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Parasite infection leads to widespread glucocorticoid hormone increases in vertebrate hosts: A meta-analysis

Katie O'Dwyer[1] | Felipe Dargent[2] | Mark R. Forbes[2] | Janet Koprivnikar[1]

[1]Department of Chemistry and Biology, Ryerson University, Toronto, ON, Canada

[2]Department of Biology, Carleton University, Ottawa, ON, Canada

Correspondence
Janet Koprivnikar
Email: jkoprivn@ryerson.ca

Present address
Katie O'Dwyer, Marine and Freshwater Research Centre, Galway-Mayo Institute of Technology, Galway, Ireland

Felipe Dargent, Department of Biology, University of Ottawa, Ottawa, ON, Canada

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Abstract

1. Parasites and pathogens (hereafter parasites) commonly challenge organisms, but the extent to which their infections are physiologically stressful to hosts remains unclear. Importantly, vertebrate hormones, glucocorticoids (GCs), have been reported to increase, decrease or show no alterations stemming from infections, challenging the generality of parasite-associated GC responses and motivating a search for important moderator variables.
2. We undertook the first meta-analysis of changes in vertebrate GCs following experimental infection with parasites, extracting 146 effect sizes from 42 studies involving 32 host and 32 parasite species to test for general patterns of GC following infection, as well as the influence of moderators.
3. Overall, infection increased GCs relative to preliminary or control levels when the single largest effect sizes from repeated measures studies were examined, suggesting that parasites of vertebrate hosts can be thought of generally as physiological stressors by elevating GCs.
4. When all effect sizes were included along with the moderator of sampling time post-infection (tPI), parasite infection still had a positive effect on host GCs. However, the strength of that effect did not relate consistently to tPI, illustrating temporal differences in GC changes during the course of infection among parasite taxa (e.g. arthropod vs. bacterial infections). Other moderator variables examined did not influence GC responses.
5. Studies broadening the range of host and parasite taxa, and sampling during critical time windows, would aid in our understanding of variation in the host stress response and its consequences for fitness of both vertebrate hosts and their parasites.

KEYWORDS
glucocorticoid, hormone, infection, parasite, pathogen, stress

1 | INTRODUCTION

Parasites and pathogens are ubiquitous natural enemies that have detrimental effects on individual hosts (Brown, Brown, & Rannala, 1995) and host populations (Anderson & May, 1978, 1979; Poulin, 1999). Such effects are likely mediated by increases in host mortality, reductions in condition or fecundity, or shifts in reproductive effort and other life-history traits (e.g. Agnew, Koella, & Michalakis, 2000; Forbes, 1993; Sánchez et al., 2018). Parasites can exert these effects by being energetically costly to their hosts, either directly or

via immune activation (Barber, Wright, Arnott, & Wootton, 2008; Brace et al., 2017). For instance, vaccinated female flycatchers had elevated immune responses and reduced reproductive output compared with unvaccinated conspecifics (Ilmonen, Taarna, & Hasselquist, 2000), indicating the cost of responding to parasite infection.

However, the focus on energetic costs of infection does not necessarily take into account the price of physiological effects such as increased stress, which may in turn have important fitness consequences for hosts. One classical physiological response of vertebrates to abiotic or biotic stressors is the activation of the hypothalamic–pituitary–adrenal (HPA) axis that results in the secretion of glucocorticoid (GC) hormones such as corticosterone and cortisol; these are generally referred to as 'stress hormones' although they perform critical day-to-day functions, and other hormones can be altered by stressors as well (see reviews by MacDougall-Shackleton, Bonier, Romero, & Moore, 2019; Sapolsky, Romero, & Munck, 2000; Wingfield et al., 1998). Despite long recognition of the key involvement of GCs in the vertebrate stress response, their complex roles and functions are still to be fully understood (Sapolsky et al., 2000). For instance, short-term increases in GCs are now considered adaptive for regaining homeostasis in response to stressors (Martin, 2009; Sapolsky et al., 2000; Wingfield et al., 1998). Conversely, long-term, sustained increases in GCs are regarded as problematic by leading to suppression of the immune response and other critical activities such as reproduction (Romero, 2004; Sapolsky et al., 2000). In the context of infection by parasites and pathogens (hereafter collectively termed parasites), GCs likely play a critical role in mediating metabolic responses by providing critical energy in response to infection and in preventing an overshoot of the inflammatory response to infection which could damage the host's own cells (Sapolsky et al., 2000).

Alongside direct effects on host condition and fitness, alterations of GCs could represent a critical route by which parasites have trait-mediated indirect effects, similar to those of predators (Buck & Ripple, 2017; Raffel, Martin, & Rohr, 2008). Such effects of predators are thought to have a greater influence on prey than direct consumption (Peacor, Peckarsky, Trussell, & Vonesh, 2013) and can be mediated by predator-induced alterations of prey GCs (reviewed by Hawlena & Schmitz, 2010). Similar investigations with parasites are critical for unifying natural enemy ecology theories by looking for commonalities and differences in response to different types of enemies (Raffel et al., 2008). Studies of GC responses to infection additionally help us understand the degree to which parasites represent physiological stressors to hosts, which are subjected to a variety of abiotic and other biotic stressors also affecting GCs (Busch & Hayward, 2009; Dantzer, Fletcher, Boonstra, & Sheriff, 2014). Critically, multiple stressors may magnify the effects of parasites and infectious diseases on hosts (Hing, Narayan, Thompson, & Godfrey, 2016), or vice versa, especially if the responses to these stressors share mechanistic pathways.

There are certain biological phenomena that are often considered as maxims and widely accepted, even in the absence of broad empirical tests to confirm their validity, including adages involving parasitism. For instance, the prevailing view of social hierarchies in vertebrates has been that individual status is inversely linked to parasite burdens, with this relationship likely mediated by stress-associated hormones; however, a recent meta-analysis spanning multiple species found the exact opposite: dominant animals generally faced higher parasite burdens than subordinates such that this might be an under-appreciated cost of high social rank (Habig, Doellman, Woods, Olansen, & Archie, 2018). Similar nuance was uncovered in a meta-analysis examining the influence of sex hormones on immune function as a broad test of the immunocompetence handicap hypothesis; testosterone was found to have some effect across studies; the effect of oestrogen, however, depended on the immune measure considered (Foo, Nakagawa, Rhodes, & Simmons, 2017). Meta-analyses such as these are needed to assess the consistency and magnitude of particular outcomes across primary studies, as well as causes of variation among study outcomes, such as moderator variables that may influence effect sizes (Gurevitch, Koricheva, Nakagawa, & Stewart, 2018). As an example, a recent study found that the relationship between host body condition and parasite infection in wildlife was strongly influenced by the condition measure used (Sánchez et al., 2018).

In a similar vein, while it has been assumed that parasite infections typically cause a sustained increase in vertebrate GCs (e.g. Apanius, 1998; Klein, 2004; Maier & Watkins, 1999), there has been no attempt thus far to quantitatively investigate whether this is broadly the case across primary studies involving experimental challenges spanning different parasite and host taxa. This is especially important given that there are reports of both GC increases and decreases in response to infection, even for the same host or parasite groups. For example, cortisol was elevated in chum salmon experimentally infected with salmon lice relative to controls, showed no difference with controls in infected pink salmon, and was actually reduced in infected Atlantic salmon (Sutherland et al., 2014). Larvae of various amphibian species also show variation in their GC alterations stemming from infection by various parasites or pathogens. While infection with ranavirus or the chytrid fungus *Batrachochytrium dendrobatidis* seems to elevate GCs in tadpoles (Gabor, Fisher, & Bosch, 2015; Warne, Crespi, & Brunner, 2011), infection with trematode helminths has no effect or even results in decreased GCs (Koprivnikar, Hoye, Urichuk, & Johnson, 2019; Marino, Holland, & Middlemis Maher, 2014).

To address such inconsistencies, it is essential to establish whether these discrepancies in GC responses stem from methodological or biological phenomena—questions suitable for meta-analysis. Regarding the impact of parasite infection on vertebrate-host GCs, quantitative methods are required to assess whether parasite-induced changes in these hormones show general responses in their direction and magnitude across host–parasite associations. It is especially important to establish the broad nature of GC responses in the context of infectious disease dynamics, such as whether they may be expected in host–parasite associations not yet studied, because chronic elevation of GCs could depress immunity and make

infected hosts more prone to secondary infections (Lutermann, Bodenstein, & Bennett, 2012).

Here, we conducted a meta-analysis of GC levels in response to experimental infection, spanning 42 studies, 32 host species and 32 parasite species, to investigate whether infections have a consistent overall effect on this group of vertebrate hormones. We also examined the importance of time post-infection (tPI) and the type of parasites involved as the main moderator variables given that those with different courses of infection may affect GCs dissimilarly.

2 | MATERIALS AND METHODS

2.1 | Data collection

In 2016, we conducted a keyword search using *ISI Web of Knowledge* for results published beginning in 2006, with an additional 2 years searched in 2018, employing the following search term: "parasit* AND (glucocorticosteroid OR glucocorticoid OR cortisol OR cortisone OR corticosterone)". These results comprised relatively large parasites (macroparasites) that followed the 'traditional' definition of a parasite (e.g. helminths and sea lice), as well as those of smaller size (microparasites), including some that may be described as pathogens (bacteria and viruses). We thus broadly defined 'parasites' based on a general consumer-resource framework (Lafferty et al., 2015), that is a natural enemy that feeds intimately on one host (Lafferty & Kuris, 2002), which is also consistent with other meta-analyses involving parasites (e.g. Sánchez et al., 2018). Subsequently, use of the term 'pathogen' hereon will specifically refer to bacteria and viruses as a sub-category of parasitism based on their host effects and transmission requirements whereas 'parasite' encompasses all natural enemies under this consumer model, including those which may be distinguished as either macro- or microparasites (see definitions in Lafferty & Kuris, 2002).

Any study involving parasites and GCs was initially examined (total of 1,751), but we subdivided studies into those investigating the effects of parasite infection on GC levels versus those examining parasitism following the manipulation of GCs—the latter were excluded. Those remaining studies were of two broad categories: investigations that examined the mean difference in GC levels between infected and uninfected individuals, and studies testing the relationship between parasite load and GCs. After assessing publication titles, 614 papers evaluating effects of parasite infection on GCs were retained. We then focused on experimental infections to investigate temporal patterns of GC levels, given the aforementioned and important distinction between possibly adaptive short-term increases versus harmful long-term elevations. Time since infection could not be evaluated for natural infections or for studies where experimental removals of parasites were done; these subsets of studies were dropped from consideration. A thorough assessment of the 614 articles, including contact with authors for whom the data could not be extracted directly from their papers, produced 186 potentially suitable studies which were carefully evaluated for eligibility; for example, by confirming that a measure of the direct relationship between parasite infection and GCs was included so that an effect size could be calculated. Following this full assessment, a total of 42 suitable studies, based on experimental infections, were identified and included in our dataset (for PRISMA flow diagram see Figure S1).

For a study to be included, it had to provide a test statistic, or the mean and variation, for the relationship between experimental infection and GC levels. In most GC response studies, samples were taken repeatedly over several time points post-infection. In some of those cases, the same control was used for 'time zero' and compared to later time points. To account for this, a conservative approach was taken by dividing the sample size for the control group by the number of times that control group was used in calculations based on differences between means (Higgins & Green, 2011). The majority of effect sizes collected were differences between means of infected and uninfected groups (controls). We note that GC levels in the latter, or those measured in individuals before parasite exposure in studies without true controls, likely include a mixture of true baseline levels and acute responses to stressors such as handling and experimental housing, and thus refer to these as control or preliminary GC levels as appropriate. Where the standard error (*SE*), confidence intervals (CI) or interquartile ranges (IQR) were reported, these were converted to the standard deviation (*SD*) using established methods (see Appendix S1). Where data were presented in figures, they were extracted using GraphClick (Arizona Software, 2017). The log proportional change between means was calculated as the log response ratio and used in our analyses following methods in Lajeunesse (2011). Multiple effect sizes from single studies were treated as separate data points in analyses, provided the different effect sizes were allied to different values/types of moderator variables (see below).

The main moderator variables examined were time post-infection (tPI) and the type of parasite involved. Random-effects meta-analysis models assume independence of data points (Nakagawa & Santos, 2012); hence, we included phylogenetic trees in our analyses (see Appendix S1 for details) to control for non-independence of data points due to the shared evolutionary histories of hosts and parasites (Harvey & Pagel, 1998). The individual parasites included in the studies which we utilized span many orders of magnitude in size and their numbers also vary considerably over their course of infection. For example, infection intensities for macroparasites, such as helminths, will be below or equal to the doses used to challenge hosts; however, infection intensities could easily be elevated beyond infection doses for microparasites that can replicate within hosts (e.g. bacteria), but this was not reported consistently. With this in mind, infection dose and parasite intensity were not considered comparable across studies and were excluded from analyses.

2.2 | Data analyses

All data analyses were performed using *R 3.3.1* (R Core Team, 2016). We used *MCMCglmm* (Hadfield, 2010) and included the

following random effects to account for correlated structure: phylogenetic relationships, species identity and study identity. We did not include an observation-level random effect as most studies dealt with single host-parasite combinations, and there were few recurrences of combinations across studies (see Dryad data). We used a topological phylogenetic tree for the 32 host species to account for phylogenetic relationships (Figure S2), converted to an ultrametric tree (see Hadfield & Nakagawa, 2010). *MCMCglmm* was used to fit generalized linear mixed models through a Markov chain Monte Carlo (MCMC) algorithm using a weakly informative prior. Heterogeneity in the data was measured using I^2 and was compared for the main model with either host phylogeny or parasite phylogeny included in the model (Figure S3). The heterogeneity accounted for by either of the two phylogenies did not vary greatly; hence, the phylogenetic signal for both hosts and parasites were extremely similar, and only the host phylogeny was used in analyses (Table S1). We assessed publication bias by inspecting funnel plots of raw effect sizes visually, by performing Egger's regression and by using the trim and fill method in the *METAFOR* package (Viechtbauer, 2010).

Our first analysis considered the single largest effect size (positive or negative) within studies containing repeated measures for differences in GC levels of infected animals versus a preliminary level or control group of uninfected hosts, irrespective of tPI. This analysis was based on 77 effect sizes. With respect to stressor-induced changes in GC levels, the magnitude of elevations or depressions is likely important if they occur within critical time periods (Martin, 2009). For instance, elevated GCs have different effects on neurological development depending on the distinct time window in which elevations occur (Welberg & Seckl, 2001). Short-term elevations or depressions also should be considered if there is potential for critical thresholds beyond which positive or negative consequences occur, for example as reported for hypertension associated with elevated GC levels (Huscher et al., 2009; del Rincón, Battafarano, Restrepo, Erikson, & Escalante, 2014). Importantly, the means of data taken at several times post-infection can 'homogenize' temporal variation and obscure increases or decreases at a specific tPI that are biologically relevant (Figure 1). Therefore, in this first analysis we sought to examine the single largest change in GC levels for each of the host–parasite combinations included.

In a second set of analyses, we used all 146 effect sizes, including those from studies with >1 tPI (i.e. repeated measures) for each host–parasite combination. We examined the influence of parasite infection on the mean effect size for studies with multiple tPIs (relating to the duration of sampling post-infection). When tPI was considered, the non-independence of data taken at several time points is treated explicitly. We examined whether the inclusion of pathogens influenced our main findings by performing a complementary analysis that excluded effect sizes for infections by bacteria and viruses. We thus focused on effect sizes of macro- and microparasites (n = 122), which are considered as 'traditional' parasites, based on their distributions within host populations, relative size and relationships between intensity and pathology (cf. Crofton, 1971).

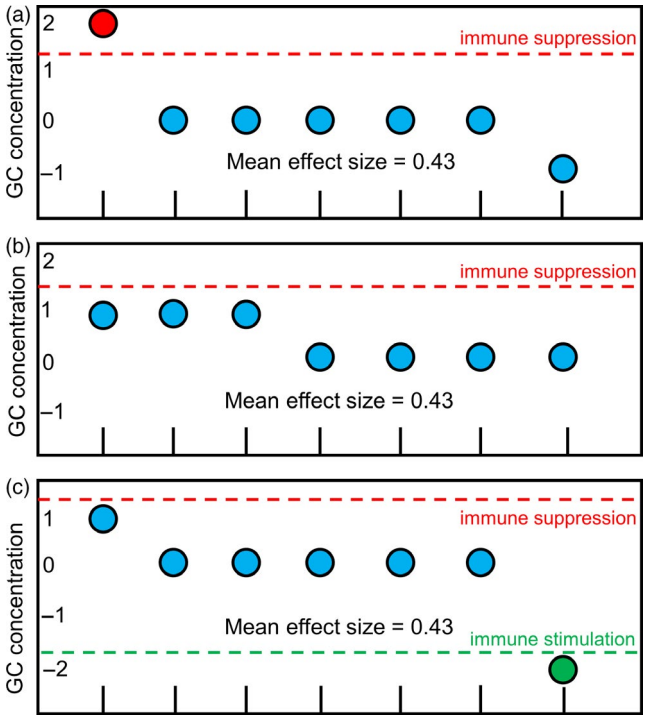

FIGURE 1 Biological significance of considering mean versus largest effect size across multiple time points for influence of parasitic infection on host glucocorticoid (GC) levels in studies that use repeated measures. Note that the mean effect size across 7 time points post-infection (P.I.) is the same in all three panels. In (a), GCs are elevated at one time point (0 indicates no change from preliminary/control) and depressed at another, but the largest effect size crosses a critical threshold for immune suppression. The direction and magnitude of the largest effect, which has biological significance, are consequently more informative than the mean effect size. In (b), GCs are elevated at three time points and depressed at none. While the largest effect size is positive in direction, it does not cross the critical threshold for immune suppression, thus essentially provides the same biological information as the mean effect size. In (c), GCs are elevated at only one time point and also depressed at only one, but the largest effect size crosses a critical threshold where immune stimulation occurs. As in the top panel, the mean effect size is therefore relatively uninformative in terms of potential biological significance

2.3 | Additional moderators

Our final set of analyses considered parasite lifestyle and type as moderators. We examined differences in GC changes with tPI for ectoparasite and endoparasites (lifestyle), and for the most common parasite types in our dataset—arthropods, bacteria, nematodes and protozoans (type). Lastly, we determined whether any relationship between the largest GC changes (largest effect sizes) and tPI differed for these parasite types. Additional moderators examined, and outlined in Appendix S1, included host type, host life stage, type of tissue sampled and year of publication.

3 | RESULTS

The final dataset consisted of 42 publications, 146 effect sizes, 32 host species and 32 parasite species (data available on Dryad). Of these effect sizes, 50% represented experimental infections by arthropods, 31% by micro- and macroparasites (e.g. protozoans and helminths), 12% by bacteria and <7% involved other infectious agents (viruses or parasitic molluscs) or used a standard substitute such as a pathogen-derived protein injection as a proxy for live infectious agents. Mammal and fish hosts each comprised 47% of the effect sizes, with the remaining 6% represented by amphibians and birds. The most common host–parasite combinations were fish with ectoparasite (27% of effect sizes), mammal and ectoparasite (25%), mammal with micro- or macro-parasite (21%), and fish with bacteria (12%). The tPI at which GC levels were measured in our dataset ranged from as little as 0.5 hr to 196 days, with a mean (±*SD*) of 106.1 ± 225.4 hr for studies with bacteria and 356.9 ± 402.9 hr for those with parasitic arthropods. No publication bias was detected in our dataset (see Appendix S1 for details).

When examining the single largest effect size for each unique host–parasite combination within individual studies with repeated measures, we found effect sizes to be significantly positive (95% credible interval [CI] does not cross zero), when considering GC levels of infected animals relative to controls or preliminary levels (posterior mean = 0.730, CI = 0.334–1.108; Table S2). Thus, infected animals typically had a doubling of GC levels (exp (0.730)) compared with controls or preliminary measures for at least one sampling tPI (Figure 2). The inclusion of tPI as a predictor of GC levels examining only the largest effect sizes did not change this overall result (posterior mean = 0.727, CI = 0.320–1.119; Table S3), with no significant relationship between GC levels and tPI detected (posterior mean = 0.015, CI = −0.124 to 0.165, Figure 2a).

In our second set of analyses, which included all effect sizes across multiple time points post-infection, we found that parasite infection elevated the level of GCs 1.42 times (posterior mean = 0.353, CI = 0.070–0.631; exp (0.353) = 1.42). We detected no significant change in GCs with tPI (posterior mean = −0.041, CI = −0.140 to 0.051). This is possibly due to a lack of consistency in the timing of elevated GC levels (Figure 3, Table S4), as was suspected also for the aforementioned analysis involving the largest effect sizes. The results of analyses that only considered 'traditional' micro- and macroparasites (i.e. excluded bacteria and viruses) were consistent with results based on the full dataset in that infection was associated with an overall increase in GCs (posterior mean 0.348, CI = 0.051–0.642; Table S5), but there was no significant and consistent effect of tPI on GCs (posterior mean = 0.006, CI = −0.119 to 0.129).

Whether a host was infected by an endoparasite or ectoparasite had no significant influence on the change in GC levels relative to the controls or preliminary measures (posterior mean = −0.099, CI = −0.504 to 0.265; Table S6). However, while not significant, GC levels tended to decrease over time following infections by endoparasites (posterior mean = −0.107, CI = −0.228 to 0.016), while for ectoparasites a slight increase in GC levels with tPI was indicated (posterior mean = 0.184, CI = −0.040 to 0.382). Bacteria and parasitic arthropods were among the most well-represented endoparasite and ectoparasite groups, respectively, and they showed opposing temporal patterns in GC response (Figure 4). Host GC levels generally decreased with the duration of bacterial infection (posterior mean = −0.220, CI = −0.431 to −0.027; Table S7); more specifically, an initial increase in GCs changed to a decrease at approximately 12 days post-infection. This differed significantly (posterior mean = 0.359, CI = 0.081–0.629) from the pattern for infection by arthropod parasites, where GC levels showed an overall increase with duration of infection. Unlike bacteria, the effect of an arthropod infection on host GCs changed from initially low levels to increases around 2 days post-infection. No significant patterns in GC levels with tPI were detected for protozoans or nematodes. When considering only the largest effect sizes, the patterns were similar, although non-significant for all groups (Table S8).

Results for the following moderators are provided in Appendix S1: host type (mammal, fish); host life stage (juvenile, adult, both); tissue sampled for GCs (e.g. plasma, feather); and year of publication (all were non-significant, see Tables S9-S12). As there were 17 studies which contributed only one sampling time point during the course of parasite infection, a sensitivity analysis was carried out with these studies removed (leaving 25 studies, 129 effect sizes, 26 host species and 20 parasite species); however, the overall results did not change from those above (Table S13). One study contributed the largest sample sizes to the dataset; thus, a sensitivity analysis was performed with it removed, but this also did not change our results (Tables S14-S15).

4 | DISCUSSION

Experimental infection with parasites was typically associated with an elevation in the level of GCs in vertebrates at some point following infection, relative to control or preliminary values. Similarly, the mean level of GCs for infected individuals was significantly higher than uninfected controls or preliminary measures when all effect sizes were considered. However, it was critical to consider the time at which host samples were taken post-infection (tPI) because GC levels were not consistent in their direction of change through time. That is, GCs either increased or decreased with tPI, depending on parasite type (i.e. for arthropods vs. bacteria, respectively). In this context, parasites generally can be considered as stressors to their vertebrate hosts through inducing a change in stress-associated hormone levels. However, infected individuals do not typically exhibit a sustained, long-term increase in their GC levels, but rather, a short-term elevation at some point during the course of infection.

It is perhaps not surprising that vertebrates are seemingly well adapted to infections by not exhibiting long-term and sustained increases in GCs that could be problematic by reducing immunocompetence and reproduction (Sapolsky et al., 2000). After all, parasites and pathogens represent ubiquitous threats and have typically coevolved with their host species such that many may be relatively

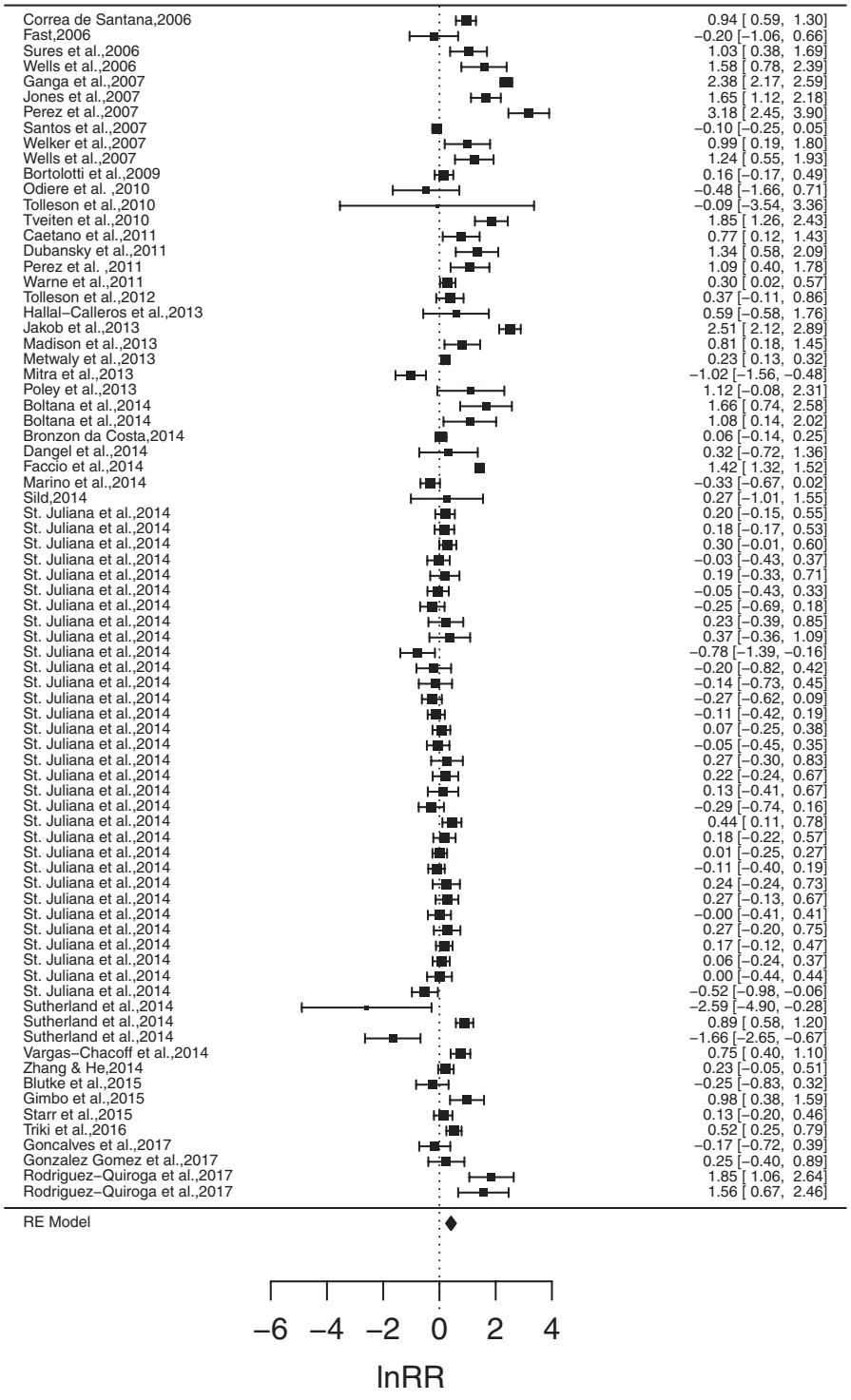

FIGURE 2 Forest plot showing 77 effect sizes included in the analysis of the largest effect (0 = no change, >0 = GC increase, <0 = GC decrease) reported from 42 published studies examining a change in glucocorticoid (GC) levels for parasitized vertebrates relative to preliminary or control values. The log response ratio (lnRR) and corresponding variance (var lnRR) are represented as points and error bars, respectively

tolerant of certain infections (i.e. have the ability to limit parasite damage vs. reducing parasite burden), and this could be reflected in only temporarily increased GC levels. For instance, elevated GCs contribute to pathways promoting host tolerance to endotoxins resulting from bacterial infection (Szabo, Thiemermann, Wu, Perretti, & Vane, 1994). This said, the general short-term stress responses involving GCs could have important implications. For instance, infection-induced GC elevations during sensitive time windows may act synergistically with other stressors (Dantzer et al., 2014), thereby affecting host resistance or tolerance to secondary infections (Hing et al., 2016). In addition, the feedback loop nature of the HPA axis can result in suppressed GC levels by animals experiencing chronic stress (Herman et al., 2011); thus, low GC levels do not necessarily indicate high tolerance to a stressor, but rather, possible pathology. Whereas the majority of parasites do not kill their hosts outright (i.e. do not have an immediate consumptive effect), their potential for non-consumptive effects via altered GCs at critical time points may be widespread and substantial, and warrants further investigation.

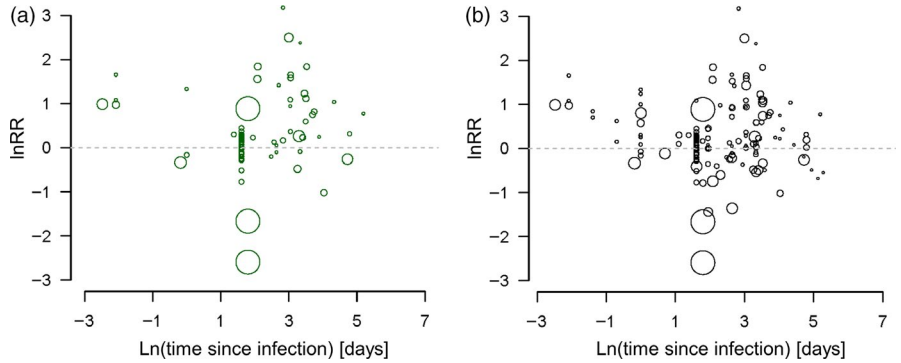

FIGURE 3 Relationship between the log response ratio (lnRR) in glucocorticoids (GCs) in response to the log-transformed variable time since infection (days) for two separate analyses: (a) the *largest* GC measurement found within each of 42 studies, constituting 77 effect sizes; and (b) for *all* GC measurements found within each of 42 studies and including all 146 effect sizes. Sample size is shown by the size of the data point, with the largest data points having a total sample size of 80

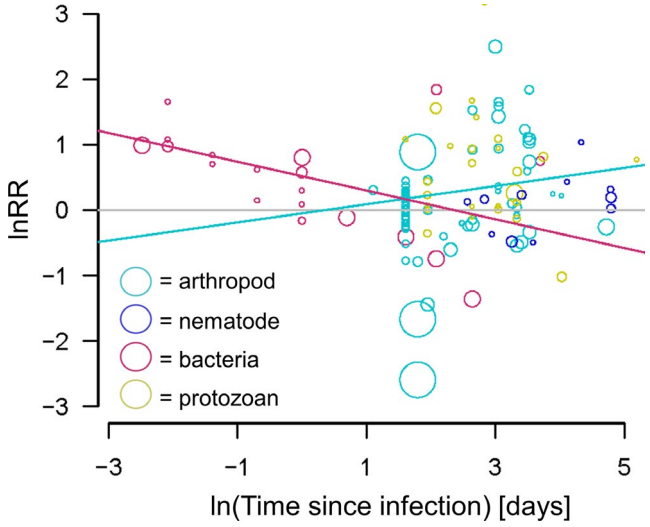

FIGURE 4 Relationship between the log response ratio (lnRR) in response to the log-transformed variable time since infection (days) for glucocorticoid (GC) measurements in vertebrates following infection by bacteria (no. effect sizes (*N*) = 19), nematodes (*N* = 11), protozoans (*N* = 26) and arthropods (*N* = 73). Sample size is shown by the size of the data point, with the largest data points having a total sample size of 80. Significant relationships are shown by the presence of the regression line through the data points (bacteria: posterior mean = −0.220, credible interval = −0.431 to −0.027; comparison with arthropods: posterior mean = 0.359, CI = 0.081–0.629)

As well as a lack of sustained GC elevations, the timing of short-term GC elevations following infection was not consistent. Such inconsistency may also be related to variation in host tolerance, but also parasite type; the latter generally displayed different temporal dynamics, with the smallest effect sizes found in the later stages of bacterial infections, but in earlier stages of infection by arthropods. This contrasting pattern likely explains the lack of a significant overall effect of infection on GCs when tPI was included in models, given that bacterial and arthropod infections represented the majority of the effect sizes in our dataset (~63%), and the non-significant influences of helminth or protozoan infections.

The temporal pattern of initially elevated GCs in response to bacterial infections corresponds to previous reports (see review by Webster & Sternberg, 2004), but ours is the first report of a general pattern of elevated GC levels following vertebrate infections by parasitic arthropods. Such time-dependent changes in GC levels based on parasite type correspond well to known differences related to the course of infection, particularly that bacterial infections establish much more quickly within hosts relative to other parasites. For example, severe symptoms from infection by pathogenic strains of *Escherichia coli* in humans can occur after an incubation period as short as 14–50 hr (Nataro & Kaper, 1998), whereas extensive pathology in fish exposed to parasitic copepods may not be evident for weeks (Fast, 2014).

Elevated GCs following bacterial infection agree with the paradigm of short-term GC increases being adaptive, owing to their anti-inflammatory actions (Sapolsky et al., 2000). The innate component of the immune system is a first-line, non-specific reaction to bacterial infection because local inflammation serves to limit the spread of the infection (Maier & Watkins, 1999). As phagocytic cells engulf the invaders, they release pro-inflammatory cytokines (e.g. interleukin-1 (IL-1) α and β, interleukin-6 (IL-6) and tumour necrosis factor α (TNF-α)) as part of the T_H1 pathway that stimulates T-lymphocytes involved in the acquired cellular immune response (Maier & Watkins, 1999; Romagnani, 1992). However, a prolonged inflammatory response can be harmful; thus, the anti-inflammatory actions of GCs play a key role in preventing 'inflammation overshoot' and maintaining homeostasis (Sapolsky et al., 2000). Diseased animals can be more susceptible to predation (Hudson, Dobson, & Newborn, 1992), and GC-mediated dampening of the stress response is likely important in reducing visible signs of infection or illness that serve as cues of vulnerability (Sapolsky et al., 2000).

Infection by ectoparasitic arthropods also seems to primarily involve a T_H1-like inflammatory response in many host–parasite systems (Buchmann, 1999; Fast, 2014). The delayed elevation in GCs for hosts with arthropod infections, relative to bacteria, may therefore occur because of inherent differences between these two parasite types and how their infections unfold. Given that pathogens such

as bacteria undergo rapid within-host replication, they ultimately achieve higher infection intensities compared with macroparasites that do not replicate in or on their hosts (Lafferty & Kuris, 2002). Whereas the within-host replication by bacteria thus necessitates a fast immune response (Maier & Watkins, 1999), infection by parasitic arthropods is often associated with distinct immune response phases that correspond to parasite development and life history (Fast, 2014). These contrasting patterns of parasitism may help to explain the discrepancy in GC temporal dynamics between bacteria and arthropods. Macroparasites also typically represent longer-lived infections relative to bacteria. For instance, sea lice, which represented a substantial proportion of arthropod infections examined here, have life spans of 1 year or more and undergo changes in their morphology and feeding habits while attached to their fish hosts (Fast, 2014). Importantly, there is a weak host inflammatory response to juvenile sea lice followed by elevations later in the course of infection in susceptible hosts (>21 days) as these parasitic copepods moult into the pre-adult and adult stages and external lesions become more pronounced (Fast, 2014). The general increase in GCs through time for hosts infected with parasitic arthropods may therefore correspond to the timing and nature of their immune responses.

Our analysis based on 'traditional' parasites (i.e. excluding bacteria and viruses) also found no sustained elevation of GCs for infected vertebrates when considering tPI, but there might be differences among parasites even within this functionally narrower group with respect to the temporal dynamics of relevant immunological responses. For instance, GC elevations stemming from infections by macroparasites such as helminths are relatively delayed or minor (e.g. Morales-Montor, Newhouse, Mohamed, Baghdadi, & Damian, 2001) compared with those by bacteria (Maier & Watkins, 1999). Notably, the vertebrate immune response to many parasitic helminths is largely governed by the T_H2 pathway of the acquired immune system (Anthony, Rutitzky, Urban, Stadecker, & Gause, 2007), compared with the T_H1 pathway that promotes inflammation in response to ectoparasites and bacteria. While cytokines are still involved in the T_H2 pathway, different cytokine types are involved, and the outcome of their signalling primarily promotes the proliferation of various leucocytes (e.g. B-lymphocytes and eosinophils) that are effective against many helminths rather than T_H1-mediated increases in cytotoxic macrophages (Anthony et al., 2007). Consequently, the inflammatory response may play a role in combating some helminth infections (Anthony et al., 2007), but is likely not as intense relative to those against bacteria and arthropods.

The co-evolutionary history between hosts and their parasites is likely to influence the extent of infection-induced GC alterations, as it does for virulence, which is often more pronounced for relatively recent host-parasite associations (Alizon & Michalakis, 2015). Even among closely related host species, there can be considerable variation in resistance or tolerance to the same parasite species. For instance, juvenile pink salmon display higher innate resistance to sea lice than chum salmon, with parasite-induced cortisol increases only observed in the latter (Jones, Fast, Johnson, & Groman, 2007). Parasites are generally thought to have an evolutionary 'upper hand' compared with hosts because they are under stronger selection owing to their obligate relationship, and may also evolve faster due to their usually larger population sizes and shorter generation times relative to their hosts (Gandon & Michalakis, 2002). Future studies could thus examine whether there is asymmetry between parasite and host rates of adaptation, and how this co-evolutionary history might relate to their GC response to infection. For instance, comparing vertebrate GCs after infection by arthropod parasites with different generation times relative to their hosts may indicate whether greater adaptation asymmetry is associated with a stronger physiological response. The contrast of GC levels from novel host–parasite combinations with those from relatively well-established relationships will also aid in elucidating the influence of shared co-evolutionary history.

Our meta-analysis provides a glimpse into the generality and nuances of vertebrate stress responses to parasite infection via changes in GC levels, with the key findings that parasitism can be viewed as a stressor when considering their peak impact (the largest effect size during infections), and that GC levels either increased or decreased over tPI depending on parasite type in a manner that corresponds to the expected host immunological response. As short-term GC elevations more typically characterized a response to infection rather than sustained elevations, these are potentially adaptive to the host if they mediate the inflammatory immune response. However, this also has implications for studies of co-infections where responses to one parasite that are thought to be optimal might not actually be so for the host or the other parasite, or even for responses to other natural enemies such as predators.

Investigations to date tended to focus on particular host–parasite associations, and thus, there is a need for experimental studies of GC alterations from a wider range of host and parasite taxa. Studies that add taxonomic breadth will be of particular benefit to further test the general patterns uncovered in our study and to aid in predicting possible exceptions, as with a previous meta-analysis of sex biases in host parasitism (Moore & Wilson, 2002). Researchers should also consider sampling design related to tPI because similar temporal windows for the sampling of host GCs are needed to compare patterns within functionally similar groups of parasites, which are expected to have similar courses of infection. For example, the mean GC sampling tPI was 106 hr for bacterial infections and 347 hr for parasitic arthropods. Although there are inherent biological differences that preclude a standardized tPI sampling protocol for all parasite types, efforts to incorporate a sufficient number of early and late time points will allow for future comparisons of stress-associated hormone alterations induced by different parasites if temporal windows overlap. The importance of tPI for GC levels here also has relevance for results obtained from observational studies related to parasitism because the time of initial infection is usually unknown, and sampling is typically opportunistic, occurring at different times of the day and year—factors also known to affect hormone levels. This underscores the need for complementary studies utilizing controlled infections if possible to establish key sampling time points.

Our findings provide a foundation for future work on GC levels during parasite infections of vertebrate hosts. For instance, studies focusing on other moderators, such as the timing of host breeding, host–parasite co-evolutionary history and co-infections will shed further light on this topic. Given that infectious diseases are a growing concern for humans, domesticated animals and wildlife (Daszak, Cunningham, & Hyatt, 2000), it will be important to determine how commonly, and at what time points, parasitic infections represent stressors, and also to continue researching key physiological mechanisms and pathways.

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AUTHORS' CONTRIBUTIONS

All authors conceived of the study and contributed to the manuscript. K.O. and F.D. collected data, and K.O. performed analyses.

DATA AVAILABILITY STATEMENT

Data are available through the Dryad Digital Repository: https://doi.org/10.5061/dryad.fn2z34tph (O'Dwyer, Dargent, Forbes, & Koprivnikar, 2019).

ORCID

Janet Koprivnikar https://orcid.org/0000-0001-8410-1041

REFERENCES

Agnew, P., Koella, J. C., & Michalakis, Y. (2000). Host life history responses to parasitism. *Microbes and Infection*, *2*, 891–896. https://doi.org/10.1016/S1286-4579(00)00389-0

Alizon, S., & Michalakis, Y. (2015). Adaptive virulence evolution: The good old fitness-based approach. *Trends in Ecology and Evolution*, *30*, 248–254. https://doi.org/10.1016/j.tree.2015.02.009

Anderson, R. M., & May, R. M. (1978). Regulation and stability of host-parasite population interactions: I. Regulatory processes. *Journal of Animal Ecology*, *47*, 219–247. https://doi.org/10.2307/3933

Anderson, R. M., & May, R. M. (1979). Population biology of infectious diseases: Part I. *Nature*, *280*, 361–367. https://doi.org/10.1038/280361a0

Anthony, R. M., Rutitzky, L. I., Urban, J. F. Jr, Stadecker, M. J., & Gause, W. C. (2007). Protective immune mechanisms in helminth infection. *Nature Reviews Immunology*, *7*, 975–987. https://doi.org/10.1038/nri2199

Apanius, V. (1998). Stress and immune defense. *Advances in the Study of Behavior*, *27*, 133–153.

Arizona Software. (2017). Retrieved from www.arizona-software.ch/graphclick/

Barber, I., Wright, H. A., Arnott, S. A., & Wootton, R. J. (2008). Growth and energetics in the stickleback–*Schistocephalus* host–parasite system: A review of experimental infection studies. *Behaviour*, *145*, 647–668. https://doi.org/10.1163/156853908792451403

Brace, A. J., Lajeunesse, M. J., Ardia, D. R., Hawley, D. M., Adelman, J. S., Buchanan, K. L., … Martin, L. B. (2017). Costs of immune responses are related to host body size and lifespan. *Journal of Experimental Zoology Part A: Ecological and Integrative Physiology*, *327*, 254–261.

Brown, C. R., Brown, M. B., & Rannala, B. (1995). Ectoparasites reduce long-term survival of their avian host. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *262*, 313–319.

Buchmann, K. (1999). Immune mechanisms in fish skin against monogeneans-a model. *Folia Parasitologica*, *46*, 1–8.

Buck, J. C., & Ripple, W. J. (2017). Infectious agents trigger trophic cascades. *Trends in Ecology and Evolution*, *32*, 681–694. https://doi.org/10.1016/j.tree.2017.06.009

Busch, D. S., & Hayward, L. S. (2009). Stress in a conservation context: A discussion of glucocorticoid actions and how levels change with conservation-relevant variables. *Biological Conservation*, *142*, 2844–2853. https://doi.org/10.1016/j.biocon.2009.08.013

Crofton, H. D. (1971). A quantitative approach to parasitism. *Parasitology*, *62*, 179–193. https://doi.org/10.1017/S0031182000071420

Dantzer, B., Fletcher, Q. E., Boonstra, R., & Sheriff, M. J. (2014). Measures of physiological stress: A transparent or opaque window into the status, management and conservation of species? *Conservation. Physiology*, *2*, cou023. https://doi.org/10.1093/conphys/cou023

Daszak, P., Cunningham, A. A., & Hyatt, A. D. (2000). Emerging infectious diseases of wildlife - threats to biodiversity and human health. *Science*, *287*, 443–449. https://doi.org/10.1126/science.287.5452.443

del Rincón, I., Battafarano, D. F., Restrepo, J. F., Erikson, J. M., & Escalante, A. (2014). Glucocorticoid dose thresholds associated with all-cause and cardiovascular mortality in rheumatoid arthritis. *Arthritis and Rheumatology*, *66*, 264–272. https://doi.org/10.1002/art.38210

Fast, M. D. (2014). Fish immune responses to parasitic copepod (namely sea lice) infection. *Developmental and Comparative Immunology*, *43*, 300–312. https://doi.org/10.1016/j.dci.2013.08.019

Foo, Y. Z., Nakagawa, S., Rhodes, G., & Simmons, L. W. (2017). The effects of sex hormones on immune function: A meta-analysis. *Biological Reviews*, *92*, 551–571. https://doi.org/10.1111/brv.12243

Forbes, M. R. (1993). Parasitism and host reproductive effort. *Oikos*, *67*, 444–450. https://doi.org/10.2307/3545356

Gabor, C. R., Fisher, M. C., & Bosch, J. (2015). Elevated corticosterone levels and changes in amphibian behavior are associated with *Batrachochytrium dendrobatidis* (*Bd*) infection and *Bd* lineage. *PLoS ONE*, *10*, e0122685. https://doi.org/10.1371/journal.pone.0122685

Gandon, S., & Michalakis, Y. (2002). Local adaptation, evolutionary potential and host–parasite coevolution: Interactions between migration, mutation, population size and generation time. *Journal of Evolutionary Biology*, *15*, 451–462. https://doi.org/10.1046/j.1420-9101.2002.00402.x

Gurevitch, J., Koricheva, J., Nakagawa, S., & Stewart, G. (2018). Meta-analysis and the science of research synthesis. *Nature*, *555*, 175–182. https://doi.org/10.1038/nature25753

Habig, B., Doellman, M. M., Woods, K., Olansen, J., & Archie, E. A. (2018). Social status and parasitism in male and female vertebrates: A meta-analysis. *Scientific Reports*, *8*, 3629. https://doi.org/10.1038/s41598-018-21994-7

Hadfield, J. D. (2010). MCMC methods for multi-response generalized linear mixed models: The MCMCglmm R package. *Journal of Statistical Software*, *33*, 1–22.

Hadfield, J. D., & Nakagawa, S. (2010). General quantitative genetic methods for comparative biology: Phylogenies, taxonomies and multi-trait models for continuous and categorical

characters. *Journal of Evolutionary Biology*, *23*, 494–508. https://doi.org/10.1111/j.1420-9101.2009.01915.x

Harvey, P. H., & Pagel, M. D. (1998). *The comparative method in evolutionary biology*. New York, NY: Oxford University Press.

Hawlena, D., & Schmitz, O. J. (2010). Physiological stress as a fundamental mechanism linking predation to ecosystem functioning. *The American Naturalist*, *176*, 537–556. https://doi.org/10.1086/656495

Herman, J. P., McKlveen, J. M., Ghosal, S., Kopp, B., Wulsin, A., Makinson, R., … Myers, B. (2011). Regulation of the hypothalamic-pituitary-adrenocortical stress response. *Comprehensive Physiology*, *6*, 603–621.

Higgins, J. P., & Green, S. (2011). *Cochrane handbook for systematic reviews of interventions. Version 5.1.0. The Cochrane Library*. Retrieved from http://www.cochrane-handbook.org

Hing, S., Narayan, E. J., Thompson, R. A., & Godfrey, S. S. (2016). The relationship between physiological stress and wildlife disease: Consequences for health and conservation. *Wildlife Research*, *43*, 51–60. https://doi.org/10.1071/WR15183

Hudson, P. J., Dobson, A. P., & Newborn, D. (1992). Do parasites make prey vulnerable to predation? Red grouse and parasites. *Journal of Animal Ecology*, *61*, 681–692. https://doi.org/10.2307/5623

Huscher, D., Thiele, K., Gromnica-Ihle, E., Hein, G., Demary, W., Dreher, R., … Buttgereit, F. (2009). Dose-related patterns of glucocorticoid-induced side effects. *Annals of the Rheumatic Diseases*, *68*, 1119–1124. https://doi.org/10.1136/ard.2008.092163

Ilmonen, P., Taarna, T., & Hasselquist, D. (2000). Experimentally activated immune defence in female pied flycatchers results in reduced breeding success. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *267*, 665–670. https://doi.org/10.1098/rspb.2000.1053

Jones, S. R., Fast, M. D., Johnson, S. C., & Groman, D. B. (2007). Differential rejection of salmon lice by pink and chum salmon: Disease consequences and expression of proinflammatory genes. *Diseases of Aquatic Organisms*, *75*, 229–238. https://doi.org/10.3354/dao075229

Klein, S. L. (2004). Hormonal and immunological mechanisms mediating sex differences in parasite infection. *Parasite Immunology*, *26*, 247–264. https://doi.org/10.1111/j.0141-9838.2004.00710.x

Koprivnikar, J., Hoye, B. J., Urichuk, T. M., & Johnson, P. T. (2019). Endocrine and immune responses of larval amphibians to trematode exposure. *Parasitology Research*, *118*, 275–288. https://doi.org/10.1007/s00436-018-6154-6

Lafferty, K. D., DeLeo, G., Briggs, C. J., Dobson, A. P., Gross, T., & Kuris, A. M. (2015). A general consumer-resource population model. *Science*, *349*, 854–857. https://doi.org/10.1126/science.aaa6224

Lafferty, K. D., & Kuris, A. M. (2002). Trophic strategies, animal diversity and body size. *Trends in Ecology and Evolution*, *17*, 507–513. https://doi.org/10.1016/S0169-5347(02)02615-0

Lajeunesse, M. J. (2011). On the meta-analysis of response ratios for studies with correlated and multi-group designs. *Ecology*, *92*, 2049–2055. https://doi.org/10.1890/11-0423.1

Lutermann, H., Bodenstein, C., & Bennett, N. C. (2012). Natural parasite infection affects the tolerance but not the response to a simulated secondary parasite infection. *PLoS ONE*, *7*, e52077. https://doi.org/10.1371/journal.pone.0052077

MacDougall-Shackleton, S. A., Bonier, F., Romero, L. M., & Moore, I. T. (2019). Glucocorticoids and "Stress" are Not Synonymous. *Integrative Organismal Biology*, *obz017*, https://doi.org/10.1093/iob/obz017

Maier, S. F., & Watkins, L. R. (1999). Bidirectional communication between the brain and the immune system: Implications for behaviour. *Animal Behaviour*, *57*, 741–751. https://doi.org/10.1006/anbe.1998.1068

Marino, J. A. Jr, Holland, M. P., & Middlemis Maher, J. (2014). Predators and trematode parasites jointly affect larval anuran functional traits and corticosterone levels. *Oikos*, *123*, 451–460. https://doi.org/10.1111/j.1600-0706.2013.00896.x

Martin, L. B. (2009). Stress and immunity in wild vertebrates: Timing is everything. *General and Comparative Endocrinology*, *163*, 70–76. https://doi.org/10.1016/j.ygcen.2009.03.008

Moore, S. L., & Wilson, K. (2002). Parasites as a viability cost of sexual selection in natural populations of mammals. *Science*, *297*, 2015–2018. https://doi.org/10.1126/science.1074196

Morales-Montor, J., Newhouse, E., Mohamed, F., Baghdadi, A., & Damian, R. T. (2001). Altered levels of hypothalamic-pituitary-adrenocortical axis hormones in baboons and mice during the course of infection with *Schistosoma mansoni*. *The Journal of Infectious Diseases*, *183*, 313–320.

Nakagawa, S., & Santos, E. S. (2012). Methodological issues and advances in biological meta-analysis. *Evolutionary Ecology*, *26*, 1253–1274. https://doi.org/10.1007/s10682-012-9555-5

Nataro, J. P., & Kaper, J. B. (1998). Diarrheagenic *Escherichia coli*. *Clinical Microbiology Reviews*, *11*, 142–201.

O'Dwyer, K., Dargent, F., Forbes, M. R., & Koprivnikar, J. (2019). Data from: Parasite infection leads to widespread glucocorticoid hormone increases in vertebrate hosts: A meta-analysis. *Dryad Digital Repository*, https://doi.org/10.5061/dryad.fn2z34tph

Peacor, S. D., Peckarsky, B. L., Trussell, G. C., & Vonesh, J. R. (2013). Costs of predator-induced phenotypic plasticity: A graphical model for predicting the contribution of nonconsumptive and consumptive effects of predators on prey. *Oecologia*, *171*, 1–10. https://doi.org/10.1007/s00442-012-2394-9

Poulin, R. (1999). The functional importance of parasites in animal communities: Many roles at many levels? *International Journal for Parasitology*, *29*, 903–914. https://doi.org/10.1016/S0020-7519(99)00045-4

R Core Team. (2016). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.R-project.org/

Raffel, T. R., Martin, L. B., & Rohr, J. R. (2008). Parasites as predators: Unifying natural enemy ecology. *Trends in Ecology and Evolution*, *23*, 610–618. https://doi.org/10.1016/j.tree.2008.06.015

Romagnani, S. (1992). Induction of TH1 and TH2 responses: A key role for the 'natural' immune response? *Immunology Today*, *13*, 379–381. https://doi.org/10.1016/0167-5699(92)90083-J

Romero, L. M. (2004). Physiological stress in ecology: Lessons from biomedical research. *Trends in Ecology and Evolution*, *19*, 249–255. https://doi.org/10.1016/j.tree.2004.03.008

Sánchez, C. A., Becker, D. J., Teitelbaum, C. S., Barriga, P., Brown, L. M., Majewska, A. A., … Altizer, S. (2018). On the relationship between body condition and parasite infection in wildlife: A review and meta-analysis. *Ecology Letters*, *21*, 1869–1884. https://doi.org/10.1111/ele.13160

Sapolsky, R. M., Romero, L. M., & Munck, A. U. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrine Reviews*, *21*, 55–89.

Sutherland, B. J., Koczka, K. W., Yasuike, M., Jantzen, S. G., Yazawa, R., Koop, B. F., & Jones, S. R. (2014). Comparative transcriptomics of Atlantic Salmo salar, chum *Oncorhynchus keta* and pink salmon *O. gorbuscha* during infections with salmon lice *Lepeophtheirus salmonis*. *BMC Genomics*, *15*, e200.

Szabo, C., Thiemermann, C., Wu, C. C., Perretti, M., & Vane, J. R. (1994). Attenuation of the induction of nitric oxide synthase by endogenous glucocorticoids accounts for endotoxin tolerance in vivo. *Proceedings of the National Academy of Sciences of the United States of America*, *91*, 271–275. https://doi.org/10.1073/pnas.91.1.271

Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, *36*, 1–48.

Warne, R. W., Crespi, E. J., & Brunner, J. L. (2011). Escape from the pond: Stress and developmental responses to ranavirus infection in wood frog tadpoles. *Functional Ecology*, *25*, 139–146. https://doi.org/10.1111/j.1365-2435.2010.01793.x

Webster, J. I., & Sternberg, E. M. (2004). Role of the hypothalamic-pituitary-adrenal axis, glucocorticoids and glucocorticoid receptors in toxic sequelae of exposure to bacterial and viral products. *Journal of Endocrinology*, *181*, 207–221. https://doi.org/10.1677/joe.0.1810207

Welberg, L. A., & Seckl, J. R. (2001). Prenatal stress, glucocorticoids and the programming of the brain. *Journal of Neuroendocrinology*, *13*, 113–128. https://doi.org/10.1111/j.1365-2826.2001.00601.x

Wingfield, J. C., Maney, D. L., Breuner, C. W., Jacobs, J. D., Lynn, S., Ramenofsky, M., & Richardson, R. D. (1998). Ecological bases of hormone-behavior interactions: The "emergency life history stage". *American Zoologist*, *38*, 191–206. https://doi.org/10.1093/icb/38.1.191

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