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Author for correspondence:
Sonia A. Cavigelli
e-mail: sac34@psu.edu

Sex, social status and physiological stress in primates: the importance of social and glucocorticoid dynamics

Sonia A. Cavigelli[1,2,3] and Michael J. Caruso[1,2]

[1]Department of Biobehavioral Health, Pennsylvania State University, 219 Biobehavioral Health Building, University Park, PA 16802, USA
[2]Center for Brain, Behavior, and Cognition, Pennsylvania State University, University Park, PA 16802, USA
[3]Huck Institute of Life Sciences, Pennsylvania State University, 101 Huck Life Sciences Building, University Park, PA 16802, USA

Social status has been associated with health consequences, although the mechanisms by which status affects health are relatively unknown. At the physiological level, many studies have investigated the potential relationship between social behaviour/rank and physiological stress, with a particular focus on glucocorticoid (GC) production. GCs are of interest because of their experimentally established influence on health-related processes such as metabolism and immune function. Studies in a variety of species, in both naturalistic and laboratory settings, have led to complex outcomes. This paper reviews findings from primates and rodents and proposes a psychologically and physiologically relevant framework in which to study the relationship between social status and GC function. We (i) compare status-specific GC production between male and female primates, (ii) review the functional significance of different temporal patterns of GC production, (iii) propose ways to assess these temporal dynamics, and (iv) present novel hypotheses about the relationship between social status and GC temporal dynamics, and potential fitness and health implications. To understand whether GC production mediates social status-related fitness disparities, we must consider social contest conditions and the temporal dynamics of GC production. This framework will provide greater insights into the relationship between social status, physiological stress and health.

1. Introduction

Individuals living in groups often develop social hierarchies [1,2]. The associations between social status and developmental, physiological, behavioural and health processes have been documented in a variety of species and settings (e.g. [3–8]). However, the proximate mechanisms by which social status has any causal influence on development, physiology, behaviour and/or health are not clear. In this paper, we examine the relationship between social status and one aspect of physiological stress, production of glucocorticoid (GC) hormones, which can have a significant influence on health, ageing, behaviour and development. We focus this review on free-ranging primates because of the abundance of studies on social status and GC production in this taxon. Studies that have investigated the relationship between social status and health and/or stress physiology have led to complex findings. We show that these findings can be clarified by comparing primate male- and female-typical social competition and by adopting a nuanced understanding of hypothalamic–pituitary–adrenal (HPA) axis regulation and the functional significance of GC production temporal dynamics. To provide insights into the functional significance of GC temporal dynamics, we examine results from studies with laboratory rodents and humans. By understanding GC temporal patterns in high- and low-ranking individuals, we will achieve a better understanding of how GC production may mediate the relationship between social status and long-term health outcomes.

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In this review, we investigate the relationship between social status and GC production by considering two important functional observations: (i) the sexes often differ in hierarchy formation processes [9] and (ii) long- versus short-term elevations in GC production have different influences on physiology and health [10,11]. We review these two phenomena, and then provide specific predictions of how social status in different societies could differentially relate to GC temporal dynamics to provide insights into proximate costs and benefits of maintaining specific social rank in different social systems.

Males and females regularly form dominance hierarchies across a variety of primate species. However, the social behaviour and associated costs involved in acquiring and maintaining rank can differ between sexes. Males typically engage in more intense and frequent aggressive interactions than females, whereas females tend to engage in more complex affiliative interactions [12–14], with some exceptions [9]. Male rank is often achieved by violent turnovers of an existing hierarchy and competition is over access to mates, whereas female rank is typically determined by more subtle aggressive and affiliative interactions and competition is often over access to quality food resources ([12–15], cf. [9]). In addition, the immediate costs of aggressive interactions are usually greater for males than females (e.g. wounding) [16,17] given increased male weaponry (teeth, claws, body size) [18–20].

Given broad differences in social and reproductive strategies between males and females, the challenges involved in attaining and maintaining social status differ between sexes. In a 'typical' species, in which males are large with significant weaponry, male dominance requires good physical condition and can be dangerous and costly to acquire during discrete periods. In a similar species where females use coalitionary and affiliative strategies, dominance may be less energetically costly and subordinate exclusion from quality resources may be more costly over longer periods. These two methods of attaining and maintaining dominance should lead to different GC production dynamics: acute elevations in typical dominant males versus chronic elevations in typical subordinate females.

In addition to considering broad differences in male versus female sociality, we consider temporal dynamics and costs/benefits of elevated GC production. GC production is a dynamic process that involves complex feedforward and feedback regulatory processes [10]. This complex regulation allows for a range of GC production temporal patterns, with differences in peak and trough amplitudes, rates of recovery to basal production and frequency of elevated production (figure 1). In laboratory studies, these differences in temporal dynamics have been associated with differences in behaviour, environment, age and genetics (reviewed below) [21–28].

Differences in GC temporal dynamics are particularly important because they may confer different health consequences. Short- versus long-term elevations in circulating GC levels may have seemingly opposite influences on metabolic, cardiovascular and immune processes. For example, short-term elevations in circulating GC levels can increase certain aspects of cellular immunity, have a negligible influence on cardiovascular function and lead to temporary weight loss; whereas long-term elevations can cause decreased cellular immune responses, increased arterial blood pressure and heart rate and increased weight gain [29–32]. These bidirectional influences of GC production are important to consider in terms of fitness consequences. If GC production mediates differential health outcomes among social ranks, then it is important to study status-specific GC production temporal patterns. To predict fitness-related outcomes, we need information on timing and duration of elevated and dampened GC production.

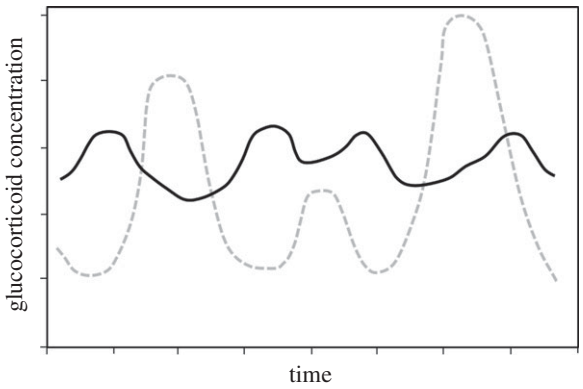

Figure 1. Stylized examples of two different circulating GC temporal profiles that would produce similar *mean* GC levels.

2. Sex differences in social status and glucocorticoid production

A decade ago, several reviews were published on social status and GC production [33–36]. These concluded that GCs are elevated in group-living individuals that have heightened metabolic demands, and that these demands are greatest during periods of social instability. The 'stress of subordination' and 'stress of dominance' hypotheses were coined, based on the realization that both high- and low-rank are associated with specific challenges [33–35,37]. Importantly, challenges associated with subordination and dominance can trigger increased GC production that fuels specific behavioural and physiological responses. These reviews, and the refinement of non-invasive faecal steroid methods, stimulated further investigation of social status and GC production in a variety of free-ranging species, particularly primates.

Primates are a useful biological system in which to investigate these questions because many species maintain relatively large and complex social groups, where quantification of social interactions is relatively easy. We focus on studies of free-ranging primates, which provide a good basis to assess the relationship between physiological stress and social status and the selection pressures associated with systematic covariation of social behaviour and physiology. We compare results according to the sex of study subjects and methods of rank attainment/maintenance (whether rank is inherited or not). Given prior results ([36,38,39], cf. [40]), we focus on studies conducted during social instability when rank acquisition or maintenance is presumably most costly (for both subordinate and dominant individuals; table 1).

The majority of primate studies indicate that dominant males produce levels of GCs that are more than or equal to subordinate males, whereas only one study has found that subordinate males excrete more GCs than dominant males (table 1—see 'MALES—not inherited') [40,48,56–70]. The opposite pattern emerges for females, where subordinate females often have greater GC production than dominant individuals, particularly when rank is not inherited

Table 1. Summary of studies that have measured GC levels among high- and low-ranking individuals in free-ranging primate groups. The table is organized by sex of study subjects and whether rank is inherited from the mother or not. Results are focused on study periods that were identified as socially unstable (e.g. mating season, social disruptions such as rank-reversals, immigration events, etc.). In studies that included both stable and unstable periods, we only present results from unstable periods. For studies that only included stable periods, we include those data in the table (for a summary that includes other species and a comparison of stable versus unstable periods, refer to [41]). The footnotes provide an explanation of the information in each column. Text provides information on literature review criteria.

sex—rank inheritance species	animals/groups[a]	sample medium[b]	months of sampling[c]	mean samples per Ind'l[d]	social stability[e]	CORT relative to rank[f]	ref.
FEMALES—inherited							
chacma baboons	10/1	faeces	17	26	?	=	[42]
chacma baboons	21/1	faeces	16	30	unstable	=	[43]
chacma baboons	18/1	faeces	8	31	unstable	=	[41]
chacma baboons	22/1	faeces	1.5	24	unstable	**S**	[44]
chacma baboons	45/1	faeces	48	?	stable	**S**	[45]
mandrills	19/1	faeces	12	18	stable	=	[46]
rhesus macaques	70/6	serum (reactivity)	5 (across 2 years)	1–2	?	=	[47]
long-tailed macaques	34/4	urine	2	~3	stable?	=	[48]
barbary macaques	8/1	faeces	5–7	16	stable	**I**	[49]
FEMALES—not inherited							
chimpanzees	18/1	urine	60	67	unstable	**S**	[50]
sykes' monkeys	11/1	faeces	16	165	unstable	**S**	[51]
common marmoset	6/3	faeces	10–16	69	unstable	**S**	[52]
ring-tailed lemurs	39/8	faeces	0.6	6	unstable	**D**	[53]
ring-tailed lemurs	45/7	faeces	4–12	~10	?	=	[54]
ring-tailed lemurs	32/3	faeces	51 (across 7 years)	43	unstable	**I**	[55]
MALES—not inherited							
chimpanzees	11/1	urine	12	AM: 31 PM: 15	stable	AM: = PM:**D**	[56]
gorilla	10/3	urine	15	21	unstable	=	[57]
olive baboons	13/1	serum (reactivity)	0.5	6–9 ?	stable	=, **D**?	[58]
				sequential	unstable	=	[59]
savannah baboons	125/5	faeces	108	36	unstable	**D,S**	[40]
chacma baboons	13/1	faeces	14	37	unstable	**D**	[60]
mandrills	16/2	faeces	1–3	20	unstable	**D**	[61]
long-tailed macaques	24/4	urine	2	3	unstable	= **D**?	[48]

(*Continued*.)

Table 1. (*Continued.*)

sex—rank inheritance species	animals/groups[a]	sample medium[b]	months of sampling[c]	mean samples per Ind'l[d]	social stability[e]	CORT relative to rank[f]	ref.
long-tailed macaques	16/1	faeces	4.5	15	unstable	=	[62]
Japanese macaques	6/1	faeces	6	42	stable	**D**	[63]
Assamese macaques	6/1	faeces	5	35	unstable	**S**	[64]
tufted capuchins	6/1	faeces	12	>14	unstable	=	[65]
white-faced capuchins	8/3	faeces	6	24	unstable?	**D**	[66]
bearded capuchins	3/1	faeces	3	15	unstable	**D**	[67]
golden lion tamarins	24/14	faeces	16	8	?	=	[68]
Verreaux's sifakas	10/5	faeces	5	32	unstable	**D**	[69]
ring-tailed lemurs	13/3	faeces	4–5 (across 3 years)	5–6	unstable	=	[70]

[a]Total number of animals/total number of social groups.
[b]Biological sample used to measure GC production.
[c]Number of months that samples were collected to measure GC production.
[d]Mean number of samples collected from each individual.
[e]Estimate of social stability based on description of social conditions in paper. Mating periods in seasonally breeding species with multiple breeding males were considered unstable. New group formation and increased aggression were considered unstable.
[f]Dominance rank with greatest GC production: 'D' indicates dominants greater than subordinates, 'S' indicates subordinates greater than dominants, 'I' indicates intermediate rank greater than subordinates/dominants, ' = ' indicates no rank effects.

(table 1—see 'FEMALES—inherited' and 'FEMALES—not inherited') ([24,35,41–52), cf. [53,54,55]). Given the role of GCs in metabolism, these findings support the hypothesis that male attainment and maintenance of high rank are associated with increased metabolic costs relative to subordinates, but that subordinate status in females is associated with greater metabolic costs relative to dominants.

Exceptions to these sex-specific patterns of GC production occur in male Assamese macaques (*Macaca assamensis*) where dominant males have lower *mean* GC levels than subordinates [64], and in female ring-tailed lemurs (*Lemur catta*) where high-ranking females have greater *mean* GC levels than subordinates [53,55]. In both cases, the social structure does not follow 'sex-typical' patterns described above. Male Assamese macaques attain high rank through male–male coalitionary support and high rank does not necessarily confer exclusive access to reproductive females [64,71]. Female ring-tailed lemurs are dominant to males, they have significant weaponry, and they are relatively aggressive within and between social groups [72,73]. These two exceptions may prove the rule that high rates of within-sex aggression for high-rank attainment predict short-term costs and GC elevations in dominant individuals, whereas in social systems with low rates of within-sex aggression, subordinate exclusion from key resources predicts longer term costs and GC elevations in subordinates.

The above summary supports the hypothesis that during periods of social instability, dominant male primates produce more GCs than subordinate males, and that the reverse is true for females. However, there are a several caveats: (i) plenty of studies indicate no relationship between GC production and dominance status, (ii) several studies indicate a nonlinear relationship between dominance rank and GC production and (iii) current studies tell us little about GC production dynamics (e.g. peak versus trough, basal versus reactivity levels) as they relate to dominance rank. In the following section, we expand on the functional significance of basal and reactive HPA activity and delve into the hypothesis that dominance status may be more closely related to the temporal *dynamics* of GC production than to *mean* production over time (as assessed by non-invasive urine and faecal sampling methods).

3. Temporal dynamics of glucocorticoid production

(a) Basic neuroendocrine-stress physiology

GCs are produced by the adrenal cortex and released into peripheral circulation in response to endocrine signalling from the anterior pituitary (adrenocorticotrophin, ACTH), mediated by hypothalamic corticotropin-releasing hormone (CRH). Stimulation of this HPA axis occurs in response to external stimulation, physical exertion, cognitive/emotional processes and circadian rhythms. Once in circulation, GCs alter the function of multiple organs simultaneously and in a sustained manner by binding receptors in brain, peripheral organs and immune cells [11,74–77]. Bound intracellular receptors stimulate slow, long-term alterations in cell function through transcriptional and epigenetic processes [78–81], and GC binding to putative membrane receptors also influences HPA axis sensitivity through non-genomic signalling [82,83]. A fine-tuned balance of receptor expression in the central nervous system moderates HPA axis responses to stress and stress coping strategies [84,85]. Based on these complex and long-lasting organism-level changes, the endocrine system may be particularly well-suited to support subtle and sustained responses to social status-related challenges and subsequent health-related outcomes.

Intermediate signalling hormones in the HPA axis have significant effects on cellular function; CRH and ACTH directly alter brain and peripheral cell function in ways that could affect health beyond the influence of GCs (e.g. [86]); these influences are discussed in depth elsewhere [87–93]. Sympathetic activation is also closely related to social behaviour, status and health consequences [94,95], but fewer social behaviour studies have focused on this metabolically relevant system, particularly in free-ranging animals.

(b) Cues that alter glucocorticoid production

Based on laboratory studies with rodents, diverse physical and social stimuli cause significant short-term elevations in circulating GC levels [28]. In these controlled situations, standardized social stressors cause twice as much GC production as physical stressors. In free-ranging animals (reptiles, amphibians, birds and mammals), rapid elevations in GC production have been documented following capture, severe weather conditions and aggressive male immigration, and long-lasting GC alterations have been documented during periods of low food supply and across seasons [58,96–100].

The time course of GC responses to environmental and internal cues is modified by stressor qualities (intensity, frequency, duration, degree of novelty, etc.), organism characteristics (age, genetics, etc.) and time of day or season. For example, in laboratory rodents and primates, repeat exposure to the same stressor leads to habituation and faster return to basal levels [101,102], and different stressor types or intensities lead to different recovery durations [24,25]. Rodent and primate genetic background further influences the duration and intensity of GC production, which are not necessarily linked to behavioural differences [23,103]. Time of day can further influence peak amplitude and duration of GC responses [104], and the sex and age of an organism affect response dynamics in humans and rodents [21,22,26,27,105,106].

These different response dynamics are significant because short- versus long-term elevations in GC production are associated with different influences on biological processes and health. In particular, GC recovery rate (time to return to baseline concentrations after a challenge) has particular functional/health significance (e.g. [107]). Social status, whether high or low, is associated with an array of different challenges, some that stimulate long-term elevations in GC production and others that stimulate short-term elevations. These different challenges may confer different influences on physiology and health.

(c) Metabolic and health effects of short- versus long-term glucocorticoid elevations

Studies with laboratory rodents suggest that short- versus long-term GC elevations have different influences on health-related processes. We review some of these findings and apply these lessons to primates based on the fact that HPA regulatory processes are evolutionarily conserved, with significant homology among vertebrate species [108–110]. Effects of

HPA axis hormones on health processes in laboratory rodents may generalize to a wide range of vertebrate organisms.

GCs are widely recognized for their effects on carbohydrate metabolism, gluconeogenesis and subsequent increased blood glucose. In addition, GCs regulate lipid metabolism in adipose tissue, enhance *de novo* lipid synthesis in the liver, and increase protein catabolism [111,112]. The release of energy-rich substrates supplies an organism with increased metabolic resources to cope with stressors. Over longer periods, these hormones can increase body mass because they tend to increase feeding behaviour and stimulate intake of high-caloric foods in humans and rodents [113–115]. Finally, GCs influence an array of other biological systems such as the cardiovascular, respiratory, immune, visual, metabolic and reproductive systems (reviewed below and in table 2) [119].

Duration of elevated GC production is an important determinant of physiological consequences. While many of the acute effects of GCs mobilize energy, chronically elevated circulating GCs enhance energy storage (table 2). For example, in mice, chronic (four-week) exposure to elevated GC caused an initial weight loss followed by significant weight gain [32,117]. Acute GC elevations can activate the adaptive immune system, whereas chronic GC elevations are linked to suppressed cell-mediated leucocyte trafficking [29]. Telomerase, an enzyme that maintains telomere length, is upregulated in human peripheral mononuclear cells 1 h after exposure to an acute laboratory social stressor, but chronic stress is associated with reduced telomere length in these cells [118,120].

Short- versus long-term effects of GCs and stressors are also important in the brain where they influence behavioural responses. Immediately after acute exposure to GC, hippocampal-dependent information processing is impaired, but an hour to days later hippocampal long-term potentiation is enhanced [121]. GC injections 90 min before behavioural testing caused enhanced exploratory behaviour and decreased fear behaviour in rats, but when exposed to repeated GC administration for 25 days, rats were less exploratory and displayed enhanced fear behaviour [116]. Acute actions of GCs may enhance processing of stress-related information, which helps the individual to cope with similar future challenges, but effects of sustained GC elevations may overpower adaptive responses to acute stress.

In regard to the stress of dominance, acute GC elevations support enhanced responding. For example, an aggressive interaction to attain or maintain dominance requires increased energy, and GC-induced carbohydrate, lipid and protein metabolism provides a sustained source of energy. Acute GC elevations also stimulate leucocyte redistribution to the skin, which can fight off infection after potential wounding. While we have discovered a great deal about the role of GCs in health and coping, there is still much to learn. For example, there are few direct comparisons of the effects of short- versus long-term GC elevations in controlled experiments (table 2), and this experimental work is primarily performed in rodents. Further research is needed to clarify open questions with regard to chronic GC elevations such as what constitutes long-term exposure and at what point detrimental effects occur.

(d) Limitations of current methods

Faecal GC metabolites (FGCMs) measures provide a non-invasive estimate of HPA axis function ideal for field studies. However, there are limitations to this method; several factors influence the amount and rate of GC metabolism and excretion [122–128]. For example, GC metabolism differs between sexes in mice, rats and other rodents, with males typically excreting higher concentrations than females, with exceptions [123,124,127,128], and the specific FGCMs excreted are sex- and species-specific [123–125]. Quantification of circadian rhythm is difficult: FGCMs can show a diurnal rhythm mirroring that of circulating GCs, but this rhythm can only be documented in animals that defecate multiple times per day [124,126,127]. Intestinal transit time, which regulates FGCM excretion rate, is influenced by physical activity; rodents excrete GCs more rapidly during the active versus passive phases [123]. Total faecal mass influences FGCM concentration, which may not reflect circulating concentrations [126]. Thus, FGCM measures provide a useful estimate of GC production in free-ranging animals with appropriate methodological considerations and biological validation for each species [125].

More relevant to this review is the fact that faeces are excreted in discrete periods, and therefore, faecal steroid measures reflect a physiological average of circulating steroid levels over several hours or days. These measures represent an estimate of overall production during both low- and high-production periods. Also, most studies necessarily use opportunistic sampling and estimate mean steroid production across long periods (weeks, months). Because GC production is affected by many variables and because faecal samples have inherent limitations, accurate quantification of individual differences in GC production requires frequent within-individual sampling over a significant period. From current studies, it is difficult to know whether high-*mean* FGCM levels reflect consistently high levels of circulating GCs (e.g. chronic stress associated with negative health consequences) or frequent or particularly high elevations in GC production in response to challenges (e.g. a profile that may activate adaptive metabolic processes; see figure 1 for different GC dynamics underlying the same GC *mean*). If GC production estimates are to provide a mechanism by which social stress/status confers specific health benefits or costs, then it is particularly important to distinguish between these two kinds of GC profiles.

4. Social status, glucocorticoid production dynamics and fitness: the 'dynamics of stress' framework

(a) Novel predictions on social dynamics, social status and glucocorticoid production dynamics

We propose two testable predictions that are sex-specific in 'typical' species where males engage in aggressive within-sex competition for limited access to mates and females engage in lower levels of aggression for access to physical resources (male challenges are more intense but shorter lived than female challenges). (i) In species that show 'stress of dominance' (dominant individuals have greater *mean* GC production), dominant individuals will have more frequent and/or higher GC elevations than subordinates as a result of acute intense metabolic demands like within-sex fighting, and trough production will not relate to social status (figure 2*a*: 'stress dynamics of dominance'). (ii) In species that show 'stress of subordination' (subordinate individuals have greater *mean* GC production), subordinate individuals will have chronically

Table 2. Examples of studies in which the duration(s) of GC production and/or stress were manipulated or controlled for to determine the influence of acute versus chronic elevations in GC/stress exposure on fitness- and health-related processes. Methods and specific dose/frequency/duration of experimental manipulations are provided, along with outcomes of acute versus chronic exposure conditions. ADX, adrenalectomy; Pred., prednisolone (synthetic GC/derivative of cortisol); min, minute; d, day; wk, week; m, month; CORT, cortisol in human studies and corticosterone in rodent studies; DEX, dexamethasone (a synthetic glucocorticoid receptor agonist); DTH, delayed-type hypersensitivity (adaptive cell-mediated immune response to a specific antigen); TSST, Trier Social Stress Test (common psychosocial stress challenge for human participants in a laboratory setting).

species	variable	method	dose/freq./dur. of 'acute' manipulation	dose/freq./dur. of 'chronic' manipulation	outcome (acute—A versus. chronic—C)	ref.
human	GC	GC (Pred.) pills	5–10 mg/1 d/7 d	5 mg/1 d/12 m	protein metabolism A: increased C: no change	[112]
rat	GC	ADX + GC implants	40 or 80%/1 d/5 d	n.a.	food consumption A: increased weight gain A: decreased	[113]
rat	GC	GC injection	5 or 20 mg/kg/1 d/1×	5 or 20 mg/kg/1 d/25 d	anxiety-like behaviour A: decreased C: increased	[116]
rat	GC	ADX + GC implant or injection	3.7 µg/g DEX/1 d/1×	238 µg DEX/1 d/3 wk and 9.5 mg CORT/1 d/1 wk	blood glucose/leptin A: increased body weight C: decreased	[117]
rat	GC	ADX + GC injection	5 mg/kg/1 d/1×	40 mg/kg/1 d/6 d	DTH response A: enhanced C: supressed	[29]
mouse	GC	GC in drinking water	n.a.	25 or 100 µg/ml/1 d/4 wk	weight gain/adiposity/food consumption C: increased locomotor activity C: decreased	[32]
human	GC reactors	TSST	TSST/1×/45 min	n.a.	sweet food calorie consumption A: High CORT reactors consumed more than low CORT reactors	[115]
human	life stress	TSST	TSST/1×/20 min	n.a.	telomerase activity C: chronic life stress group lower than low stress group	[118]

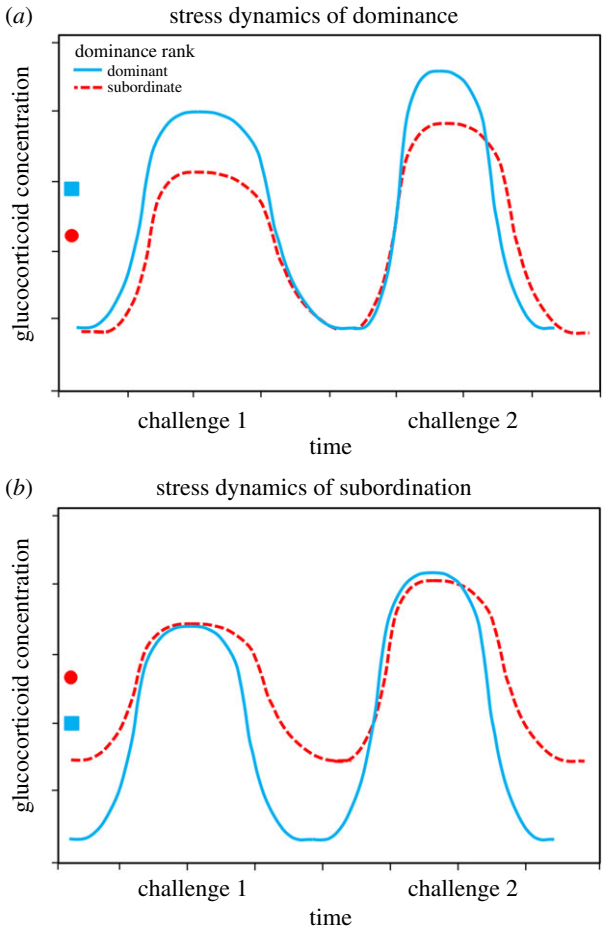

Figure 2. Predictions about adaptive temporal patterns of GC production in a dominant versus subordinate individual in two different social systems: (*a*) where dominant individuals maintain elevated *mean* GC production relative to subordinate individuals and (*b*) where subordinate individuals maintain elevated *mean* GC production relative to dominant individuals. Square indicates *mean* GC concentration for dominant individuals, circle indicates *mean* GC concentration for subordinate individuals. (*a*) In the 'stress dynamics of dominance' scenario, the dominant individual has elevated *mean* GC production as a result of greater *peak* production compared with subordinate individuals; this is a pattern that may confer metabolic, reproductive, immune and/or cognitive benefits to the dominant individual and support increased survival/fitness. (*b*) In the 'stress dynamics of subordination' scenario, the subordinate individual has elevated *mean* GC production as a result of greater *trough* production and/or slower returns to baseline compared with dominant individuals, and this pattern may incur decreased fitness/survival benefits. (Online version in colour.)

elevated GC production and/or fewer periods of return to expected basal production relative to dominants as a result of chronic low-grade metabolic demands like exclusion from key resources. In this scenario, peak GC production will not differ between subordinate and dominant individuals (figure 2*b*: 'stress dynamics of subordination'). These distinct temporal profiles may have different consequences for health and fitness.

We expect that these status-related GC production patterns will be apparent during periods of instability, in both sexes, and in social groups in which competition more often involves contest than scramble. In addition, we expect the 'stress dynamics of dominance' scenario to be more frequent in males in species in which male–male fighting is particularly aggressive and wounding is significant, and the 'stress dynamics of subordination' to be frequent in females in species in which female–female aggression and wounding are not frequent and high-quality food supplies are easily monopolized [20]. We expect these patterns to be reversed between the sexes when specific characteristics of dominance rank acquisition and maintenance are not 'sex-typical' (e.g. where males compete for access to clumped food resources, and/or females compete in a particularly aggressive manner that involves enhanced weaponry). In the following section, we provide one example of how the above predictions may be tested with existing datasets with frequent GC sampling.

(b) Example of social status-related glucocorticoid production dynamics

This kind of analysis will work best when many samples from the same individual are available. We re-analysed published data from wild female ring-tailed lemurs [129], which live in relatively small social groups (5–30 individuals) in extremely arid environments in Madagascar [130–132]. All females are dominant to all males, and this behavioural adaptation is thought to have evolved as a result of very limited resource availability [72,133].

Faecal samples were analysed from 10 females across two social groups during two months of mid-to-late dry season when females were lactating (mean of 39 samples for each female; range of 32–47 samples/female) [129]. Samples and behaviour were collected during four alternating one-week periods for each group, with approximately 10 samples/female/week, and no differences in sample size between high- and low-ranking females. Dominance rank was quantified using agonistic interaction matrices based on all observed interactions. Prior analyses of these data indicated that the two highest-ranking females in unstable social groups produced more FGCMs than the three lowest-ranking females in these groups, and that FGCM levels were positively related to aggressive behaviour [53]. To determine potential health consequences of elevated GC levels, it is imperative to understand whether elevated faecal levels reflect frequent or intense acute GC elevations (figure 2*a*) or chronically elevated basal circulating GC levels (figure 2*b*). Frequent or intense GC elevations in an individual may confer certain health benefits, whereas long-term basal GC elevations or protracted GC responses may have more negative health consequences.

One way to distinguish between the two GC response profiles is to analyse minimum versus maximum FGCM levels from each individual. With enough samples from the same individuals, one can compare individual minimum versus maximum production across time. As the number of samples from an individual increases so too will the range, with greater maximum and lower minimum levels obtained as sample size increases [134]. Therefore, studies of minimum and maximum FGCM levels require many samples from the same individual and comparable sample sizes across individuals or controls for variable sample sizes. With enough samples, it is possible to refine faecal steroid analyses to estimate temporal dynamics, and the potential functional significance of individual GC production profiles. Specifically, if high-*mean* FGCM levels result from relatively frequent or intense GC spikes in circulation, then minimum FGCM levels should be similar in animals with high- or low-*mean* FGCM levels, but maximum FGCM levels may be greater in the high- versus low-*mean* FGCM individual (figure 2*a*). On the other hand, if high-*mean* FGCM levels

result from chronically elevated circulating GC levels, then minimum FGCM levels will be higher than those from an individual that has chronically lower circulating GC levels (figure 2*b*).

With the ring-tailed lemurs we were able to determine individual minimum and maximum FGCM values for each one-week observation period. High-ranking females with high *mean* FGCM levels (ranks 1–2) had similar minimum FGCM levels to low-ranking females (ranks 3–5; 9–19 versus 7–14 ng g^{-1}, repeated measures ANOVA $F_{1,8} = 2.2$, n.s.). However, maximum FGCM levels were twice as high in high- versus low-rank females (34–155 versus 27–44 ng g^{-1}, repeated measures ANOVA $F_{1,8} = 10.2$, $p < 0.05$). Results were not affected by sample size (as a covariate), nor by inclusion of more samples from other seasons. These results suggest that high-rank ring-tailed lemur females do not necessarily have chronically elevated GC levels, but rather that they experience higher, longer or more frequent elevations in circulating GC levels with similar trough levels to subordinate females. Further analysis revealed that high-ranking females had greater FGCM levels one day following a significant challenge (territory invasion, predation threat) compared with low-ranking females, suggesting that high-ranking females have a physiological stress response that is more responsive to environmental stressors [1]. Based on the prior review of GC dynamics, heightened GC responses may confer certain fitness advantages.

The analysis of minimum versus maximum FGCM levels in female ring-tailed lemurs supports the prediction that elevated GC production in dominant aggressive versus subordinate less-aggressive individuals probably occurs in a discrete or acute fashion, and may thus confer different fitness consequences from those associated with chronically elevated GC production. This information will be important to collect in future studies of social status-associated GC production. Only by documenting the relative variability in individual GC production can we infer the potential costs or benefits of differential GC production among high- versus low-ranking individuals (e.g. [135,136]). Because social dynamics among ring-tailed lemurs are exceptional [72,73], future studies in species with more prototypical social structures are required.

5. Conclusion and future directions

Quantification of the temporal patterns of GC production among individuals is necessary to understand potential fitness costs and benefits of status-specific GC production. We must distinguish between high-GC individuals with a responsive HPA axis to acute threat and those with more chronically elevated GC production either in the absence of, or as a result of, chronic threat. The former profile of GC production may confer specific fitness benefits (increased coping responses), whereas the latter profile may confer specific health costs (e.g. slower wound healing, decreased memory, decreased energy availability). It is also important to distinguish between low-GC individuals that are hyporesponsive to threat and those with low basal levels and short elevations in GC production at appropriate times. Dissection of individual GC production temporal dynamics as they relate to environmental cues will provide the best estimate of HPA axis regulation efficiency—a key factor in predicting health outcomes. Furthermore, different social structures [137] may help explain different temporal dynamics in stress physiology and predict status-related fitness consequences.

There are several key areas for future work on GC production (and HPA axis regulation) as it relates to health-related outcomes for high- versus low-status individuals. First, it will be important to document individual HPA axis regulation. To this end, frequent measures of GC production within the same individual will facilitate estimation of GC responses to environmental stimuli (e.g. [58,61,129]). Non-invasive GC measures have greatly advanced our understanding of GC production in free-ranging animals and we have suggested a method to assess variability (HPA regulation) within individuals that is feasible with relatively crude estimates of GC production. Moreover, peripheral GC sensitivity assays can provide estimates of HPA axis regulation. Given ethical and logistical constraints for some study populations, one blood sample per study animal could facilitate indirect estimation of GC function. For example, *in vitro* immune system challenges, with cells from whole blood samples, can be performed to assess GC receptor sensitivity (e.g. [100,138–140]). Second, to understand the specific environmental factors that stimulate stress responses in high- versus low-status individuals, further work is required to document individual GC production in response to specific challenges and benefits associated with high- and low-social status (e.g. physical activity, exposure to aggression, access to social support, access to food/shelter, social stability, costs of reproduction) [33–36,38,40,53,141–144]. Third, the relationship of GC production to specific health outcomes for high- versus low-status individuals will provide information on the moderating role of GC production on status-related outcomes. For example, some studies have related GC production (versus social status) to specific health outcomes like mortality and illness/resilience, and to functional immune measures like wound healing and parasite clearance (e.g. [61,145–148]). The same GC receptor sensitivity assays in cultured immune cells described above can also provide insights into molecular correlates of immune system function in high-GC animals [140]. Finally, experimental work (and taking advantage of naturally occurring shifts in social status) will provide insights into the relative causal relationship between social status costs/benefits and GC production, and between GC production and health-related outcomes [139,144,146,149–152].

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