their young. They also show increased baseline corticosterone levels and have enhanced response to capture stress (19). Some avian mating systems have marked differences in degree of paternal care. Those species in which males are polygynous and provide little or no parental care retain a high sensitivity of the HPA axis to stress whereas females, that provide all parental care, show reduced adrenocortical responses to stress (20, 21). Conversely, in polyandrous species in which females provide no parental care, sensitivity to stress is retained whereas males that provide all care reduce adrenocortical responses to stress (21).

Glucocorticosteroids, semelparity and programmed death

Some vertebrates are semelparous, compressing their lifetime reproductive output into a single breeding effort and then dying (case D, Table 1). Species in which there is only a single round of breeding per lifetime should be uncoupled from potentially inhibitory effects of stress (where, in fact, such reproduction triggers a programmed die-off shortly afterward in many individuals). In other words, it would also be maladaptive for a stressor to be reproductively suppressive at the time of that single opportunity to breed.This phenomenon has been studied in lampreys (*Petromyzon* and *Lampetra* sp.), eels (*Anguilla* Sp.) and Pacific salmon (*Oncorhynchus* sp. 22), and a group of dasyurid marsupials (23). One of the hallmarks of semelparity in these organisms is progression of reproductive development despite deteriorating body condition and symptoms of severe stress. Some fish species stop feeding weeks or months before spawning and development of the reproductive system occurs at the expense of body tissues (24).

Why would such a life history strategy evolve? In Pacific salmon, it is possible that the long upstream migration from the ocean, where they spend most of their lives and grow to adult size, is energetically demanding. However, the gonads are maturing during migration and may comprise more than 30% of body weight. By the time they reach the spawning grounds, body reserves are so depleted there is no energy left for a migration back to the ocean. Programmed death may thus be selected for. Rivers of the Pacific North-west and Alaska are often glacial fed and poor in nutrients resulting in low food resources. Decaying corpses of postspawned adults do fertilize waters of the spawning grounds potentially increasing food for the hatchling salmon (alevins) (22), although this is a group selection argument.

The behavioural and physiological profiles of animals at this time are well understood. Maturing Pacific salmon stop feeding and the gastrointestinal tract atrophies as they enter rivers to begin the upstream migration to spawning grounds. Furthermore, male salmon fight to establish territories and attract mates, females dig nests (redds) in the gravel of streams, both metabolically taxing behaviours (22, 24). Not surprisingly, this period is associated with high circulating levels of glucocorticosteroids (25) accompanied by hypertrophy of inter-renal tissue (homologous to adrenocortical tissue of mammals (26). These high levels, which are likely to reduce immune responses, coupled with exhaustion of

metabolizable energy stores, leads to massive infection by fungus and bacteria, and eventually to their demise (22). Experimental force feeding of maturing and spawned sockeye salmon, *Oncorhynchus nerka*, reversed the deterioration of body condition and prolonged life for up to 10 weeks (22). However, because apparently healthy post spawned fish also die eventually without a second attempt at breeding, it is clear that some endogenous program, or other factors, underlie the semelparous strategy. Furthermore, in landlocked kokanee salmon, *O. nerka kennerlyi*, in the upper Colorado River, plasma levels of cortisol are elevated during the spawning migration (27). This suggests that the increase in cortisol during spawning migration of semelparous salmon may not be primarily related to long-distance migration and salinity change.

The pathogenic profile seen in these species at this time would result in suppressed reproductive development in most vertebrates. Despite that, both sexes shed gametes, and circulating levels of gonadotropins and sex steroids such as oestradiol and 11-ketotestosterone increase in maturing Pacific salmon peaking several weeks before spawning (22, 28). Such high circulating levels of gonadal hormones occur despite elevated glucocorticosteroid levels, and they appear to be the stimulus for such adrenocortical hypersecretion at this time. As evidence, gonadectomy reverses glucocorticosteroid hypersecretion (29), whereas androgen injections in gonadectomized males increase secretion (30).

The actual mechanisms by which these semelparous fish are able to breed despite hyper-adrenocortical function remains unknown. From studying Table 2, it is possible that case C would be appropriate. One possible prediction here is that glucocorticosteroid receptors in the brain and HPG axis are down regulated so that behavioural and reproductive traits are not inhibited. This would allow metabolic effects of glucocorticosteroids to act but without inhibiting breeding. However, this does not appear to be the case. Glucocorticosteroid receptors have been characterized in the brains of Chinook salmon, *Oncorhynchus tshawytscha*. There appear to be two receptors in cytosolic extracts showing high affinity, low capacity and differing pharmacology of binding (31). An immunohistochemical study of the number of glucocorticoid receptor-immunoreactive staining neurones in the brains of sexually immature and mature spawning kokanee salmon indicated wide distribution of glucocorticoid receptor in the brain, similar to the mammalian pattern (32). Moreover, brains from spawning fish had the same pattern of glucocorticoid receptor as immature fish and, in contrast to predictions in Table 2, olfactory regions had greater numbers of glucocorticoid receptor-immunoreactive neurones with predominantly nuclear locations in spawning fish. In immature fish, glucocorticoid receptor-immunoreactive staining appeared to be largely cytoplasmic (32). Compensatory stimulatory inputs to the gonad axis are a possible mechanism (case D, Table 2) that remains to be tested.

Semelparity in mammals: dasyurid marsupials

In Australia, small, shrew-like, marsupials, *Antechinus* sp. and *Phasogale calura*, reproduce once a year during a short mating period and then the males die (33). Most females die after lactation ceases although a few breed through two seasons (34). The mass mortality of males is thought to reduce competition for food when females are lactating. Their death may also allow an increase in litter size above that seen in closely related species which are iteroparous (i.e. which breed more than once), going through at least two cycles of reproductive development (23). Again, this is a group selection argument that needs to be rethought in more conventional evolutionary theory.

In many ways, this story parallels that of the salmonids, and constitutes another example of case D in Table 1. During the breeding period, circulating cortisol levels are elevated, and weights of the adrenal glands increase in size in male *A. stuarti* at mating (35). Furthermore, CBP levels decline below the capacity to bind increasing plasma levels of cortisol (36–38); when combined with the increased cortisol levels, this produces an enormous increase in unbound, biologically active cortisol. In female *Antechinus*, that do not die until later, circulating levels of cortisol are as high as in males, but CBP titres remain high and match circulating levels of cortisol (36, 37).

Some of the elevated cortisol levels are probably related to the aggressiveness of males during this breeding period. In addition, there are alterations in adrenocortical function at a number of levels in the axis. Dexamethasone inhibits plasma cortisol levels 2 months before the mating period, but not during the mating period (39). By contrast, intramuscular injection of ACTH results in a significant increase in cortisol levels at both stages in the annual cycle, indicating that responsiveness of the adrenal cortex does not change. As another regulatory feature, the elevated ACTH concentrations decrease CBP levels (37).

As with the salmonids, glucocorticosteroid excess appears to play a role in the programmed death. As breeding commences, males develop classic symptoms of chronic stress such as

TABLE 2. Potential Mechanisms Underlying Resistance of the Hypothalamic-Pituitary-Gonadal Axis to Stress.

Mechanism	Examples
A: Blockade at the CNS level: stressors are not perceived as stressful	Lekking species, breeding snow bunting
B: Blockade at the level of the HPA: failure to secrete glucocorticosteriods	Many avian species, breeding Lapland Longspurs, redpolls, garter snakes
C: Blockade at the level of the HPG: resistance of the gonadal axis to glucocorticosteriod actions	Male olive baboons, Arctic songbirds
D: Compensatory stimulatory inputs to the gonad axis to counteract inhibitory glucocorticosteriod actions	Male olive baboons, male Arctic ground squirrels, dark-eyed junco
E: Protection from the actions of glucocorticosteriods by, for example, steroid-binding proteins	Tree lizards

Sources include references (49, 82–85, 90, 102, 104). CNS, Central nervous system; HPA, hypothalamic-pituitary-adrenal; HPG, hypothalamic-pituitary-gonadal.

moderate anaemia, elevated parasite load, hepatic necrosis and abscesses, ulcers, haemorrhaging gastrointestinal tracts and involuted splenic follicles (37, 40). The agglutination response of the immune system in male *Antechinus* is greater than in females prior to breeding. As breeding approaches, agglutination titres rise in females but decline precipitously in males. Serum immunoglobulin is lower in males than females, resulting in a marked increase in endoparasite infection in males accompanied by the pathologies noted above (37, 40). In the terminal stages, these males lose fur and body mass, become lethargic and show signs of being moribund (41), nitrogen balance is lost, and they finally die (35). As evidence that cortisol excess plays a role in these pathologies, injections of cortisol acetate intramuscularly into males before the mating period result in increased mortality compared with controls (42).

Despite this adrenocortical profile, plasma levels of androgens rise in males in July to a peak in August coincident with mating, followed by rapid declines after mating and during senescence (37, 38, 43). Furthermore, as in salmonids, activation of the gonadal axis even helps bring about hyperadrenocorticism and subsequent pathologies. As evidence, if males are experimentally isolated from mating, they survive longer (44), and castrated males survive longer than intact males (37). In the latter study, maximum corticosteroid binding capacity of CBP in blood did not decline compared with intact males. Moreover, injection of testosterone into castrates decreased CBP (38).

Thus, in male *Antechinus*, the breeding season is associated with increases in circulating testosterone concentrations and in aggression; these result in ACTH release followed by cortisol. Testosterone and ACTH together reduce CBP levels in blood resulting in extreme hyperadrenocorticism. Over several days to weeks around the mating period this ultimately leads to pathologies of chronic stress and finally death (44). Clearly, during this period, the reproductive system remains unaffected and mating is successful. It is of particular interest that dexamethasone treatment decreases circulating testosterone levels two and a half months before mating, but not when testosterone is near its peak (39). This adrenocortical profile is specific to semelparity. In another small marsupial that is iteroparous, the fat-tailed dunnart, *Smithsopsis crassicaudata*, males survive beyond a single season. There is no marked peak in circulating cortisol as in the semelparous species, and they are always below the maximum binding capacity of CBP (38). As for semelparous fish, the mechanisms by which reproduction proceeds in the face of elevated glucocorticosteroid secretion is unknown. Again, case C (Table 2) is most plausible and could involve down regulation of receptors for cortisol in the HPG axis. Case D (Table 2) cannot be ruled out, however.

These profiles may not be universal in semelparous marsupials. In another larger dasyurid, the quoll, *Dasyurus hallucatus*, all males die after mating and show the same symptoms of senescence (except gastric ulceration). However, there is apparently no increase in plasma cortisol in males; they remain similar to the profiles in females despite high circulating levels of testosterone. CBP levels remain unchanged (45, 46). This might be case A rather than C or D in Table 2. Male quolls can store relatively more fat than the much smaller *Antechinus*. Quolls also have a specialized fat storage organ in the tail and may be able to 'prepare' for the mating season by utilizing these stores, thus protecting protein breakdown. Smaller animals are not able to store enough fat and this results in protein catabolism, accompanied by elevation of circulating cortisol levels (45). From these studies, the authors suggest that hyper-secretion of glucocorticosteroids may be a result of programmed senescence and not its cause in semelparous marsupials.

Social conflict and glucocorticosteroids in male olive baboons

Resistance to the suppressive effects of stress would make sense in some social systems. This is relevant to 'tournament species', in which males compete for opportunities for polygamous mating. In such species, a dominant male may be under considerable stress due to competitive challenges to his high rank. It would be adaptive to have evolved resistance to the suppressive effects of such stressors, if males are dominant for only a short period and will have the majority of matings during this time (e.g. also, in lekking species, case E, Table 1). In other examples, dominance status may influence the adrenocortical response to stress even though the mating period may not be short.

Olive baboons (*Papio anubis*) live in large multimale troops in the savannas of East Africa. Such baboons are a tournament species with high degrees of sexual dimorphism, minimal male parental investment, and extensive male–male competition for reproductive females. Males form fairly linear dominance hierarchies and, among the rewards of dominance, high-ranking males have a somewhat disproportionately large reproductive success, although not as much as once believed (47). Male rank changes over time, as a function of health and age of individuals, or formation or dissolution of cooperative coalitions. As a result, a male will be high-ranking only transiently (as opposed to the hereditary rank system seen among females of many Old World primates, including olive baboons), and is often subject to stressful challenge during that tenure. Because of the transience of such high rank, this constitutes a situation where it would be adaptive to have reproductive access be resistant to suppressive effects of stress (case E, Table 1).

Rather than having elevated basal cortisol levels, high-ranking male baboons have levels that are, in fact, significantly lower than among subordinate males (48). This difference has generally been interpreted as being due to the fact that subordinate males are subject to: (i) more physical stressors (they must work harder to obtain their food, are subject to high rates of displacement aggression); (ii) more psychological stressors (a marked lack of social control and predictability comes with subordinance); and (iii) fewer coping responses (such as social grooming) are available. The low basal cortisol levels in dominant males appear to arise from low levels of ACTH and of hypothalamic secretagogues, as well as from enhanced sensitivity of the adrenocortical axis to negative-feedback inhibition (49).

During periods of acute stress and elevated cortisol concentrations, the testicular axis in subordinate males is promptly inhibited. LH and testosterone concentrations decline within minutes and hours, respectively, after stressor onset (50). The decline in LH concentrations is secondary to a decline in GnRH secretion, and the inhibition of the latter is due to stress-induced secretion of opiates, working through the μ- and κ-opiate receptors (51). Moreover, cortisol blunts the responsiveness of the testes to LH (50).

By contrast, the testicular axis in high-ranking males is relatively resistant to the suppressive effects of stress. Thus, during the

first few hours after stressor onset, when testosterone concentrations are declining in subordinate males, levels are not reduced in dominant individuals, but are transiently elevated (52). The mechanisms underlying this resistance are understood. Stress suppresses LH secretion in dominant individuals to the same extent as in subordinates, indicating that resistance does not occur at the level of the pituitary or higher. However, the testes of dominant males are less vulnerable to the disruptive effects of cortisol than are those of subordinates (50).

Testicular resistance would explain why testosterone concentrations in high-ranking males do not decline as much as in subordinates. However, in addition, one must explain why they increase transiently. This is due to the actions of the sympathetic nervous system (SNS) (53), something also observed in male rodents (54). During stress, the increase in SNS tone appears to be greater in dominant than in subordinate animals (55). Either of two mechanisms could explain how this would lead to enhanced testosterone secretion/unit LH stimulation. First, there is direct SNS innervation of the primate testes, and SNS stimulation could potentially enhance testicular steroidogenesis. Second, sympathetic catecholamines can vasodilate the testicular parenchyma, increasing testicular blood flow and the absolute amounts of LH delivered. Thus, among male olive baboons, there is a selective logic for resistance of the gonadal axis to the suppressive effects of stress during the transient period when a male is high ranking. Mechanistically, this is due to a combination of decreased sensitivity of the gonadal axis to the suppressive effects of glucocorticosteroids (case C, Table 2), plus the counteracting effects of sympathetic activation (case D, Table 2).

Short breeding seasons and male arctic ground squirrels

In male Arctic ground squirrels, *Spermophilus parryi plesius*, breeding in spring lasts only 2–3 weeks (case B, Table 1). Males roam widely, suffer more injuries (from fighting with other males), consume less food and lose more weight than females, followed by higher mortality after breeding compared with females (56). Adult breeding males had the highest plasma levels of free cortisol, lowest CBP capacity, were dexamethasone resistant, had lower haematocrits and reduced white-blood cell count indicating prolonged stress. Juvenile males dispersing in mid-August also showed dexamethasone resistance in boreal habitat *vs* juvenile males in an alpine habitat in the Yukon, Canada. Juvenile females that generally do not disperse, did not show these differences (57).

In breeding male Arctic ground squirrels, circulating testosterone levels remained high despite the apparent chronic stress. Dexamethasone treatment did decrease testosterone levels whereas ACTH injection increased testosterone levels. High baseline testosterone levels in blood and its augmentation by ACTH may be unique and may serve to maintain aggression as males compete for mates (case D, Table 2).

This profile represents a classic trade-off of survival and reproduction (56, 57). This is in contrast to red squirrels, *Tamiasciurus hudsonicus*, in the same boreal forest and may be related to the ecology of the two species. Red squirrels have a stable social system, do not hibernate, are long-lived and have individual territories (58). By contrast, Arctic ground squirrels hibernate, are short-lived with males competing intensely for females in a social system based on female kin groups and male dispersal (58, 59).

Neuroendocrine mechanisms underlying the resistance of gonadal function to stress

There are a number of scenarios in which the reproductive axis of an organism has evolved insensitivity to the suppressive effects of stress. We now discuss in more detail potential neuroendocrine mechanisms (basic mechanisms are shown in Figs 1 and 2) that would allow for gonadal function to be maintained despite an ongoing stressor.

Working in a top-down manner using Table 2 as a template, a first possible mechanism by which gonadal function can be maintained in the face of stress, is that the perturbation may simply not be perceived as a stressor (case A, Table 2). Depending on one's disciplinary origins, this can be an obvious and meaningless truism: events that are not stressful do not provoke stress responses. From a different perspective, however, this can be far from meaningless, built around two facts that are central to much of stress management and behavioural medicine: (i) the psychological filters with which an external event is perceived greatly influence whether the event is 'stressful' and activates a stress response; (ii) such filters are malleable. An extensive literature demonstrates that external challenges are far less likely to provoke a stress response if the organism perceives itself to have control, to have predictive information about the nature of the challenge, if the organism interprets the challenge as occurring in a context of an improving situation, or has effective coping outlets (60–62). Framed in the context of the issues being discussed in this review, consider a species that migrates annually between the Arctic and the tropics. In such a case, a day in the tropics in which the temperature is, unexpectedly, 15 °C rather than the usual 30 °C may be more of a psychological and physiological stressor than a −10 °C day in the Arctic that is precisely as cold as anticipated. Moreover, a bird that has excellent body condition and high stores of subcutaneous fat will not perceive a restriction of food as stressful compared with another individual in poor condition and virtually no stores of fat (63).

As a next possible mechanism, the event may be perceived and may activate afferent pathways to the paraventricular nucleus of the hypothalamus, but may fail to provoke glucocorticosteroid secretion (case B, Table 2). Such a blockade of the HPA axis could occur at the level of the brain, pituitary or adrenal, and could involve: (i) depletion of relevant hormones (CRH, ACTH, etc.); (ii) loss of hormone receptors; (iii) inactivation of postreceptor transduction mechanisms; and (iv) enhanced clearance rate of an HPA hormone so as to block its capacity to influence a target tissue.

Moving further down, conceptually, an event may be perceived as stressful and activate glucocorticosteroid secretion, but some key element of the HPG system loses its vulnerability to the suppressive effects of glucocorticosteroids (case C, Table 2). Such resistance could occur at any level(s) of the HPG axis and, on a mechanistic level, would most likely be explained by a loss of glucocorticosteroid receptors. It is also possible that a perceived stressor may provoke secretion of glucocorticosteroids that exert inhibitory effects on the gonadal axis. However, these inhibitory effects are accompanied by some additional physiological effect that counteracts this inhibition (case D, Table 2). As a purely speculative model, some stressor might lead to decreased secretion of a gonadal steroid. However, if accompanied by a

marked decrease in hormone clearance rate, the net result might be no change in circulating levels. As already discussed in male olive baboons, precedent exists for at least one example of this.

Finally, mechanisms may exist that protect the organism from actions of glucocorticosteroids, at least at certain times in the life cycle. For example, CPBs at high capacity may be able to protect the HPG axis from inhibitory effects by keeping free (unbound) glucocorticosteroid concentrations low and effectively unchanged (case F, Table 2). Individuals with a lower capacity of CBP may not be able to 'absorb' stress-induced increases in glucocorticosteroids thus resulting in higher free fractions that may then inhibit the HPG. Thus, a number of possible circumstances occur where selection logically favours resistance of the gonadal axis to the suppressive effects of stress, and a number of neuroendocrine mechanisms exist to mediate such resistance.

Decreased sensitivity of adrenocortical responses to perturbations of the environment

Cases A and B in Table 2 focus on instances where an external event that would logically be viewed to be a stressor fails to activate the HPA axis. This could be because the event is not actually perceived to be stressful (case A), or because of some mechanistic blockade in activation of the axis (case B). Numerous studies indicate that whether or not an external event activates the HPA axis can be highly context-dependent. This implies that the sensitivity of the HPA axis can be modulated (4, 62, 64), although such individual variation can make it difficult to compare effects of stress in different taxa (65). Evidence for modulation of adrenocortical responses to stress is now widespread and, in many cases, occurs so that reproduction can proceed in the face of potentially stressful environmental conditions. This modulation can be roughly divided into four sections as follows [modified from (3)]: (i) variation among populations of the same, similar, or other species reproducing in different habitats (66); (ii) variation from season to season (e.g. breeding and nonbreeding seasons), time of day, and sexual dimorphism within a population (4, 67–70); (iii) facultative variation within a population, season or life history stage (e.g. a change in responsiveness of the HPA axis to chronic stress) (19, 71); and (iv) individual variation within a population e.g. adrenocortical sensitivity to stress may vary as a function of social status (62, 64, 72, 73), body condition (4), infection (74), and other factors (67).

Variation in and among populations according to age (case A, Table 1)

There is evidence in a pelagic seabird, Leach's petrel, *Oceanodroma castro*, that older individuals show greater resistance to acute stress when breeding. A population on Kent Island, Maine, has been ringed for over 30 years and thus the age of these petrels is known. The adrenocortical response to a standardized capture, handling and restraint protocol (stress series) decreases as individuals age and the potential for future breeding events declines (75, 76). Mechanisms for this change in response to the stress series are unknown but could involve cases A or B in Table 2.

Variation among and within populations across seasons (case B, Table 1)

Spring weather is often very severe in extreme environments, such as at high latitudes, and frequent weather perturbations may disrupt breeding. Because the breeding season is attenuated in these environments, it would be advantageous to temporarily reduce sensitivity of the HPA axis to stress. Any 'costs' associated with impaired ability to respond to acute stress would be outweighed by increased reproductive success. Birds breeding in the Sonoran Desert of Arizona, also show suppression of the adrenocortical responses to stress (66). In the Arctic, sensitivity of the HPA axis to capture, handling and restraint stress in breeding snow buntings, *Plectrophenax nivalis*, female redpolls, *Carduelis flammea,* and Lapland longspurs, *Calcarius lapponicus*, are generally lower than those of passerine species sampled in temperate zone regions (77–79). Additionally, two breeding populations of semipalmated sandpiper, *Calidris pusilla*, studied in the low arctic near Nome, Alaska, and in the high arctic at Barrow/Prudhoe Bay, Alaska, show that circulating levels of corticosterone following capture, handling and restraint, are lowest at the most northerly sites with most severe weather (20, 21). An analysis of several different breeding seasons near Barrow, Alaska, revealed that corticosterone levels in several passerines do not increase in response to inclement weather, but do so after breeding has been terminated. These data bolster the hypothesis that the adrenocortical responses to acute stress are being suppressed (80).

There is a possible phylogenetic component to species differences in adrenocortical responses to acute stress (81) because mean maximum corticosterone levels in plasma of charadriiformes (a group that includes shore birds, gulls, etc.) is significantly higher than in both passeriformes (song birds) and galliformes (chicken-like birds) sampled while breeding in the Arctic (81). Nonetheless, sexual dimorphism in profiles of corticosterone plasma levels following capture, handling and restraint suggest that parental care by each sex may be related to modulation of adrenocortical responses to acute stress independently of phylogeny (81). Arctic-breeding birds exhibiting less parental care show greater adrenocortical responses to the capture stress protocol. Moreover, in several shorebird species breeding in northern Alaska, males and females display varying degrees of parental care. The sex showing most parental care has a lower response to the capture stress protocol (20, 21). Here, phylogenetic problems are minimized because these shorebird species are closely related. Thus, it is possible that expression of parental behaviour is an ecological base for suppression of the adrenocortical response to acute stress. This modulation may be more evident if the species also breeds in extreme environments. Mechanisms by which these modifications of the adrenocortical responses to acute stress occur are beginning to be explored. In some species (e.g. Lapland longspur and King penguin), the blockade appears to be at the central nervous system (CNS) level (case A, Table 2) (63, 82). In others (e.g. snow buntings and redpolls), it appears to be a failure of the HPA axis to secrete glucocorticosteroids (case B, Table 2) (83–85).

One additional way to modulate the response to stress is to change sensitivity of the target tissues, including the brain, to high circulating levels of glucocorticosteroids (case C, Table 2) (62, 86). It is also possible that behavioural responses to glucocorticosteroids may be regulated independently of the response of the

HPA axis itself, and that the regulation may occur at population and individual levels. Evidence for this is sparse but American tree sparrows, *Spizella arborea*, breeding on the arctic tundra showed no behavioural response to implants of corticosterone. Males defended territories normally, and continued to feed young (86), unlike the effects of corticosterone implants in birds breeding at lower latitudes that cause abandonment of territory and termination of parental care (87). This is potentially an exciting new area especially in relation to field studies. Whether the mechanisms for behavioural insensitivity to glucocorticosteroids lie at the level of changes in receptor numbers and distribution remains to be determined. It is also possible that intracellular enzymes (e.g. 11β-hydroxysteroid-dehydrogenase) (88, 89), that deactivate glucocorticosteroids to inactive 11-keto forms could be a site of regulation (2).

One novel mechanism that would support compensatory mechanisms to stimulate the gonadal axis and possibly counteract inhibitory actions of glucocorticosteroids (case D, Table 2) has recently come to light. In white-crowned sparrows breeding on the Alaskan tundra, there is a marked increase in the adrenocortical response to acute stress, especially in males (70) that is accompanied by a parallel increase in CBP in blood. When bound to such proteins with high affinity, steroid hormones are generally regarded as inactive because they cannot enter target cells. In dark-eyed juncos, Junco *hyemalis hyemalis*, these binding proteins also have a high affinity for testosterone (but less than for corticosterone) that is circulating at high levels early in the breeding season (90). High testosterone levels may actually increase CBP levels (91) and in nonstressful conditions, high levels of CBP probably bind most circulating corticosterone and testosterone. Therefore, in response to acute stress, corticosterone levels increase, interact with CBP, thus displacing testosterone that would then be free to enter cells and counteract the inhibitory glucocorticosteroid actions (90).

Terrestrial oviposition in pelagic female sea turtles

There is now abundant evidence that reptiles show similar adrenocortical responses to acute stress as other vertebrates. However, there is considerable species variation in the rate of response, across seasons, and with gender (69, 92–95). Sea turtles spend almost their entire lives at sea, but females must come ashore to lay eggs in the sand of tropical beaches. At this time, they are susceptible to predation and if they do not return to the sea by dawn, they can be exposed to overheating. In all, the period of oviposition can be stressful with the potential to interfere with nesting behaviour. Both male and female Ridley sea turtles, *Lepidochelys kempii*, loggerhead sea turtles, *Caretta caretta* and green sea turles, *Chelonia mydas*, show marked increases in circulating corticosterone levels in response to capture and handling (96–99). Adult females coming ashore to nest either singly or en masse (arribada) (97) show a decrease in the adrenocortical response to stress of capture and overturning. Even when exposed to severe heat stress, the following elevation of plasma levels of corticosterone in nesting female green sea turtles was less than in males and nonbreeding females (98). This is consistent with very brief breeding events (case B, Table 1). Although the mechanisms involved remain unknown, failure to perceive overheating as stress and blockade of the HPA axis (cases A and B, Table 2) are possible. There also is evidence that such phenomena may occur in the female whistling frog, *Litoria ewingi* (100).

Alternate reproductive tactics and stress in territorial male lizards

Males of many vertebrate species show alternative reproductive morphs that have varying degrees of reproductive success. Tree lizards in Arizona have two major male morphs, one that is highly territorial and another that is not territorial and 'floats' between and among the territories of the other morph (i.e. a satellite strategy). Territorial morphs have orange-blue dewlaps (throat fans) that they extend in displays against other males, whereas males of the other morph have only orange dewlaps and are less aggressive. Both morphs show identical adrenocortical responses to acute stress (physical restraint), but only the morph with orange dewlaps (nonterritorial) shows an accompanying decline in plasma testosterone. Males with orange dewlaps maintain high circulating testosterone levels despite high corticosterone responses to stress (case F, Table 1) (101).

This resistance to acute stress may be mediated through steroid binding globulins in blood. Tree lizards have a sex hormone binding globulin (SHBG) that binds testosterone and oestradiol with high affinity. The capacity (amount) of SHBG in blood is similar in the two male morphs. These lizards also have a second protein (CBP) that binds C21 steroids such as corticosterone and also binds testosterone. This protein binds oestradiol with much less affinity and is best called an androgen-glucocorticosteroid binding globulin (AGBG). The capacity of AGBG is much higher than SHBG, but the capacity of AGBG is greater in territorial *vs* nonterritorial morphs (102). Therefore, it is possible that as plasma levels of corticosterone increase following acute stress, then the fraction of free (unbound) corticosterone will be relatively higher in the nonterritorial morph that has a lower capacity of AGBG. This could explain why high corticosterone is accompanied by suppression of testosterone in this morph and not in the territorial morph (case E, Table 2) (102).

Population differences in breeding season length in garter snakes

Red-sided garter snakes, *Thamnophis sirtalis*, are distributed widely throughout North America. However, in northern populations, breeding may be highly restricted to just a few days in the year. In Manitoba, Canada, males in a population of garter snakes, *T. s. parietalis*, with such a brief breeding season showed no changes in plasma levels of corticosterone or testosterone in response to capture, handling and restraint. However, later in the summer, after breeding was over, these males showed a marked increase in corticosterone and a decrease in testosterone to the same stress protocol. In autumn, when mating may also occur, the same capture stress protocol in males resulted in a decrease in testosterone but corticosterone levels did not change (case B, Table 1) (103). In contrast, red-spotted garter snakes, *T. s. concinnus*, breeding in western Oregon mate over an extended period. Adrenocortical responses to the capture stress protocol were similar throughout spring, summer and fall. Although testosterone levels declined during acute stress in spring, circulating testosterone did not decline, despite high levels of corticosterone,

during the period of gametogenesis in summer and autumn (case C, Table 2) (103).

Mechanisms underlying the complete suppression of the adrenocortical response to stress in the red-sided garter snake of Manitoba may involve some combination of cases A, B or C in Table 2. Intraperitoneal injections of corticosterone into males suppressed mating behaviour when they were subsequently exposed to females, but this treatment had no effect on plasma levels of testosterone (104). Thus, it is possible that either the capture stress protocol is not perceived as stressful during mating, or there is some blockade of the HPA axis to stress at this time. Simultaneously, the HPG axis becomes resistant to the effects of acute stress, but the brain can respond to high corticosterone levels if given exogenous testosterone.

Facultative variation within a population

Modulation of the adrenocortical responses to environmental perturbations is generally thought to be temporary (i.e. over minutes to hours). More prolonged suppression of the stress response may result in severe debilitation as the individual incurs considerable cost by maintaining the reproductive effort in the face of deteriorating conditions. If the perturbation is transient then the cost may be greatly compensated for by enhanced reproductive success. If this is true, then modulation of the HPA axis may be far more labile than we previously thought. A recent field study showed that a prolonged snow storm (four days in mid-June) at Toolik Lake, Alaska, was endured by breeding Lapland longspurs for at least three days. Females continued incubating eggs in nests under snow. By the end of the third day, snow and subfreezing temperatures persisted and first males and then females began to abandon nests and territories. They formed flocks typical of the nonbreeding season and began wandering over the tundra. A number of birds were captured and sampled as they abandoned nesting. The rate of increase in corticosterone levels in response to capture, handling and restraint had increased by almost an order of magnitude over that before the storm while females were incubating (71). These birds were apparently able to up-regulate their responsiveness to acute stress within a few hours once environmental conditions had deteriorated to the point that both reproductive success and survival were in jeopardy. Because the breeding season of these birds in the Arctic is so short, the storm resulted in zero reproductive success for that year. However, individuals were able to survive and breed another year thereby maximizing reproductive success in the long term. Mechanisms for reactivation remain unknown, but probably involve a reversal of blockades at the CNS or HPA levels (case A or B, Table 2) (83–85, 105).

Individual variation

It has long been known that individual profiles of blood glucocorticosteroid levels in response to stress are highly variable and represent an independent source of variation to that seen at the population level (cases C and E, Table 1). Individual variation can occur in either sex, at any stage in the life cycle and includes differences in initial level of glucocorticosteroids, the rate of increase and maximal level attained (4). There is increasing evidence for individual variation in coping mechanisms that may have a genetic basis, or may be moulded by experience during development, or be a result of environmental variables as an adult (106, 107). Here, we restrict our discussion to environmental effects. What basis, if any, is there for this pronounced individual variation, especially in relation to reproduction?

The most common relationship with individual variation in stress responses is body condition. This could be a result of social status, quality of the territory and resources on it, parasite load, and experience during development (2, 3). Studies in the field show that breeding birds in the Arctic that have more fat tend to have a more suppressed adrenocortical response to stress although this relationship is by no means universal (78, 79, 81). As discussed, in olive baboons (48, 108), social status may have profound influences on sensitivity of the HPA axis to acute stress. Usually, the dominant animal is more resistant than the subordinate animal such as the reduced response of dominants to the same stress in the green anole, *Anolis carolinensis* (109). In contrast, fecal glucocorticosteroid levels indicate that the reverse may be true in free-living Cape hunting dogs of Africa (110). Clearly, much more work is needed to unravel the complex interrelationships of social status and resistance to stress. As pointed out by Creel (73), glucocorticosteroid levels do not just depend upon rank, but on what rank means in a particular species or group.

Individual experience may also play a role. In many passerines, both sexes feed young in the nest. If one member of the pair dies (taken by a predator), or is abandoned by its mate, then the other may compensate by feeding young more intensively. The result is that the surviving individual may lose body mass as its daily energetic requirements increase, but the endpoint is successful breeding. In free-living pied flycatchers in Sweden, some males are sequentially bigamous. However, the male usually abandons his second mate and returns to help the first mate feed young. These abandoned females have higher baseline levels of corticosterone and show a greatly enhanced adrenocortical response to stress (19). Nonetheless, they are able to raise young alone, although it is possible they are more vulnerable to perturbations of the environment than a female who is assisted in parental care by a male. Mechanisms involved are unknown, but because both baseline and stress-induced levels are higher than in females receiving assistance from a male when feeding young, then cases C or D (Table 2) appear likely.

Conclusions

There is abundant evidence that environmental and social stresses have deleterious effects on reproductive function in vertebrates. Thousands of studies cover medical, agricultural and basic biological aspects of stress and reproductive suppression. In recent decades, global climate change, human disturbance and endocrine disruption from pollutants are increasingly likely to pose additional stresses that could have dire import for human society worldwide. Indeed, the consequences of stress to reproductive function have far reaching social, economic and environmental costs.

Despite this discouraging scenario, examples are emerging in which some populations of animals are able to resist environmental and social stresses, at least temporarily, and breed successfully. These cases span the full spectrum of vertebrates from fish to mammals. They appear to be classified into examples of evolutionary logic behind maintaining reproduction during stress (i.e. a classical trade-off of reproductive success for potential survival).

We define five examples (Table 1): (i) aged individuals with minimal future reproductive success that should attempt to breed despite potential acute stressors; (ii) seasonal breeders when time for actual breeding is so short that acute stress should be resisted in favour of reproductive success; (iii) when both members of a breeding pair provide parental care, then loss of a mate should be compensated for by the remaining individual working twice as hard to raise young successfully; (iv) semelparous species in which there is only one breeding period followed by programmed death; and (v) species where because of the transience of dominance status in a social group, individuals may only have a short window of opportunity for mating. There is also accumulating evidence for the mechanisms underlying resistance of the gonadal axis to stress. Possible scenarios (Table 2) include: (i) blockade at the CNS level (i.e. an individual no longer perceives the perturbation as stressful); (ii) blockade at the level of the HPA axis (i.e. failure to secrete some critical component of the axis and thus no increase in glucocorticosteroids); (iii) blockade at the level of the HPG axis (i.e. some form of resistance of the reproductive system to the actions of glucocorticosteroids); and (iv) compensatory stimulation of the gonadal axis to counteract inhibitory glucocorticosteroid actions. Future research is needed to provide valuable information on the biology of stress and how organisms cope. Such mechanisms would be particularly insightful as the spectre of global change continues to unfold.

Although it is intuitive that mechanisms allowing reproduction to occur despite stressful conditions are genetic, it is much less clear whether the variation among and within populations is also genetically determined. In other words, some individuals may have a 'coping style' very different from other individuals in a population. This may be a result of genetic differences underlying such coping styles. There may be selection for several styles if those individuals are successful and reproduce despite stressful conditions. On the other hand, environmental factors may contribute directly to the degree to which an individual can resist stress and these environmental effects may or may not be further influenced by genetics. Much research remains to be done to tease apart genetic and environmental influences on resistance to stress.

Acknowledgements

J.C.W. is grateful for several grants from the Division of Integrated Biology and Neuroscience, and the Office of Polar Programs, National Science Foundation. He also acknowledges a John Simon Guggenheim Fellowship, a Benjamin Meaker Fellowship (University of Bristol, UK), and a Russell F. Stark University Professorship (University of Washington). The work of R.M.S. that has contributed to this review was supported by the Harry Frank Guggenheim Foundation and the Templeton Foundation. Drs Susan Wray and Barry Sinervo, and two anonymous reviewers provided valuable comments on earlier drafts.

Accepted 20 February 2003

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