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Ticks and Tick-borne Diseases

Original article

To cool or not to cool? Intestinal coccidians disrupt the behavioral hypothermia of lizards in response to tick infestation

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A B S T R A C T

It is generally accepted that parasites exert negative effects on their hosts and that natural selection favors specific host responses that mitigate this impact. It is also known that some components of the host immune system often co-evolve with parasite antigens resulting in a host-parasite arms race. In addition to immunological components of the anti-parasitic response, host behavioral responses are also important in this arms race and natural selection may favor avoidance strategies that preclude contact with parasites, or shifts in the host's thermoregulatory strategy to combat active infections (e.g., behavioral fever). Ticks are widespread parasites with direct and indirect costs on their vertebrate hosts. Their saliva provokes hemolysis in the blood of their hosts and can transmit a plethora of tick-borne pathogens. We enquired whether tick infestation by *Ixodes pacificus* can provoke a thermoregulatory response in *Sceloporus occidentalis*. For this, we compared the thermoregulatory behavior of tick-infested lizards against tick-infested lizards co-infected with two different species of coccidians (*Lankesterella occidentalis* and *Acroeimeria sceloporis*). After this, lizards were kept in individual terraria with a basking spot and fed ad libitum. We found that tick-infested lizards sought cooler temperatures in proportion to their tick load, and this response was independent of the co-infection status by *L. occidentalis*. This was consistent in April and June (when tick loads were significantly lower) and suggests a conservative strategy to save energy which might have been selected to overcome tick infestations during phenological peaks of this parasite. However, this behavior was not observed in lizards co-infected with *A. sceloporis*, suggesting that co-infection with this intestinal parasite prompt lizards to be active. Cost of tick infestation was confirmed because housed lizards lost weight at a constant ratio to initial tick load, independently of other infections. The broader implications of these findings are discussed in the context of climate change.

1. Introduction

Ectothermic animals have a limited physiological capacity to modify their body temperature and must compensate through selecting thermal microhabitats that match their physiological requirements (Stevenson, 1985; Zimmerman et al., 1994; Schultz, 1998). Indeed, ectotherms tend to maintain their body temperature in a range close to their thermal preference (Sinervo, 1990; Seebacher and Franklin, 2005). However, interspecific interactions may influence thermal preferences of competing organisms and this represents a particular case of behavioral interference (e.g., Downes and Bauwens, 2002). For example, naïve endemic lizards may select lower temperatures when they interact with more competitive species for basking spots (Downes and Bauwens, 2002; Žagar et al., 2015). Similarly, host-parasite interactions represent a particular case of interference competition and a systemic inflammation provoked by a parasite may induce an alteration of the thermoregulatory response of the host (*sensu* Birch, 1957). This especially occurs when parasites differ in optimal growth temperatures with their host's thermal preferences and "manipulate" the thermoregulatory behavior of hosts, which may result in the parasite's benefit (Schmid-Hempel, 2011). Alternatively, post-infection changes in the host's thermoregulatory behavior might benefit both the host and the parasite

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(e.g., Campbell et al., 2010). However, by definition, parasites exert a negative effect on their hosts' fitness (e.g., Martínez-de la Puente et al., 2010; Sarasa et al., 2011) and thus, in general, selection may favor thermoregulatory behaviors that reduce the negative effects of infection and increase host lifespan, typically by increasing the host's preference for higher temperatures (Kluger et al., 1975; Ouedraogo et al., 2004; Richards-Zawacki, 2010). However, increasing body temperature may compromise other physiological functions (Baracos et al., 1987) and we may expect that the intensity and direction of the thermoregulatory response will depend on the virulence of the parasite (Żbikowska, 2011). Indeed, it is expected that infections will provoke a behavioral response when benefits of such response outweigh its physiological costs (Adamo, 1998; Zamora-Camacho et al., 2016).

To complicate things, the thermoregulatory response to infections may be sequential, especially in endotherms, and alternates between two sickness patterns: hypothermia and fever (Romanovsky and Székely, 1998; Almeida et al., 2006). However, this sequential thermoregulatory pattern has rarely been reported in ectotherms. For example, after injection with a bacterial lipopolysaccharide most of the tested yearling green iguanas, *Iguana iguana*, developed a cold-seeking behavior, resulting in hypothermia, but some developed a heat-seeking behavior, resulting in behavioral fever. This last group of iguanas shifted towards a cold-seeking behavior after several days post-injection (Deen and Hutchison, 2001). This was interpreted as a conservative thermoregulatory strategy aimed to save energy in response to the drop in mass of the individuals during the trial period (Deen and Hutchison, 2001). Thus, as compared to endotherms, infected ectotherms may select lower temperatures, which cools their body (= hypothermia) (Lefcort and Bayne, 1991; Moore and Freehling, 2002; Paranjpe et al., 2014), or alternatively, they can develop behavioral fever through selection of warmer temperatures (Kluger et al., 1975; Campbell et al., 2010; Richards-Zawacki, 2010). Nonetheless, Romanovsky and Székely (1998) suggested that both behavioral responses, fever and hypothermia, are not exclusive but complementary strategies of survival during systemic inflammation. Despite associated costs, the former ensures the active fight against the infection, whereas hypothermia is an important adaptive response that protects vital organs during bouts of metabolic trauma, including infections (Romanovsky and Székely, 1998; Deen and Hutchison, 2001; Peterson et al., 2003).

Projected models of climate change forecast a profound impact on thermal niches with dramatic repercussions in the next decades (Sinervo et al., 2010; Hoffmann and Sgro, 2011). Thermal alteration of ecosystems is already affecting populations across taxa (reviewed in Walther et al., 2002) and it is also affecting ecological interactions (e.g., Winder and Schindler, 2004; Yang and Rudolf, 2010). Alterations of host-parasite assemblages and parasite phenological cycles are also among the predicted consequences of climate change (e.g., Ogden et al., 2008; Levi et al., 2015). In this study, we aim to explore the role of parasitic infections in the thermal ecology of an ectothermic vertebrate model species, a matter poorly explored before. We focus here on the association between the western fence lizard, *Sceloporus occidentalis*, and the western black-legged tick, *Ixodes pacificus*. Although this tick species can use small mammals and birds as hosts, it prefers the western fence lizard (Eisen et al., 2004). Infestation by this tick may induce hemolysis in the blood of *S. occidentalis*, and appears to reduce the lizard's body condition when tick infestation concurs with malarial infection (Dunlap and Mathies, 1993). In addition, during feeding, ticks pump their saliva into the host's blood stream (Francischetti et al., 2009; Šimo et al., 2017) and this fluid contains immunomodulatory molecules that enable the contingent invasion by a wide plethora of tick-borne pathogens (Šimo et al., 2017). Furthermore, this tick species is an important vector for the Lyme disease spirochete, *Borrelia burgdorferi* sensu stricto (Burgdorfer et al., 1985; Clover and Lane, 1995). Interestingly, an active compound in the blood of lizards kills spirochetes of the Lyme borreliosis (Lane and Quistad, 1998; Lane et al., 2006) and, may be important natural filters limiting the transmission of

some pathogen genotypes associated to this disease (Lane, 1990; Schall et al., 1999 but also see Majláthová et al., 2008). Therefore, tick infestations are costly to host lizards and, hence, we hypothesize that lizards may show behavioral responses that mitigate symptoms. In this sense, we predict that lizards infested with more ticks will choose lower temperatures than lizards infested with less ticks to save energy. To test this, we recorded the preferred temperatures of lizards in an experimental thermal gradient and then fed and housed them for 11 days in terraria with thermal gradients that mimic natural conditions. Our prediction that tick infestation is costly to lizards would be supported if 1) lizards respond to tick infestation with behavioral hypothermia, which might limit the costs of tick infection and reduce blood drawn, rather than behavioral fever, which is unlikely to harm the ticks, and may only increase the ticks' ability to draw resources from the lizards; and 2), as a likely consequence of blood drawn, they will lose weight proportionally to their initial tick load.

2. Material and methods

2.1. Sampling

In 2014 we captured 77 adult (males = 47, females = 30) coast range fence lizards, *Sceloporus occidentalis bocourtii* (Squamata: Phrynosomatidae), at Santa Cruz County, CA, USA (36.9852, -122.0614) during two sampling periods in April and June (beginning and ending of the host breeding season, respectively). In mid-April we captured 42 lizards and in early June 35 lizards. All lizards were caught using a noose and were transported to the lab facilities in a cooler. The sex of the individuals was determined by the presence of enlarged post-anal scales (Cox et al., 2005; Megía-Palma et al., 2018). As a measure of body size, snout to vent length (SVL) of the lizards was measured with a ruler to the nearest millimeter and their mass to the nearest gram using a digital scale. A body condition index was estimated using the Scaled Mass index (SMi). This estimation accounts for the growth effect on body size as well as for the scaling relationship between mass and body length (Peig and Green, 2009, 2010), and it is calculated using the standardized major-axis of the mass on body length (following Bohonak, 2004).

2.2. Housing

A second mass measurement of the lizards captured in April (N = 42) was taken 11 days post-capture. Thus, during this period, the lizards were housed individually in plastic terraria with a damp substrate of peat moss and sand, and were provided with water and food (crickets dusted with vitamins and calcium) ad libitum. The terraria were kept in an environmental chamber with a 12L:12D photoperiod provided by natural spectrum fluorescent and ultraviolet lights and a cycling thermal regime. We used one empty terrarium with substrate to register standard temperatures 24 h/day every 5 min during 11 days with a data logger (hobo U23-002, Onset, Cape Cod, Massachusetts, USA). We set one probe of the data logger in one corner of the cage under the heat source (i.e., 40 W bulb) and other probe in the opposite corner.

2.3. Thermal behavior

Within two days of capture lizards were allowed to select temperatures in experimental thermal gradients (i.e., 48-25 °C) and their body temperature was recorded every minute during the 120 min trial (as in Paranjpe et al., 2013). Preferred temperature (T_p) was later calculated as the arithmetic mean of measured body temperatures (Pough and Gans, 1982). Standard deviations of body temperatures (SD) were also calculated. Thus, lizards with high SD have low precision of thermoregulation (Paranjpe et al., 2013). Maximum and minimum body temperatures of each individual were also registered as measures of

voluntarily selected temperatures ($T_{max.v}$, and $T_{min.v}$). In addition to these measurements of thermal preference, we also investigated the parasitic infections of these lizards. The same person (RM-P) quantified the number of ticks on the lizards (i.e., tick load) within the first day of capture and at day 11. We differentiated between non-fed and fed ticks and classified them based on their turgor, quantifying them separately. Nymphs and larvae of *I. pacificus* have been described to infect *S. occidentalis* in California (Castro and Wright, 2007), unfortunately we were unable to differentiate the tick development stages based on their differential number of legs (3 in larvae and 4 in nymphs) because they keep them hidden under their body during feeding. In addition, following the methods described in Megía-Palma et al. (2018), the same person (RM-P) diagnosed chronic infections by hematic (i.e., *Lankesterella occidentalis*) and intestinal (i.e., *Acroeimeria sceloporis*) coccidians only once at the beginning of the trials.

2.4. Statistical analyses

2.4.1. Parasitic infections

Generalized linear models (GLMs) were used to investigate factors explaining tick prevalence and total tick load. To test tick prevalence we fitted a GLM with binomial distribution linked to a logit function with tick presence as response and month, sex, SVL, SMi, and presence of *A. sceloporis* and *L. occidentalis* as predictors. To analyze predictors explaining total tick load we fitted a GLM with negative binomial distribution, which suits the typically over-dispersed distribution of parasite counts (Pennycuick, 1971). The error term of the model was linked to a logit function with total tick load as response and month, sex, SVL, SMi, and presence of *A. sceloporis* and *L. occidentalis* as predictors. Furthermore, we ran three non-parametric Wilcoxon matched pairs tests to compare 1) total tick load, 2) number of fed, and 3) number of non-fed ticks of the lizards maintained in captivity between the beginning and the end of the experiment. We also investigated factors explaining the prevalence (absence/presence) of *A. sceloporis*, and *L. occidentalis*. For this, we fitted two separated GLMs with binomial distribution linked to a logit function with *A. sceloporis* and *L. occidentalis* as response and month, sex, SVL, SMi, and tick load as predictors.

2.4.2. Effect of infections on thermoregulatory behavior

We investigated different parasitic infections, and their interactions, as predictors on both lizards' thermal preferences in the laboratory and mass loss. As a preliminary analysis and to ascertain independence among the thermal variables used here (i.e., T_p, SD, $T_{max.v}$, and $T_{min.v}$), we ran a correlation matrix for these parameters. Then, we performed general linear analyses including month of capture, sex, SVL, SMi, tick load, co-infection status: 0 = none, 1 = *A. sceloporis*, 2 = *L. occidentalis*, 3 = *A. sceloporis* + *L. occidentalis*, and tick load*co-infection status as predictors of T_p, SD, maximum, and minimum temperatures in separate analyses. We confirmed normality of all models after testing their deviance residuals with Shapiro-Wilk's normality tests. In addition, we controlled the observed heteroscedasticity of model residuals by applying a "sandwich" correction (Zeileis, 2006). Thus, we present the coefficients for corrected models. All analyses were performed in R v.3.4.3 (R core Team, 2017).

2.4.3. Effect of infections on body mass

We also studied the within-individual body mass change as a function of the different parasites investigated here. For this, we ran a general linear mixed analysis (GLMM) where individual was set as random factor and body mass as response variable. Day of measurement, sex, body size (SVL), tick load, and co-infection status were set as predictors. In addition, environmental temperature and temperature preferences of the lizards may influence the metabolic activity of the lizards and, therefore, their energy expenditure (Seebacher and Franklin, 2005). Therefore, we compared the suitability of two

alternative models: one that included $T_{max.v}$ as predictor, and other model that included T_p as predictor. The model that included $T_{max.v}$ had a $\Delta AICc = -2.05$ as compared to the alternative model that included T_p. Thus, along with the remaining predictors commented, we also included $T_{max.v}$ in the final model.

3. Results

3.1. Thermal characteristic of plastic terraria

Lizards captured in April were maintained in captivity during 11 days. During the day time (7 AM – 7 PM) and in the warmest spot of the model terrarium, mean ± SE substrate temperature was 31.5 ± 0.09 °C (mode = 30.2 °C; maximum = 39.1 °C, minimum = 17.6 °C). The soil temperatures reflect the water loss from the peat/soil mixture, and a basking lizard (under the heat source) can readily attain preferred body temperatures, or retreat to the opposite side of the terraria to achieve lower body temperatures (T_b). In the coolest spot of the terrarium, mean ± SE substrate temperature was 25.6 ± 0.1 °C (mode = 24.9 °C; maximum = 38.8 °C, minimum = 16.8 °C). Thus, the modal difference between the two thermal extremes in the model terrarium evaluated was 4.8 °C. During the night period (7 PM – 7 AM), with no heat source connected, substrate mean ± SE temperature was 19.7 ± 0.02 (mode = 19.5 °C; maximum = 29.3 °C, minimum = 16.0 °C).

3.2. Parasitic infections

There were significant differences in parasite prevalence between April and June (Fig. 1). Lizards captured in April were more often infected by ticks, *I. pacificus* (100% vs. 54.3%), and intestinal coccidians, *A. sceloporis* (73.8% vs. 28.6%). However, the observed difference in prevalence of the hematic coccidian, *L. occidentalis* (16.7% vs. 37.1%, $\chi^2 = 4.2$, $P = 0.04$) was not significant when the model was controlled by other co-variables (Table 1). The prevalence of *A. sceloporis* (53.2%) doubled the prevalence of *L. occidentalis* in the sample (26%) ($\chi^2 = 11.97$, $P = 0.0005$). Mean ± standard error tick load was also significantly higher in April than in June (April mean ± SE infestation = 18.4 ± 2.2, mode = 20, range = 1–61 vs. June mean ± SE infestation = 1.02 ± 0.2, mode = 0, range = 0–7, $Z = -11.00$, $P < 0.0001$, estimate = 1.60). The prevalence of double co-infections (*A. sceloporis* + *L. occidentalis*) was 13%, which did not significantly differ between April and June ($\chi^2 = 0.15$, $P = 0.69$). Furthermore, total tick load decreased significantly after the 11 days that lizards were maintained in terraria (day 1 = 18.4 ± 2.2, day 11 = 7.8 ± 1.3) (Wilcoxon matched pairs test: $Z = 3.66$, $P < 0.001$). Specifically, the number of non-fed ticks did not change during this period ($Z = 1.09$, $P = 0.27$), but the number of fed ticks significantly decreased ($Z = 5.31$, $P <$
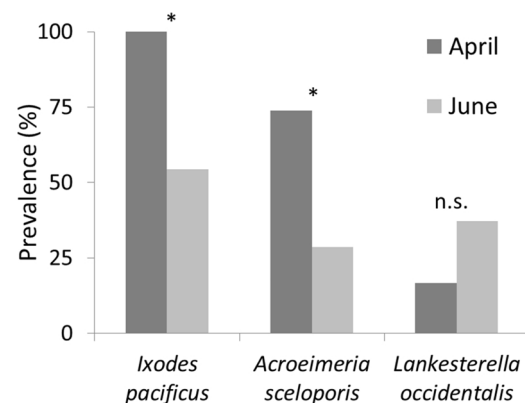
Fig. 1. Monthly distribution of tick and coccidian prevalence. Asterisks show significant differences (n.s. = non-significant difference).

Table 1

Generalized linear ANCOVAs showing main effects of month (April = 1, June = 2), sex (males = 1, females = 2), body size, body condition, and the other parasites studied here on the presence of coccidians, and the presence and abundance of ticks (0 = uninfected, 1 = infected). Asterisks indicate significance level (* P < 0.05, ** P < 0.01, *** P < 0.001). Estimate coefficients are shown for significant predictors.

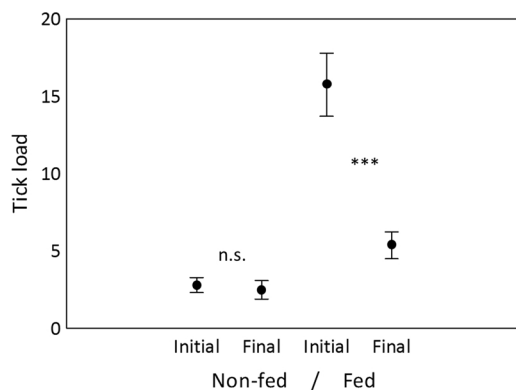|	Tick load$_{total}$		Tick prevalence		*A. sceloporis* prevalence		*L. occidentalis* prevalence	
	Estimate (SE)	z value	Estimate (SE)	z value	Estimate (SE)	z value	Estimate (SE)	z value
Month	**1.60 (0.14)**	**11.36***	**9.79 (0.36)**	**19.43***	**0.95 (0.28)**	**3.18**	–	−1.50
Sex	–	1.26	–	−0.10	–	−0.39	–	1.28
A. sceloporis	–	0.78	–	−0.16	–	–	–	−1.18
L. occidentalis	–	−0.68	–	−0.52	–	−0.68	–	–
Tick load$_{total}$	–	–	–	–	–	−0.44	–	0.24
SVL	**0.10 (0.04)**	**2.52***	–	−0.82	–	1.54	–	−0.48
SMi	–	−1.53	–	0.91	–	−1.50	–	1.13
Residuals	70							

Fig. 2. Mean ± standard error load of fed versus non-fed ticks at the beginning and the end of the 11 days that lizards were kept in captivity. Asterisks show significant differences (n.s. = non-significant difference).

0.0001; Fig. 2). Beside differences in tick load between April and June, total tick load was also positively and significantly related to body size (Z = 2.52, P = 0.014, estimate = 0.10) (Table 1).

3.3. Effects of infections of thermoregulatory behavior

The correlation matrix revealed a high correlation of T_p with $T_{max.v}$ (r = 0.73) and a low significant correlation with $T_{min.v}$ (r = 0.27). SD was significantly correlated with both $T_{max.v}$ and $T_{min.v}$ (r = 0.44 and r = -0.69, respectively). Lizards' mean T_p was 35.6 ± 0.2 °C. However, this varied between April (34.9 ± 0.2 °C, range = 37.3-31.3 °C) and June (36.4 ± 0.2 °C, range = 38.9-33.6 °C) (Table 2). Lizards in April tended to be more precise in selecting temperatures (SD = 0.9 ± 0.06) than in June (SD = 1.4 ± 0.08). In addition to the effect of the month, lizards' T_p was significantly explained by the interaction total tick load*co-infection status (Table 2). Total tick load was highly correlated with both the number of fed (r = 0.98, P < 0.0001) and non-fed ticks (r = 0.70, P < 0.0001). Thus, identical conclusions were obtained when they were alternatively included in the model of T_p (maximum ΔAICc between the three alternative models = 1). Importantly, tick load and T_p were negatively and significantly related in non-co-infected lizards (r = -0.66, P = 0.0003) or in lizards co-infected with *L. occidentalis* (i.e., hematic coccidian) (r = -0.69, P = 0.03). However, this relationship was lost when individuals were co-infected with intestinal coccidians (i.e., *A. sceloporis* alone: r = -0.17, P = 0.36; or *A. sceloporis* + *L. occidentalis*: r = 0.27, P = 0.44) (Fig. 3). In addition, independent of parasitic infections, there was a marginally significant difference in T_p between April (mean ± SE T_p = 34.9 ± 0.2 °C) and June (36.4 ± 0.2 °C). Similarly, and likely associated to the high correlation between T_p and $T_{max.v}$, variation in voluntary maxima ($T_{max.v}$) was best explained by differences between April (37.2 ± 0.3 °C) and June (39.3 ± 0.17 °C) and the interaction total tick load*co-infection status. Thus, $T_{max.v}$ values were negatively and significantly correlated with tick load in lizards if these were infested with ticks only (r = -0.57, P = 0.002), or co-infected with *L. occidentalis* (r = -0.89, P = 0.0006). However, this relationship was not significant in co-infected lizards with *A. sceloporis* alone (r = -0.30, P = 0.10), or *A. sceloporis* in combination with *L. occidentalis* (r = -0.18, P = 0.61). Variation in voluntary minima ($T_{min.v}$) was significantly explained by body size: the larger the lizards the lower their $T_{min.v}$. In addition, there was a significant quadratic relationship between $T_{min.v}$ and tick load, although it was only marginally significant (Table 2).

Table 2

General linear ANCOVAs showing main and interaction effects of tick load and co-infections (0 = ticks only, 1 = *A. sceloporis*, 2 = L. *occidentalis*, 3 = *A. sceloporis* + L. *occidentalis*) on mean selected temperature (T_p), thermoregulation precision (SD), and voluntary minimum ($T_{min.v}$) and maximum ($T_{max.v}$) temperatures selected by *S. occidentalis* under laboratory conditions. Degrees of freedom = d.f. Significant results at *P*-value < 0.05 are shown in bold. Global r-squared (R^2) is provided for each model. Estimate coefficients are shown for significant predictors.

|	d.f.	T_p Estimate (SE)	F	P	SD Estimate (SE)	F	P	$T_{max.v}$ Estimate (SE)	F	P	$T_{min.v}$ Estimate (SE)	F	P
Month	1	−0.67 (0.29)	**4.36**	**0.04**	–	3.50	0.07	−1.17 (0.32)	**14.50**	**< 0.0001**	–	0.00	0.97
SVL	1	–	0.09	0.77	–	1.71	0.19	–	0.13	0.72	−0.26 (0.11)	**5.23**	**0.025**
SMi	1	–	0.03	0.87	–	0.25	0.62	–	0.02	0.88	–	2.79	0.10
Sex	1	–	0.00	0.98	–	0.11	0.73	–	0.91	0.34	–	1.51	0.22
Co-infection	3	–	0.87	0.46	–	0.77	0.51	–	1.34	0.27	–	1.24	0.30
Tick load	1	–	0.00	0.97	–	2.09	0.15	–	0.08	0.78	**0.06 (0.03)**	**4.10**	**0.047**
Tick load : co-infection	3	−0.04 (0.02), −0.001 (0.02), -0.01 (0.03)	**4.51**	**0.006**	–	0.49	0.69	−0.02 (0.02), −0.02 (0.02), −0.01 (0.04)	**3.09**	**0.033**	–	0.69	0.56
Residuals	65												
R^2			0.31			0.35			0.39			0.34	
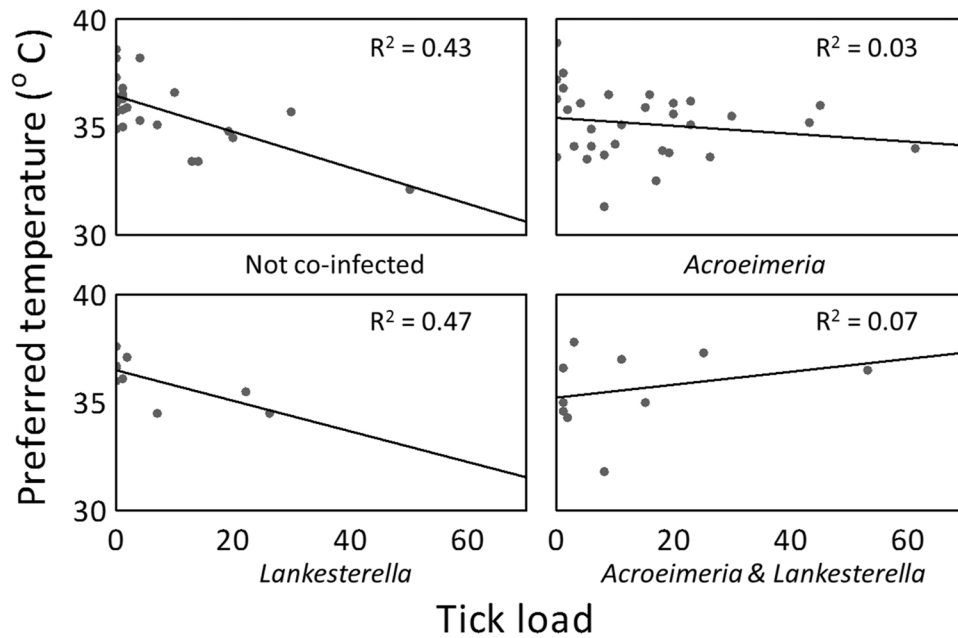
Fig. 3. Relationship between preferred temperatures (T_p) and tick load in lizards. Co-infections are indicated below each graph. Lizards **co-i**nfected with intestinal coccidians of the genus *Acroeimeria* showed non-significant relationship between T_p and tick load (see results).

3.4. Effects of infections on body mass

There was a general and significant loss of body mass after 11 days ($\chi^2_{1,\,29} = 87.74$, $P < 0.0001$; Table 3) and three lizards died. Mean ± SE mass of lizards was 8.15 ± 0.48 g at first day, and 7.23 ± 0.43 g at day 11. Thus, mean ± SE body mass loss was 0.92 ± 0.07 g, and this ranged from 0.11 to 1.8 g. Body mass loss was significantly and negatively related to tick load at capture ($\chi^2_{1,\,29} = 6.04$, $P = 0.014$; Fig. 4), SVL ($\chi^2_{1,\,29} = 591.82$, $P < 0.0001$), and $T_{max.v}$ ($\chi^2_{1,\,29} = 6.35$, $P = 0.011$) (Table 3). Thus, larger lizards lost more body mass. Independent of this, lizards that voluntarily selected higher temperatures at the beginning of the experiment and had more ticks also experienced a higher body mass loss during the 11 days.

4. Discussion

Tick infestation was related to cold-seeking behavior in *S. occidentalis*, as both T_p and $T_{max.v}$ negatively related to total tick load, except in those individuals co-infected with intestinal coccidians, *A. sceloporis*. This first supports a differential effect of the two coccidian parasites studied here which had already been suggested in a previous study on this population (Megía-Palma et al., 2018). In that study, a
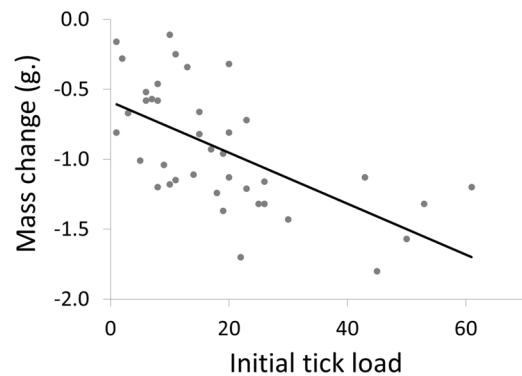
Table 3
Result of GLMM analysis showing in bold significant predictors (at $P < 0.05$) for within-individual body mass change of the lizards sampled in April and kept in captivity. $R^2(m)$ shows the proportion of variance in within-individual body mass change explained by fixed terms in the model. Estimate coefficients (± standard errors) are shown for significant predictors.

| | d.f. | Estimate (SE) | Body mass | |
			$X^2_{1,\,33}$	*P*-value
(Intercept)	1	**−17.10 (2.14)**	**63.72**	**< 0.0001**
Day of measurement	1	**0.39 (0.04)**	**87.74**	**< 0.0001**
SVL	1	**0.33 (0.01)**	**591.82**	**< 0.0001**
Tick load	1	**0.01 (0.005)**	**6.04**	**0.014**
Sex	1	–	0.34	0.55
Co-infection status	3	–	1.62	0.65
$T_{max.v}$	1	**0.14 (0.05)**	**6.35**	**0.011**
$R^2(m)$				0.95

Fig. 4. Relationship between mass change (mass day 11 – mass day 1) and tick load (day 1). All lizards were infested by ticks (range = 1–61). None of the lizards gained mass.

poorer nuptial coloration was associated in both males and females to the infection by *A. sceloporis*, but not to the infection by *L. occidentalis* suggesting already a higher virulence of the former. This is congruent with the observed prevalence of *A. sceloporis* which doubled the prevalence of *L. occidentalis* and also with the fact that *A. sceloporis* (and *I. pacificus*) was more abundant in April when the lizards' hormonal state associated to reproduction (see seasonal differences in e.g., Robinson and Gifford, 2019) may increase susceptibility to some parasites (Folstad and Karter, 1992). Secondly, it also suggests that infested free-ranging lizards, like captive ones, seek out cool temperatures which may help them to overcome acute tick infestations. Indeed, as demonstrated by the significant relationship found between mass loss with both total tick load and the initial voluntary selection of maximum temperatures in the lizards kept in captivity, tick infestation has negative impacts on the host's physiology (Dunlap and Mathies, 1993), which can be aggravated under a warm environment. Moreover, our data suggest that the thermal physiology of *S. occidentalis* is plastic because we found significant differences in T_p and $T_{max.v}$ between April and June, independent of the parasitic infections studied here and as a likely response to the typical seasonal rise of temperatures during the summer in Mediterranean regions (e.g., Díaz et al., 2006). This plasticity in the thermal physiology of *S. occidentalis* might be added to other

compensatory behaviors performed by this species to cope with warm thermal regimes (e.g., Adolph, 1990). For example, Western fence lizards use more shaded microhabitats or perch off the ground more often at low than at high elevations in California. This highlights the importance of thermal microhabitat availability for this species to cope with environmental constraints (Adolph, 1990). Anthropogenic perturbation at low elevations in California is favoring a rapid homogenization of microhabitats with yet quantifiable impacts on biodiversity (Holway and Suarez, 2006; Schwartz et al., 2006; Simovich et al., 2013). However, despite some high infestation levels (i.e., 61 ticks), our data showed that tick infestation resulted in a modal 4.6% reduction of lizard body temperature below the preferred temperatures of *S. occidentalis* (i.e., 35 °C) which is very likely within the available range of thermal microhabitats at present.

Tick parasites infest lizards worldwide (e.g., Schall et al., 1999; Main and Bull, 2000; Václav et al., 2007). However, there is scarce empirical evidence of the negative effect on lizard hosts of this association despite the fact that some infestations can be massive (Gomes et al., 2013; Megía-Palma et al., 2017). For example, infested Australian lizards, *Tiliqua rugosa*, have smaller home ranges, move less, and have lower sprint speed and endurance in the lab than experimentally disinfested lizards, suggesting that ticks might limit both mating opportunities and fleeing success (Main and Bull, 2000). Ticks also reduce the period that male Iberian green lizards, *Lacerta schreiberi*, maintain their nuptial coloration during the breeding season, suggesting a possible reduction in sexual attractiveness (Megía-Palma et al., 2017). The results of our study demonstrate that tick infestation is costly to lizards because, in support of our predictions and at a ratio proportionally to initial tick load, 1) infested lizards selected lower temperatures, resulting in hypothermia, and 2) they lose weight. Body mass is a universal predictor of fighting and mating success in male lizards (e.g., Gullberg et al., 1997; Huygue et al., 2005) and is positively related to individual quality and offspring body condition in females of the closely related *S. virgatus* (Weiss, 2006; Weiss et al., 2009), thus, if tick infestation reduces body mass of their lizard hosts, it may result in a direct fitness cost.

Two non-excluding hypotheses may explain the average 11.61% weight loss at a constant ratio to initial tick load. On the one hand, ticks not only induce sickness in lizards but direct wounds in the skin surface and blood vessels of their hosts (Francischetti et al., 2009). The host immune system reacts immediately healing the wounds. This is associated with cytokines secretion which, in turn, induce lethargic behavior and anorexia (Johnson, 2002; Werner and Grose, 2003; Barrientos et al., 2008). For example, the closely related side-blotched lizard, *Uta stansburiana*, reduced metabolic rate in response to wound healing and lost weight at a constant ratio to the number of cutaneous wounds (Smith et al., 2017). In addition to the costs associated to the healing process, an infestation of 8–10 ticks may provoke an average 10% reduction of hematocrit in lizards weighing 5–15 g (Dunlap and Mathies, 1993). The same authors posit that a fully fed tick nymph may consume 3.6 mg of blood and an average lizard (here weighing 7.8 g) may have between 178.75 and 243.75 mg of blood (extrapolated from Dunlap and Mathies, 1993). Thus, in our study, only 5–7 tick nymphs would be sufficient to reduce the lizard hematocrit by 10%. In April, when tick loads were higher at Santa Cruz County, the lizards had on average 15.7 fed ticks. Fed ticks had probably been feeding on the lizards during the previous days, and based on their large size were nymphs (Megía-Palma pers. obs.). Due to their larger size, tick nymphs may consume more blood than tick larvae. Thus, the blood consumed by the numerous tick nymphs counted on the lizards in April might represent a non-trivial mean hematocrit reduction between 23.2 and 31.6%. This might explain, along with the physiological costs of the healing process already commented, the observed weight loss in the host lizards.

Similarly, the concomitant effects of blood extraction, blood hemolysis, and the amount of tick saliva pumped into the blood stream of hosts (dependent on the number of ticks) may explain the significant

relationship found between tick load and the thermal behavior observed in *S. occidentalis*. Hematocrit is directly linked to oxygen pressure (pO2) in vertebrates (Thorling and Erslev, 1968) and, hence, sickness associated to tick infestations includes hypoxia and lethargy (Felz et al., 2000). Behavioral hypothermia is an adaptive strategy both in ectotherms and endotherms in response to hypoxia (Wood, 1991; Peterson et al., 2003) which protects vital organs with high oxygen demand (e.g., heart, brain) (Wood, 1991; Romanovsky and Székely, 1998). This is attributed to the left shift of the oxyhemoglobin dissociation curve and the reduction in brain metabolic rate (Carlsson and Siesjo, 1976 in Wood, 1991). Peterson et al. (2003) demonstrated that low pO2 in lizards induces behavioral hypothermia and that this effect was reverted when lizards were provided with an adenosine antagonist, demonstrating the role of adenosine in the process (Seebacher and Franklin, 2005). Thus, a hematocrit reduction with associated hypoxia provoked by blood removal and hemolysis may explain the sign of the relationships found in our study. Furthermore, as commented, shifts in body temperature were proportional to the dose of a bacterial lipopolysaccharide in green iguanas, suggesting that behavioral hypothermia in lizards is also influenced by the degree of the immune perturbation (Deen and Hutchison, 2001). Thus, similarly, the dose of tick saliva injected during feeding might also be influencing the extent of the thermoregulatory response in our study because, besides the volume of blood extracted by each tick parasite, tick saliva also burdens active proteins and pathogens that pass into the host blood stream (Francischetti et al., 2009; Šimo et al., 2017).

This contribution aimed to elucidate the adaptive value of the thermoregulatory behavioral response against parasitic infections in *S. occidentalis* and our results suggest that behavioral hypothermia could be an adaptive response during seasonal peaks of tick infestation. In one study, most nymphs of *I. pacificus* that fed on guinea pigs became replete in nine days (range = 7–11) (Arthur and Snow, 1968) and according to this, ticks on lizards kept in captivity in our study were reduced significantly after 11 days, although this was particularly true for fed ticks. This suggests that lizards sustain low metabolic activity during seasonal peaks of tick abundance. This would also reduce the circulation of peripheral blood (Maclean et al., 1975) which, in turn, may limit the blood intake of ticks. In our experiment while the number of fed ticks was significantly reduced after 11 days this did not occur with the non-fed ticks, suggesting a reduction of blood intake of the latter and supporting the idea that the hypothermia response of lizards can be adaptive to fight ticks during phenological peaks of tick abundance. In addition, we repeatedly observed lizards buried in the substrate of the terraria which reduces the body temperature of lizards and might be an avoidance mechanism (*sensu* Hausfater and Meade, 1982) selected to reduce tick re-infestations, although Lane et al. (1995) reported that questing ticks are able to find lizard hosts despite this behavior. Indeed, both cold-seeking and burying behaviors would have only partially mitigated the potential prejudice of tick infestation as suggested by the important mass loss and the death of three lizards despite being allowed to thermoregulate in their terraria and were fed ad libitum. Therefore, besides the existing negative effects of parasites on hormone secretion or color production in *S. occidentalis* (Dunlap and Schall, 1995; Megía-Palma et al., 2018), tick infestations might also limit foraging or mating opportunities during the breeding season of this host species because severely infested lizards may remain in shaded microhabitats, with cooler temperatures, compared to lowly or non-infected lizards as was observed in free-ranging lizards infected with malarial parasites, *Plasmodium mexicanum* (Schall and Sarni, 1987).

Our data support the notion that parasitic infections are costly to *S. occidentalis* and behavioral hypothermia may be an adaptive response to either seasonal (e.g., ticks) or infections with mild effect (i.e., *L. occidentalis*). However, when lizards were co-infected with intestinal coccidians, *A. sceloporis*, they presumably interrupted the cold-seeking response to tick infestation as suggested by the non-significant relationship found when lizards co-infected with *A. sceloporis* were

analyzed. This suggests a higher cost of co-infection *by A. sceloporis* than tick infestations either alone or in combination with hematic coccidians that outweighs benefits of hypothermia (Adamo, 1998; Zamora-Camacho et al., 2016) and, hence, remaining inactive during co-infection with *A. sceloporis* might not be adaptive due to concomitant costs (Budischak et al., 2012). Interestingly, the maintenance of the activity of the lizards infected by *A. sceloporis* during phenological peaks of tick abundance, when other lizards not infected by this parasite remain inactive, might be beneficial to the infected lizards since could increase their mating opportunities despite the duller coloration associated to the infection by *A. sceloporis* (i.e., Megía-Palma et al., 2018). However, if this interruption of the behavioral hypothermia response in the lizards infected by *A. sceloporis* forms part of a compensatory strategy of the host (e.g., Gustafsson et al., 1994; Bowers et al., 2015) or, alternatively, is a mechanism induced by the parasite for its own benefit, will require further research.

5. Conclusions

Our results suggest that behavioral hypothermia is an adaptive response to tick infestations in *S. occidentalis*, although it may not be adaptive when tick infestation concurs with *A. sceloporis*, an intestinal coccidian infection. Thus, this thermal response found here is added to the plethora of morphological (e.g., skin pockets see Salvador et al., 1999), biochemical (i.e., hematic borreliacid factor see Lane and Quistad, 1998), and behavioral adaptations (e.g., burying in the sand, which lower T_b see Lane et al., 1995) that have likely been selected in the western fence lizard to reduce the negative impact of tick infestations. Since free-ranging lizards may have similar cold-seeking behavior during parasitic bouts, the loss of thermal microhabitats by climate change and human concomitant perturbations might, in a future scenario, have negative consequences on the response to infections in ectotherms (Raffel et al., 2006). This is because parasites (e.g., bacteria, virus, protozoa, nematodes) are ubiquitous and, although behavioral fever may also be an adaptive response to infections in some ectotherm host-parasite associations (e.g., Ouedraogo et al., 2004), hypothermia is a widespread response across taxa including e.g. snails (Lefcort and Bayne, 1991), insects (Müller and Schmid-Hempel, 1993; Moore and Freehling, 2002), and most lizard species studied (e.g., Deen and Hutchison, 2001; Merchant et al., 2008; Paranjpe et al., 2014; Zamora-Camacho et al., 2016). Given the expected levels of climate warming predicted for the planet by 2070, under business as usual scenarios or even with controls on CO_2 production (e.g., RCP 8.5 vs 4.5, Vth climate assessment IPCC, 2013), with warmer seasons and longer summers, impact of climate change as important erosive agent on ectotherm diversity (Deutsch et al., 2008; Sinervo et al., 2010; Bosch et al., 2018) should be re-examined considering pathogenic host-parasite associations (Martin et al., 2010).

Declaration of Competing Interest

None.

References

Adamo, S.A., 1998. The specificity of behavioral fever in the cricket Acheta domesticus. J. Parasitol. 84, 529–533.

Adolph, S.C., 1990. Influence of behavioral thermoregulation on microhabitat use by two Sceloporus lizards. Ecology 71, 315–327.

Almeida, M.C., Steiner, A.A., Branco, L.G.S., Romanovsky, A.A., 2006. Cold-seeking behavior as a thermoregulatory strategy in systemic inflammation. Eur. J. Neurosci. 23, 3359–3367.

Arthur, D.R., Snow, K.R., 1968. Ixodes pacificus Cooley and Kohls, 1943: its life-history and occurrence. Parasitology 58, 893–906.

Baracos, V.E., Whitmore, W.T., Gale, R., 1987. The metabolic cost of fever. Can. J. Physiol. Pharm. 65, 1248–1254.

Barrientos, S., Stojadinovic, O., Golinko, M.S., Brem, H., Tomic-Canic, M., 2008. Growth factors and cytokines in wound healing. Wound Rep. Regen. 16, 585–601.

Birch, L.C., 1957. The meanings of competition. Am. Nat. 91, 5–18.

Bohonak, A.J., 2004. RMA, Software for Reduced Major Axis Regression Version 1.17 [computer Program]. Available: http://www.bio.sdsu.edu/pub/andy/rma.html. Last accessed: 03/14/2019.. .

Bosch, J., Fernández-Beaskoetxea, S., Garner, T.W., Carrascal, L.M., 2018. Long-term monitoring of an amphibian community after a climate change-and infectious disease-driven species extirpation. Glob. Change Biol. 24, 2622–2632.

Bowers, E.K., Bowden, R.M., Sakaluk, S.K., Thompson, C.F., 2015. Immune activation generates corticosterone-mediated terminal reproductive investment in a wild bird. Am. Nat. 185, 769–783.

Budischak, S.A., Jolles, A.E., Ezenwa, V.O., 2012. Direct and indirect costs of co-infection in the wild: linking gastrointestinal parasite communities, host hematology, and immune function. Int. J. Parasitol. 1, 2–12.

Burgdorfer, W., Lane, R.S., Barbour, A.G., Gresbrink, R.A., Anderson, J.R., 1985. The western black-legged tick, Ixodes pacificus: a vector of Borrelia burgdorferi. Am. J. Trop. Med. Hyg. 34, 925–930.

Campbell, J., Kessler, B., Mayack, C., Naug, D., 2010. Behavioural fever in infected honeybees: parasitic manipulation or coincidental benefit? Parasitology 137, 1487–1491.

Carlsson, C.H.M., Siesjo, B.K., 1976. Protective effect of hypothermia in cerebral oxygen deficiency caused by arterial hypoxia. Anesthesiology 44, 27–35.

Castro, M.B., Wright, S.A., 2007. Vertebrate hosts of Ixodes pacificus (Acari: Ixodidae) in California. J. Vector Ecol. 32, 140–149.

Clover, J.R., Lane, R.S., 1995. Evidence implicating nymphal Ixodes pacificus (Acari: Ixodidae) in the epidemiology of Lyme disease in California. Am. J. Trop. Med. Hyg. 53, 237–240.

Cox, R.M., Skelly, S.L., Leo, A., John-Alder, H.B., 2005. Testosterone regulates sexually dimorphic coloration in the Eastern Fence Lizard, Sceloporus undulatus. Copeia 2005, 597–608.

Deen, C.M., Hutchison, V.H., 2001. Effects of lipopolysaccharide and acclimation temperature on induced behavioral fever in juvenile Iguana iguana. J. Therm. Biol. 26, 55–63.

Deutsch, C.A., Tewksbury, J.J., Huey, R.B., Sheldon, K.S., Ghalambor, C.K., Haak, D.C., Martin, P.R., 2008. Impacts of climate warming on terrestrial ectotherms across latitude. PNAS 105, 6668–6672.

Díaz, J.A., Iraeta, P., Monasterio, C., 2006. Seasonality provokes a shift of thermal preferences in a temperate lizard, but altitude does not. J. Therm. Biol. 31, 237–242.

Downes, S., Bauwens, D., 2002. An experimental demonstration of direct behavioural interference in two Mediterranean lacertid lizard species. Anim. Behav. 63, 1037–1046.

Dunlap, K.D., Mathies, T., 1993. Effects of nymphal ticks and their interaction with malaria on the physiology of male fence lizards. Copeia 4, 1045–1048.

Dunlap, K.D., Schall, J.J., 1995. Hormonal alterations and reproductive inhibition in male fence lizards (Sceloporus occidentalis) infected with the malarial parasite Plasmodium mexicanum. Physiol. Zool. 68, 608–621.

Eisen, R.J., Eisen, L., Lane, R.S., 2004. Habitat-related variation in infestation of lizards and rodents with Ixodes ticks in dense woodlands in Mendocino County, California. Exp. Appl. Acarol. 33, 215–233.

Felz, M.W., Swift, T.R., Hobbs, W., 2000. Tick paralysis in the United States: a photographic review. Arch. Neurol.-Chicago 57, 1071–1072.

Folstad, I., Karter, A.J., 1992. Parasites, bright males, and the immunocompetence handicap. Am. Nat. 139, 603–622.

Francischetti, I.M., Sa-Nunes, A., Mans, B.J., Santos, I.M., Ribeiro, J.M., 2009. The role of saliva in tick feeding. Front. Biosci. 14, 2051–2088.

Gomes, V., Zagar, A., Carretero, M.A., 2013. A case of massive infestation of a male green lizard Lacerta viridis/bilineata by castor bean tick Ixodes ricinus (Linnaeus, 1758). Nat. Slov. 15, 57–61.

Gullberg, A., Olsson, M., Tegelström, H., 1997. Male mating success, reproductive success and multiple paternity in a natural population of sand lizards: behavioural and molecular genetics data. Mol. Ecol. 6, 105–112.

Gustafsson, L., Nordling, D., Andersson, M.S., Sheldon, B.C., Qvarnström, A., 1994. Infectious diseases, reproductive effort and the cost of reproduction in birds. Philos. Trans. Biol. Sci. 346, 323–331.

Hausfater, G., Meade, B.J., 1982. Alternation of sleeping groves by yellow baboons (Papio cynocephalus) as a strategy for parasite avoidance. Primates 23, 287–297.

Hoffmann, A.A., Sgro, C.M., 2011. Climate change and evolutionary adaptation. Nature 470 (7335), 479.

Holway, D.A., Suarez, A.V., 2006. Homogenization of ant communities in Mediterranean California: the effects of urbanization and invasion. Biol. Conserv. 127, 319–326.

Huygue, H., Vanhooydonck, B., Scheers, H., Molina-Borja, M., Van Damme, R., 2005.

Morphology, performance and fighting capacity in male lizards, Gallotia galloti. Funct. Ecol. 19, 800–807.

IPCC, 2013. Climate Change 2013 – the Physical Science Basis. Summary of Policymakers. . http://www.ipcc.ch/report/ar5/wg1/#.Ulu4Tz8udZi.

Johnson, R., 2002. The concept of sickness behavior: a brief chronological account of four key discoveries. Vet. Immunol. Immunopathol. 87, 443–450.

Kluger, M.J., Ringler, D.H., Anver, M.R., 1975. Fever and survival. Science 188, 166–168.

Lane, R.S., 1990. Susceptibility of the western fence lizard (Sceloporus occidentalis) to the Lyme borreliosis spirochete (Borrelia burgdorferi). Am. J. Trop. Med. Hyg. 42, 75–82.

Lane, R.S., Kleinjan, J.E., Schoeler, G.B., 1995. Diel activity of nymphal Dermacentor occidentalis and Ixodes pacificus (Acari: Ixodidae) in relation to meteorological factors and host activity periods. J. Med. Entomol. 32, 290–299.

Lane, R.S., Mun, J., Eisen, L., Eisen, R.J., 2006. Refractoriness of the western fence lizard (Sceloporus occidentalis) to the Lyme disease group spirochete Borrelia bissettii. J. Parasitol. 92, 691–696.

Lane, R.S., Quistad, G.B., 1998. Borreliacidal factor in the blood of the western fence lizard (Sceloporus occidentalis). J. Parasitol. 84, 29–34.

Lefcort, H., Bayne, C.J., 1991. Thermal preferences of resistant and susceptible strains of Biomphalaria glabrata (Gastropoda) exposed to Schistosoma mansoni (Trematoda). Parasitology 103, 357–362.

Levi, T., Keesing, F., Oggenfuss, K., Ostfeld, R.S., 2015. Accelerated phenology of blacklegged ticks under climate warming. Philos. Trans. R. Soc. B 370, 20130556.

Maclean, G.S., Lee, A.K., Withers, P., 1975. Haematological adjustments with diurnal changes in body temperature in a lizard and a mouse. Comp. Biochem. Phys. A 51, 241–249.

Main, A.R., Bull, C.M., 2000. The impact of tick parasites on the behaviour of the lizard Tiliqua rugosa. Oecologia 122, 574–581.

Majláthová, V., Majláth, I., Hromada, M., Tryjanowski, P., Bona, M., Antczak, M., Víchová, B., Dzimko, Š., Mihalca, A., Peťko, B., 2008. The role of the sand lizard (Lacerta agilis) in the transmission cycle of Borrelia burgdorferi sensu lato. Int. J. Med. Microbiol. 298, 161–167.

Martin, L.B., Hopkins, W.A., Mydlarz, L.D., Rohr, J.R., 2010. The effects of anthropogenic global changes on immune functions and disease resistance. Ann. N. Y. Acad. Sci. 1195, 129–148.

Martínez-de la Puente, J., Merino, S., Tomás, G., Moreno, J., Morales, J., Lobato, E., García-Fraile, S., Belda, E.J., 2010. The blood parasite Haemoproteus reduces survival in a wild bird: a medication experiment. Biol. Lett. 6, 663–665.

Megía-Palma, R., Martínez, J., Merino, S., 2017. Manipulation of parasite load induces significant changes in the structural-based throat color of male Iberian green lizards. Curr. Zool. 64, 293–302.

Megía-Palma, R., Paranjpe, D., Reguera, S., Martínez, J., Cooper, R.D., Blaimont, P., Merino, S., Sinervo, B., 2018. Multiple color patches and parasites in Sceloporus occidentalis: differential relationships by sex and infection. Curr. Zool. 64, 703–711.

Merchant, M., Fleury, L., Rutherford, R., Paulissen, M., 2008. Effects of bacterial lipopolysaccharide on thermoregulation in green anole lizards (Anolis carolinensis). Vet. Immunol. Immunopathol. 125, 176–181.

Moore, J., Freehling, M., 2002. Cockroach hosts in thermal gradients suppress parasite development. Oecologia 133, 261–266.

Müller, C.B., Schmid-Hempel, P., 1993. Exploitation of cold temperature as defence against parasitoids in bumblebees. Nature 363, 65–67.

Ogden, N.H., Bigras-Poulin, M., Hanincova, K., Maarouf, A., O'callaghan, C.J., Kurtenbach, K., 2008. Projected effects of climate change on tick phenology and fitness of pathogens transmitted by the North American tick Ixodes scapularis. J. Theor. Biol. 254, 621–632.

Ouedraogo, R.M., Goettel, M.S., Brodeur, J., 2004. Behavioral thermoregulation in the migratory locust: a therapy to overcome fungal infection. Oecologia 138, 312–319.

Paranjpe, D., Bastiaans, E., Pattern, A., Cooper, R.D., Sinervo, B., 2013. Evidence of maternal effects on temperature preference in side-blotched lizards: implications for evolutionary response to climate change. Ecol. Evol. 3, 1977–1991.

Paranjpe, D.A., Medina, D., Nielsen, E., Cooper, R.D., Paranjpe, S.U., Sinervo, B., 2014. Does thermal ecology influence dynamics of side-blotched lizards and their microparasites? Integr. Comp. Biol. 54, 108–117.

Peig, J., Green, A., 2009. New perspectives for estimating body condition from mass/length data: the scaled mass index as an alternative method. Oikos 118, 1883–1891.

Peig, J., Green, A., 2010. The paradigm of body condition: a critical reappraisal of current methods based on mass and length. Funct. Ecol. 24, 1323–1332.

Pennycuick, L., 1971. Frequency distributions of parasites in a population of three-spined sticklebacks, Gasterosteus aculeatus L., with particular reference to the negative binomial distribution. Parasitology 63, 389–406.

Peterson, A.M., Gleeson, T.T., Scholnick, D.A., 2003. The effects of oxygen and adenosine on lizard thermoregulation. Physiol. Biochem. Zool. 76, 339–347.

The vocabulary of reptilian thermoregulation. In: In: Pough, F.H., Gans, C. (Eds.), Biology of Reptilia 12. Academic Press, London, pp. 17–23 Physiology C. Physiological Ecology.

R Core Team, 2017. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna.

Raffel, T.R., Rohr, J.R., Kiesecker, J.M., Hudson, P.J., 2006. Negative effects of changing temperature on amphibian immunity under field conditions. Funct. Ecol. 20, 819–828.

Richards-Zawacki, C.L., 2010. Thermoregulatory behaviour affects prevalence of chytrid fungal infection in a wild population of Panamanian golden frogs. Proc. R. Soc. Lond.

B 277, 19–28.

Robinson, C.D., Gifford, M.E., 2019. Intraseasonal changes of patch color in prairie lizards (Sceloporus consobrinus). Herpetologica 75, 79–84.

Romanovsky, A.A., Székely, M., 1998. Fever and hypothermia: two adaptive thermoregulatory responses to systemic inflammation. Med. Hypotheses 50, 219–226.

Salvador, A., Veiga, J.P., Civantos, E., 1999. Do skin pockets of lizards reduce the deleterious effects of ectoparasites? An experimental study with Psammodromus algirus. Herpetologica 55, 1–7.

Sarasa, M., Serrano, E., Soriguer, R.C., Granados, J.E., Fandos, P., González, G., Joachim, J., Pérez, J.M., 2011. Negative effect of the arthropod, Sarcoptes scabiei, on testes mass in Iberian ibex, Capra pyrenaica. Vet. Parasitol. 175, 306–312.

Schall, J.J., Prendeville, H.R., Hanley, K.A., 1999. Prevalence of the tick, Ixodes pacificus, on western fence lizards, Sceloporus occidentalis: trends by gender, size, season, site, and mite infestation. J. Herpetol. 34, 160–163.

Schall, J.J., Sarni, G.A., 1987. Malarial parasitism and the behavior of the lizard, Sceloporus occidentalis. Copeia 1987, 84–93.

Schmid-Hempel, P., 2011. Evolutionary Parasitology: The Integrated Study of Infections, Immunology, Ecology and Genetics. Oxford University Press Inc., New York.

Schultz, T.D., 1998. The utilization of patchy thermal microhabitats by the ectothermic insect predator, Cicindela sexguttata. Ecol. Entomol. 23, 444–450.

Schwartz, M.A., Thorne, J.H., Viers, J.H., 2006. Biotic homogenization of the Californian flora in urban and urbanizing regions. Biol. Conserv. 127, 282–291.

Seebacher, F., Franklin, C.E., 2005. Physiological mechanisms of thermoregulation in reptiles: a review. J. Comp. Physiol. B 175, 533–541.

Šimo, L., Kazimirova, M., Richardson, J., Bonnet, S., 2017. The essential role of tick salivary glands and saliva in tick feeding and pathogen transmission. Front. Cell Infect. Microbiol. 7, 281.

Simovich, M.A., Davis, K.B., Bohonak, A.J., 2013. Landscape homogenization threatens the genetic integrity of the endangered San Diego fairy shrimp Branchinecta sandiegonensis (Branchiopoda: Anostraca). J. Crust. Biol. 33, 730–740.

Sinervo, B., 1990. Evolution of thermal physiology and growth rate between populations of the western fence lizard (Sceloporus occidentalis). Oecologia 83, 228–237.

Sinervo, B., Méndez-de-la-Cruz, F., Miles, D.B., Heulin, B., Bastiaans, E., Villagrán-Santa Cruz, M., Lara-Resendiz, R., Martínez-Méndez, N., Calderón-Espinosa, M.L., Meza-Lázaro, R.N., Gadsden, H., Avila, L.J., Morando, M., De la Riva, I., Sepulveda, P.V., Duarte Rocha, C.F., Ibargüengoytía, N., Aguilar Puntriano, C., Massot, M., Lepetz, V., Oksanen, T.A., Chapple, D.G., Bauer, A.M., Branch, W.R., Clobert, J., Sites Jr, J.W., 2010. Erosion of lizard diversity by climate change and altered thermal niches. Science 328, 894–899.

Smith, G.D., Neuman-Lee, L.A., Webb, A.C., Angilletta, M.J., DeNardo, D.F., French, S.S., 2017. Metabolic responses to different immune challenges and varying resource availability in the side-blotched lizard (Uta stansburiana). J. Comp. Physiol. B 187, 1173–1182.

Stevenson, R.D., 1985. The relative importance of behavioral and physiological adjustments controlling body temperature in terrestrial ectotherms. Am. Nat. 126, 362–386.

Thorling, E.B., Erslev, A.J., 1968. The "tissue" tension of oxygen and its relation to hematocrit and erythropoiesis. Blood 31, 332–343.

Václav, R., Prokov, P., Fekiač, V., 2007. Expression of breeding coloration in European green lizards (Lacerta viridis): variation with morphology and tick infestation. Can. J. Zool. 85, 1199–1206.

Walther, G.R., Post, E., Convey, P., Menzel, A., Parmesan, C., Beebee, T.J., Fromentin, J.M., Hoegh-Guldberg, O., Bairlein, F., 2002. Ecological responses to recent climate change. Nature 416, 389–395.

Weiss, S.L., 2006. Female-specific color is a signal of quality in the striped plateau lizard (Sceloporus virgatus). Behav. Ecol. 17, 726–732.

Weiss, S.L., Kennedy, E.A., Bernhard, J.A., 2009. Female-specific ornamentation predicts offspring quality in the striped plateau lizard, Sceloporus virgatus. Behav. Ecol. 20, 1063–1071.

Werner, S., Grose, R., 2003. Regulation of wound healing by growth factors and cytokines. Physiol. Rev. 83, 835–870.

Winder, M., Schindler, D.E., 2004. Climate change uncouples trophic interactions in an aquatic system. Ecology 85, 2100–2106.

Wood, S.C., 1991. Interactions between hypoxia and hypothermia. Annu. Rev. Physiol. 53, 71–85.

Yang, L.H., Rudolf, V.H.W., 2010. Phenology, ontogeny and effects of climate change on the timing of species interactions. Ecol. Lett. 13, 1–10.

Žagar, A., Carretero, M.A., Osojnik, N., Sillero, N., Vrezec, A., 2015. A place in the sun: interspecific interference affects thermoregulation in coexisting lizards. Behav. Ecol. Sociobiol. 69, 1127–1137.

Zamora-Camacho, F.J., Reguera, S., Moreno-Rueda, G., 2016. Elevational variation in body-temperature response to immune challenge in a lizard. PeerJ 4, e1972.

Żbikowska, E., 2011. One snail – three Digenean spcies, different strategies in host-parasite interaction. Anim. Biol. 61, 1–19.

Zeileis, A., 2006. Object-oriented computation of sandwich estimators. J. Stat. Softw. 16, 1–16.

Zimmerman, L.C., O'Connor, M.P., Bulova, S.J., Spotila, J.R., Kemp, S.J., Salice, C.J., 1994. Thermal ecology of desert tortoises in the eastern Mojave Desert: seasonal patterns of operative and body temperatures, and microhabitat utilization. Herpetol. Monogr. 8, 45–59.