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Elevated basal corticosterone levels increase disappearance risk of light but not heavy individuals in a long-term monitored rodent population

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1 **Elevated basal corticosterone levels increase disappearance risk of light**
2 **but not heavy individuals in a long-term monitored rodent population**

3

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25

26 **Abstract**

27 According to the cort-fitness hypothesis, glucocorticoid levels correlate negatively with
28 fitness. However, field studies found mixed support for this hypothesis, potentially
29 because the association between glucocorticoids and fitness might depend on prevailing
30 environmental conditions. Based on the long-term monitoring of a natural rodent
31 population, we tested whether individuals with elevated corticosterone levels were more
32 likely to disappear, accounting for individual condition and among-year variation in food
33 availability, population density and predation pressure. We used basal corticosterone
34 levels measured at the onset of the pre-breeding season in 331 African striped mice from
35 six generations. While basal corticosterone levels were highly repeatable within
36 individuals, between-individual variation was large. Survival analysis revealed that
37 disappearance risk over the pre-breeding season increased with elevated basal
38 corticosterone levels for light but not for heavy individuals. High levels of corticosterone
39 may be more deleterious to smaller individuals (i.e. through allostatic overload),
40 eventually increasing their mortality risk, and disappearance would represent actual
41 death. An alternative non-exclusive explanation could be that high levels of
42 corticosterone selectively trigger dispersal in light individuals, and disappearance would
43 rather reflect their departure from the population. Although environmental conditions
44 varied considerably among generations, none of the interactions between corticosterone
45 and environmental variables were significant. Disappearance probability was positively
46 correlated with both predation pressure and food availability, a factor favoring dispersal.
47 In sum, elevated basal corticosterone levels increased disappearance in light striped mice,
48 either directly via reduced survival prospects and/or indirectly via dispersal.

49

50 **Keywords:** basal corticosterone level; body mass; cort-fitness hypothesis; disappearance;
51 dispersal; environmental challenge; food availability; survival

52

53 **Introduction**

54 Adaptive physiological change in response to challenging periods of energy limitation is
55 crucial to enhance survival probability. Organisms need to constantly adjust to both
56 predictable and unpredictable changes in their environment (i.e. allostasis; McEwen and
57 Wingfield, 2010; Romero et al., 2009; Wingfield, 2005). Among physiological processes,
58 endocrine control mechanisms mediate the relationship of the organism to its
59 environment (Ricklefs and Wikelski, 2002). They integrate both external cues and
60 internal condition to release hormones that regulate many aspects of the phenotype (Zera
61 et al., 2007). Hormones enable individuals to respond to changes in their environment
62 through modifications of metabolism, osmoregulation, reproductive status and social
63 behaviour (Wingfield, 2009). Such environmental changes include short-term stressors
64 (e.g. inclement weather) or seasonal food shortage (McEwen and Wingfield, 2010). Thus,
65 hormone secretion varies as an adaptive response to environmental stimuli, and endocrine
66 response is expected to increase individual fitness (Hau et al., 2016; Wikelski and
67 Ricklefs, 2001).

68 Glucocorticoids are important mediators of physiological adjustment as they
69 regulate energy balance (Sapolsky et al., 2000), hence promoting allostasis, which is the
70 physiological stability through change of specific mediators (McEwen and Wingfield,
71 2003). Corticosterone, the main glucocorticoid hormone in most vertebrates, regulates
72 metabolic processes to support energetically demanding activities (basal levels), as well
73 as to overcome environmental challenges (stress-induced levels). Thus, the corticosterone
74 regulatory network offers an efficient mechanism to deal with variation in energy
75 requirements and periods of reduced resource availability (Reeder and Kramer, 2005;
76 Romero et al., 2009). However, even though the adaptive value of the glucocorticoid
77 stress response has been acknowledged (Boonstra, 2013; McEwen and Wingfield, 2003;
78 Romero et al., 2009), elevated corticosterone levels have often been regarded as
79 detrimental (Reeder and Kramer, 2005). According to the cort-fitness hypothesis, which
80 predicts that baseline corticosterone correlates negatively with fitness (Bonier et al.,
81 2010, 2009), elevated corticosterone levels would reflect individuals of poor condition
82 with reduced survival prospects and/or reproductive success (Angelier et al., 2010;
83 Bonier et al., 2009; Henderson et al., 2017).

84 Many field studies have investigated fitness correlates of glucocorticoid levels,
85 but several reviews report no general trend (Bonier et al., 2009; Crespi et al., 2013; Hau
86 et al., 2016). Instead, variation in basal glucocorticoid levels was sometimes negatively
87 (Bonier et al., 2007), positively (Cyr and Romero, 2007; Lancaster et al., 2008), or not at
88 all correlated with reproductive success (Magee et al., 2006). For instance in a population
89 of great tits (*Parus major*) in Germany, high glucocorticoid levels at the beginning of the
90 breeding season were associated with a large number of fledglings while such levels were
91 associated with a low number of fledglings later in the season (Ouyang et al., 2013).
92 Similarly, survival rates were either negatively related to (stress-induced) corticosterone
93 levels (Blas et al., 2007; Romero and Wikelski, 2001), or positively related to baseline
94 levels (Cabezas et al., 2007; Patterson et al., 2014). Mixed results were also found when
95 comparing different population of American redstarts (*Sethophaga ruticilla*; Angelier et
96 al., 2009) or the same population of song sparrows (*Melospiza melodia*) over several
97 years (Macdougall-shackleton et al., 2013). It has been argued that this inconsistency
98 might relate to variation in individual condition (life history stage, age, sex) as well as in
99 environmental conditions (Bonier et al., 2009) between studies, most of which were
100 conducted for only one season.

101 It is now acknowledged that the relationship between glucocorticoid levels and
102 fitness might be context-dependent (Henderson et al., 2017). In periods of low resource
103 availability, elevated glucocorticoid levels may be detrimental and reduce fitness when
104 energy demand exceeds available resources, causing allostatic overload (McEwen and
105 Wingfield, 2003; Romero et al., 2009). By contrast, elevated levels might have no effect
106 or even be beneficial, and potentially increase fitness, when resources are not limited (i.e.
107 allostatic load can be negated by available resources). Thus, the effects of glucocorticoids
108 on fitness may change according to environmental conditions, especially food
109 availability, but also predation pressure and population density (Dingemanse et al., 2010;
110 Henderson et al., 2017). Variation in these additional environmental factors should be
111 accounted for when studying the fitness consequences of basal glucocorticoid levels.
112 Long-term, individual based studies monitoring several generations of a given species
113 under varying environmental conditions would contribute to our understanding of

114 whether elevated basal glucocorticoid levels are associated with reduced fitness, and how
115 this relationship depends on intrinsic and extrinsic parameters.

116 In the African striped mouse (*Rhabdomys pumilio*), an annual rodent, a generation
117 born in spring has to survive the forthcoming summer and autumn (i.e. the pre-breeding
118 season) characterised by low food availability, before reproducing in the next
119 winter/spring, and typically die before the subsequent pre-breeding season (Schradin et
120 al., 2012). While food availability decreases annually from spring to summer, the
121 harshness of the pre-breeding season (i.e. extent and duration of reduction in food
122 availability) differs unpredictably from generation to generation (Table 1). In striped
123 mice, corticosterone is a potential trigger for dispersal (Schoepf and Schradin, 2013), and
124 dispersal occurs mainly when food availability is high (Schoepf and Schradin, 2012).

125 We investigated whether basal corticosterone levels were related to disappearance
126 over the pre-breeding season in striped mice. According to the cort-fitness hypothesis,
127 elevated corticosterone levels are associated with poor condition or health, which would
128 translate into a negative relationship between basal corticosterone levels and survival.
129 Nonetheless, the relationship between basal corticosterone levels and survival may vary
130 according to environmental conditions, including food availability, population density
131 and predation pressure. We had three independent, non-exclusive hypotheses. First, the
132 negative effects of elevated basal corticosterone levels are expected to be stronger in pre-
133 breeding seasons with relatively lower food availability, but weaker (or even absent) in
134 pre-breeding seasons with relatively high food availability. Second, if corticosterone
135 mediates dispersal, then elevated basal levels should be related to disappearance in
136 smaller (but not large) striped mice, which are most likely to disperse (Solmsen et al.,
137 2011). Third, elevated basal corticosterone levels may enhance survival probability under
138 high predation pressure, since energy mobilised by corticosterone secretion would
139 promote predator escape responses.

140

141 **Material and methods**

142 *Study period and study area*

143 The study was conducted at the Succulent Karoo Research Station in Goegap Nature
144 Reserve in South Africa (S29°42.414' E18° 02.526'), which lies within the Succulent

145 Karoo semi-desert. Data were collected over 6 years (2009-2014) from free-ranging
146 striped mice on a 10-ha field site at the beginning of the pre-breeding season (January-
147 February). Data were collected from philopatric striped mice of 6 weeks old minimum
148 (born in the previous breeding season between July and December), since we know
149 striped mice can breed from that age (Schoepf and Schradin, 2013; Schradin and Pillay,
150 2004). Striped mice had to survive the pre-breeding season from summer to onset of
151 winter (January-June) to reproduce during the subsequent breeding season, usually
152 starting in July. We did not include breeders because less than 1% of them survive their
153 second dry season (Schradin, unpublished data), making it impossible to study the effects
154 of corticosterone on dry season survival in breeders. Summers are hot and dry with low
155 food availability, while rains in autumn/winter increases food availability. The onset of
156 rain varies, such that the period of food shortage (less than 4 food plants/2sqm associated
157 with physiological parameters of starvation: reduced blood glucose levels and increased
158 blood ketone levels; Schradin, unpublished data) varies from year to year (Table 1).
159 Animal ethics clearance for our study was provided by the University of the
160 Witwatersrand (AESC 2007/10/01 and 2007/39/04).

161

162 *Trapping, behavioural observations and radio-tracking*

163 The study population has been continuously monitored since 2002 by a combination of
164 trapping, behavioural observations and radio-tracking (Schradin, 2006; Schradin and
165 Pillay, 2004). Striped mice live in groups consisting of one breeding male, 1-4 breeding
166 females, and non-reproductive offspring of both sexes that remain in their natal group
167 after reaching adulthood (Schradin and Pillay, 2004). We typically monitored 12 focal
168 groups at one time, although groups went extinct and new groups were formed every
169 year. Each group was trapped at least twice a month at its nesting site for 3 days
170 (minimum of 6 days per month) and observed at least twice a month for two days
171 (minimum of 4 days per month) to confirm group composition.

172 Trapping was done with locally produced metal traps of Sherman style, baited
173 with a mixture of bran flakes, sunflower oil, and dried currants. Trapped striped mice
174 were weighed (± 1 g), sexed, and permanently marked with ear tags (National Band and
175 Tag Co., USA). All individuals above 25g were marked with hair dye (Inecto Rapido,

176 Pinetown, South Africa) to facilitate individual recognition during behavioural
177 observations. Each group had at least one adult breeder (which was not part of the study)
178 carrying a collar-mounted radio-transmitter (models BD-2C and PD-2C, Holohil,
179 Canada; hereafter referred as transmitter). Striped mice that were initially trapped at a
180 nest as juveniles (body mass < 30g) and trapped there subsequently were regarded as
181 being philopatric to that group (as opposed to immigrants).

182

183 *Food availability*

184 Striped mice do not cache food but feed on plant leaves (Schradin and Pillay, 2006).
185 Plant surveys were conducted on the 15th of each month, using the Braun-Blanquet
186 Method (Werger, 1974). The number of food plants species (palatability known from
187 behavioural observations; Schradin and Pillay, 2006) was recorded in each of eight
188 monitoring plots of 2 x 2 m on the field site, located within the home ranges of eight
189 different groups), and values were averaged monthly over all the plots. Every year, the
190 mean value covering the period from January to June was then used as an estimate of
191 food availability over the pre-breeding season.

192

193 *Population density*

194 Population density was calculated every year as the number of striped mice per hectare,
195 based on the total number of striped mice present at the onset of the pre-breeding season
196 (January) and the size of the field site estimated using Google Earth.

197

198 *Predation pressure*

199 Predation pressure during the pre-breeding season was estimated as the percentage of
200 striped mice carrying transmitters known to have been predated among the total number
201 of striped mice with transmitters. On average, 13.2 ± 4.9 mice were carrying transmitters
202 during the dry season, typically one or two mice per group. As the number of groups
203 varied less between years than group size, this led to a larger variation of the percentage
204 of mice from the total population carrying transmitters ($11.1 \pm 10.8\%$ of the population,
205 ranging from 3.3% in the year with highest population density to 37.4% in the year with
206 lowest density). A striped mouse's death was attributed to predation when its transmitter

207 was found lying in an open area (indicating the individual had been eaten by a mammal
208 or a raptor at this spot), at a predator's den or nest, or inside a snake.

209

210 *Disappearance probability*

211 To determine when individuals disappeared from the population, trapping was performed
212 continuously throughout the year and continued after the present study ended. A striped
213 mouse was regarded as having disappeared after it had not been trapped and not been
214 observed for at least one year, more than the average life span of striped mice at our site.
215 The last day an individual was trapped was therefore determined as its day of
216 disappearance. Striped mice initiate long-distance dispersal (outside of our study area) at
217 the onset of the breeding season, dispersal being male biased although females also
218 disperse (Solmsen et al., 2011). The breeding season typically starts in July/August, and
219 thus striped mice that were still present on the 1st of July were regarded as having
220 survived the pre-breeding season.

221

222 *Immigration*

223 Immigration was determined every month between 2005 and 2016 from the number of
224 adult individuals that immigrated into the field site. This included males that immigrated
225 into existing groups as the new breeding male, females that formed new groups (one or
226 several adult females), and solitary breeding males (roamers) that did not originate from
227 the field site.

228

229 *Blood sampling and basal corticosterone levels*

230 Striped mice were trapped early in the morning before they left their nest to forage. Basal
231 corticosterone levels have a circadian rhythm and striped mice display higher
232 corticosterone levels in the morning than in the afternoon (Schradin, unpublished data).
233 To avoid any bias, all samples were collected within the first hour after the sun started to
234 illuminate the field site and striped mice became active (Schradin et al., 2007). Traps
235 were observed (average distance of 10m) so that as soon as a striped mouse entered a
236 trap, it was removed. Striped mice were anaesthetized with diethyl ether and blood was
237 sampled from a sub-lingual vein. The vein was pricked with a needle and blood was

238 collected in a 2mL Eppendorf tube. The entire procedure (i.e. from the moment a striped
239 mouse entered a trap until the end of blood sampling) lasted no longer than 3min (mean \pm
240 sd: 2.68 ± 0.38 min, min-max: 1.40-3.00min), a period short enough to ensure the
241 measurement of basal, rather than stress-induced, corticosterone levels (correlation
242 between corticosterone levels and sampling time: Pearson $r = -0.02$, $n = 325$, $p = 0.737$;
243 Romero and Reed, 2005). Striped mice were weighed after blood collection. Blood was
244 left to clot at room temperature (approx. 25°C) for 45 min, centrifuged to allow the
245 extraction of the serum, which was then stored at -20°C . Serum samples were analysed
246 for total corticosterone using commercial ELISA kits (Immuno Biological Laboratories,
247 Hamburg; previously validated for striped mouse serum; Schradin, 2008). For two
248 different pools, intra-assay variability was 4.0% and 9.4%, inter-assay variability was
249 8.1% and 17.2%.

250

251 *Statistical analyses*

252 Blood samples collected each year from mid-January to mid-February (onset of the pre-
253 breeding season) were used for the survival analysis. At this time of the year, food
254 availability was already low (Table 1) compared to the breeding season when the food
255 plant index was above 5.0. For cases where the same individual had been sampled more
256 than once over the period of interest, we considered the blood sample collected the
257 closest to the 1st of February in the analysis. In total, data from 331 striped mice (159
258 males and 172 females) were considered in the analysis.

259 Data were analysed with R 3.4.2 (R Development Core Team, 2008).
260 Repeatability of basal corticosterone levels was examined using a second measurement
261 from 65 (31 males and 34 females) out of the 331 individuals. Paired measurements were
262 taken less than 7 weeks apart between January and March. The repeatability coefficient
263 (R), its standard error (se) and the 95% confidence intervals (CI) were calculated from
264 paired data using the 'rptR' package.

265 Survival over the pre-breeding season was analysed using a Cox Proportional
266 Hazards model (function 'coxph' of the 'survival' package), with survival time since the
267 1st of January being the dependent variable. The censoring date (i.e. time from which
268 survival was no longer monitored) was set to the 1st of July to coincide with the onset of

269 both mating and male long-term dispersal, when immigration peaks (see results).
270 Survival time was then calculated as the number of days from the 1st of January till last
271 trapped or censoring date if still present and trapped later. In addition to basal
272 corticosterone levels measured at the onset of the pre-breeding season, the initial model
273 also included the following set of intrinsic and extrinsic factors: body mass at the onset of
274 the pre-breeding season as an indicator of body condition; sex - behaviour is sex specific
275 (e.g. male biased dispersal) and the reasons of disappearance may differ between sexes;
276 mean food availability over the pre-breeding season as an indicator of the harshness of
277 the pre-breeding season; predation pressure throughout the pre-breeding season as the
278 percentage of striped mice that had transmitters being predated; and population density at
279 the onset of the pre-breeding season as the number of adult striped mice/ha present in
280 January. The interactions of basal corticosterone level with body mass, sex, duration of
281 the pre-breeding season and each of the three environmental variables were also included
282 in the initial model since: 1. leaner individuals could suffer from allostatic overload due
283 to elevated corticosterone levels, while larger ones may be able to better cope allostatic
284 overload thanks to their body reserves; 2. corticosterone may modulate sex-specific
285 behaviours and strategies, resulting in one sex being more sensitive than the other to
286 elevated corticosterone levels; 3. the effect of corticosterone levels on survival might
287 depend on the harshness of the pre-breeding season, with elevated levels being
288 detrimental to survival only when food availability is low; 4. the effect of corticosterone
289 levels may differ according to predation pressure, with elevated levels being
290 advantageous only when predation level was high and energy is required to escape
291 predators; and 5. the effect of corticosterone levels might also be density-related, with
292 elevated levels triggering dispersal in individuals of low competitive ability under low
293 population density. The model also included a frailty term which allows for fitting a
294 random effect for year, since data were collected over multiple years. We checked
295 whether our initial model satisfied the proportional hazard assumption using scaled
296 Schoenfeld residuals. Because there was evidence for non-proportional hazard for sex,
297 we computed a second model where sex was including as a stratifying variable (allowing
298 different baseline hazard functions for males and females). The Schoenfeld residuals of
299 this final stratified model no longer indicated non-proportionality. Note that this

300 procedure prevents from examining the effect of the stratifying covariate, but because
301 neither sex nor any of its interaction with corticosterone were significant in the initial
302 model, we considered the model with sex as a stratifying variable. Nonlinearity was
303 checked through visual inspection of Martingale residuals, which exhibited no obvious
304 trends. The significance level was set to $p \leq 0.05$.

305 Significant effects of covariates on hazard ratios and marginal effects of
306 covariates in interactions were visualized by parametric simulations (package ‘simPH’;
307 Gandrud, 2015). Ribbons indicate the areas containing the central 95% and 50% of 1000
308 simulations, respectively, reflecting an empirical confidence interval. All variables were
309 standardized (mean = 0 and sd = 1) so that estimates and simulations refer to effects with
310 all other covariates set to their means, and effect sizes are in units of standard deviation.
311 Increased hazard ratios therefore reflect increased disappearance rate relative to the
312 average rate at mean covariate values and increased marginal effects reflect increased
313 effect size at the respective value of the interacting covariate. Immigration and
314 disappearance rates were compared using paired t-tests and effect sizes for these paired
315 analyses are reported as Cohen’s d estimates.

316

317 **Results**

318 *Inter-individual variation and intra-individual repeatability for baseline corticosterone*

319 Inter-individual variation in basal corticosterone levels at the onset of the pre-breeding
320 season was large, ranging from 134 to 2577 ng.mL⁻¹ (mean \pm sd = 978.54 \pm 451.2 ng.mL⁻¹).
321 Nonetheless, corticosterone levels measured at that same period of the year were
322 repeatable among individuals ($R = 0.51$, se = 0.09, CI = 0.30-0.67, $p < 0.001$; Fig. 1).
323 Corticosterone levels did not significantly differed between sexes (991.5 \pm 491.6 versus
324 966.5 \pm 411.3 ng.mL⁻¹ for males and females, respectively; $t_{329} = 0.502$, $p = 0.616$).

325

326 *Variation of environmental conditions among years*

327 Mean food availability over the pre-breeding season significantly varied between years
328 (Kruskal-Wallis $\chi^2 = 17.128$, df = 5, $p = 0.004$), indicating that the six generations of
329 striped mice considered in this study experienced pre-breeding seasons of different

330 harshness. Population density and predation pressure also varied considerably among
331 years (Table 1).

332

333 *Corticosterone and disappearance probability*

334 High basal corticosterone levels were associated with increased disappearance probability
335 in light but not heavy individuals (significant interaction baseline corticosterone x body
336 mass; Table 2; Fig. 2). None of the interactions between baseline corticosterone and food
337 availability, population density and predation pressure were significant. Environmental
338 conditions impacted disappearance probability, since disappearance was positively
339 related to both food availability and predation pressure (Table 2; Fig. 3a,b).

340

341 *Immigration and disappearance throughout the year*

342 Immigration and disappearance occurred in all months, including the pre-breeding
343 season, but both peaked at the onset of the breeding season (July-August; Fig. 4).
344 Immigration rate (males: $3.0 \pm 1.7\%$ of adult population, females $1.3 \pm 0.2\%$ of adult
345 population) was always lower than disappearance rates (males: $7.90 \pm 6.4\%$ of adult
346 population, paired $t_{11} = 2.816$, $p = 0.02$, Cohen's $d = 0.85$; females $7.58 \pm 4.31\%$ of adult
347 population, paired $t_{11} = 5.230$, $p < 0.001$, Cohen's $d = 1.57$). The Cohen's d estimates
348 indicate that we can accept with great confidence that the disappearance rates are greater
349 than immigration, suggesting that disappearance represented death in most cases (even if
350 occurring during dispersal, see discussion). More males than females immigrated (paired
351 $t_{11} = 4.117$, $p = 0.002$; Cohen's $d = 1.24$), while there was no sex difference in the
352 probability of disappearance, neither for the entire year (paired $t_{11} = 0.1896$, $p = 0.85$;
353 Cohen's $d = 0.06$), nor for the pre-breeding season alone (paired $t_5 = 0.129$, $p = 0.90$
354 Cohen's $d = 0.06$). The extremely low Cohen's d estimates support the non-significant
355 sex differences.

356

357 **Discussion**

358 Our long-term analysis of the relationship between baseline corticosterone and
359 disappearance in a natural population of striped mice indicates that elevated basal
360 corticosterone levels were associated with higher risk of disappearance in light but not

361 heavy individuals. This suggests either that high corticosterone levels are increasing
362 mortality risk in striped mice of low body mass, or that they trigger dispersal in striped
363 mice of low body mass. Although the fitness costs of glucocorticoids were expected to be
364 stronger under harsh conditions, none of the interactions between basal corticosterone
365 levels and any of the environmental variables considered here was significant.
366 Disappearance risk nevertheless increased under high predation pressure, and more
367 surprisingly also under high food availability, which might support the hypothesis of
368 corticosterone mediating dispersal.

369 Previous short-term field studies found mixed support for the cort-fitness
370 hypothesis, which postulates that glucocorticoids negatively relate to fitness (Bonier et
371 al., 2009; Crespi et al., 2013; Hau et al., 2016). This hypothesis is based on the idea that
372 elevated basal glucocorticoid levels could serve as physiological indicators of poor
373 individual condition or health and thus of low fitness, especially under harsh
374 environmental conditions (Bonier et al., 2010, 2009). The pre-breeding season in the
375 natural habitat of our study population is characterised by low food and water availability
376 combined with ambient temperatures regularly exceeding 40°C at ground level, where
377 striped mice live. Striped mice must survive these harsh conditions to reach the next
378 breeding season. It has been shown previously that the health status (evaluated through
379 12 different blood parameters) at the onset of the pre-breeding season was related to
380 survival probability in our study population, and that health progressively deteriorates
381 over the pre-breeding season (Schoepf et al., 2016). More importantly, striped mice that
382 disappeared had impaired health status compared to survivors, especially blood
383 parameters indicative of nutritional state (albumin, glucose and total protein; Schoepf et
384 al., 2016). In contrast, here we found no evidence for an overall negative effect of
385 corticosterone, as we showed that elevated basal corticosterone levels were associated
386 with increased disappearance risk in light but not heavy individuals. This suggests that
387 high corticosterone levels in the pre-breeding season might only indicate poor condition
388 in individuals of lower body mass.

389 Body mass might correlate with overall condition, in which case striped mice of
390 low body mass would be more sensitive to the physiological costs of elevated
391 corticosterone levels, resulting in increased mortality risk and thus disappearance.

392 Individuals exhibiting high basal glucocorticoid levels face the risk of increased energy
393 expenditure, since glucocorticoids stimulate activity by mobilising energy stores (Reeder
394 and Kramer, 2005; Sapolsky et al., 2000). This could be detrimental when energy
395 availability is low, and particularly so for lean individuals with limited body reserves.
396 These individuals could enter allostatic overload (i.e. negative energy balance) much
397 more rapidly, with potential detrimental consequences for their physiology and health,
398 and ultimately their fitness (McEwen and Wingfield, 2010, 2003; Romero et al., 2009). In
399 contrast, heavier individuals with greater body reserves could be more capable of
400 overcoming energy shortage, preventing them going into allostatic overload. Endogenous
401 energy reserves (i.e. fat stores) might serve as a buffer against energetically constraining
402 conditions. In Galapagos marine iguanas (*Amblyrhynchus cristatus*), the increase in
403 corticosterone in response to an environmental challenge was disproportionately higher as
404 body condition worsened (Romero and Wikelski, 2001), supporting the idea that
405 glucocorticoids and body condition can covary in a nonlinear manner, with potentially
406 different effects on fitness.

407 Elevated basal corticosterone levels could also trigger dispersal in individuals of
408 lower competitive ability, thus accounting for the positive association between
409 corticosterone and disappearance in striped mice of low body mass. Glucocorticoids are
410 thought to influence dispersal behaviour in mammals (Wada, 2008), including the striped
411 mouse (Schoepf and Schradin, 2013) in which small individuals of low competitive
412 ability are more likely to disperse (Solmsen et al., 2011). The most competitive males
413 only disperse into neighbouring territories, where they become breeders with high
414 reproductive success (Schradin and Lindholm, 2011). Although dispersal is male-biased
415 in striped mice, females also disperse (Solmsen et al., 2011). Hence, the significant
416 interaction between corticosterone and body mass may reflect different dispersal
417 strategies among individuals with high corticosterone levels, where small individuals
418 leave while larger competitive individuals would remain in the study population.

419 The success of light striped mice initiating long-distance dispersal to emigrate
420 into another population remains unknown, however. Dispersing striped mice must travel
421 up to several kilometres over unoccupied and unsuitable habitat until they find (or not)
422 another population along another dry riverbed (see Fig. 1 in Solmsen et al., 2011), and

423 such behaviour is expected to be risky and to induce high mortality. This hypothesis is
424 supported by the comparison of long-term immigration data in our field site with
425 disappearance from the population over the course of the study (Fig 4). Around five times
426 more males, and eight times more females, disappeared than immigrated over the pre-
427 breeding season. If most striped mice which disappear from a population disperse and
428 successfully join other populations, the difference between disappearance and
429 immigration rates should not be so marked, and immigration rate would likely be closer
430 to disappearance rate. However, a lower immigration rate into our study population
431 suggests that most striped mice that left their natal population did not reach another
432 population, indicating that most striped mice that disappeared likely died, including those
433 which dispersed. This supports the idea that dispersal is a risky strategy associated with
434 high fitness costs. Overall, our results suggest that elevated corticosterone levels in
435 striped mice of low (but not high) competitive ability (i.e. low body mass) could be
436 regarded as an indicator of low fitness, either through direct deleterious physiological
437 effects or through dispersal-induced mortality.

438 While increased disappearance probability under higher predation pressure was
439 expected and supports our approach, the positive association between food availability
440 and disappearance risk seemed counterintuitive at first. Instead, we predicted a negative
441 association, as well as the effects of elevated corticosterone to be more pronounced when
442 food availability (and thus energy availability) was low. Indeed, striped mice are more
443 likely to disperse when food availability was high (Schoepf and Schradin, 2012),
444 meaning that higher food abundance would promote dispersal. Furthermore, a
445 demographic study conducted on the same population from a larger capture-mark
446 recapture dataset (1609 females over 11 years) also documented that female striped mice
447 disappearance was positively related to food availability and likely due to dispersal
448 (Nater et al., 2016). Additionally, previous studies showed that philopatric male striped
449 mice with high corticosterone levels are more likely to disperse than males with low
450 corticosterone levels under low population density (Schoepf and Schradin, 2013, 2012).
451 However, we found no evidence that population density or its interaction with
452 corticosterone, influenced disappearance risk. Altogether, these results indicate that food
453 availability might be an important ecological factor influencing dispersal, and that this

454 risky behaviour could be modulated by the interplay between basal corticosterone levels
455 and individual condition.

456 The diverse results from studies that investigated the relationship between
457 glucocorticoids and fitness (Bonier et al., 2009) implies that the fitness consequences of
458 elevated glucocorticoid levels could be species and context specific (Hau et al., 2016).
459 Importantly, the endocrine phenotype reflects a plastic response where hormone levels
460 are adjusted according to specific environmental conditions and current individual
461 condition, including social tactic, reproductive and nutritional states (Crespi et al., 2013;
462 Hau et al., 2016). Thus, between individual variation in basal hormone levels might not
463 be related to fitness if different levels represent individually optimised levels (Bonier and
464 Martin, 2016). The strength and direction of the relationship between glucocorticoids and
465 fitness might also depend on environmental conditions (Henderson et al., 2017). Apart
466 from basal glucocorticoid levels, stress-induced levels would be interesting to measure in
467 striped mice, together with the form of their stress response. Indeed, stress-induced
468 glucocorticoid levels in barn swallows have been reported to predict their offspring
469 survival (Vitousek et al., 2014), and the negative feedback of the stress response in
470 marine iguanas to predict their survival during starvation (Romero, 2012). Although we
471 considered the interaction between basal corticosterone levels and different
472 environmental variables, we found no evidence that the relationship varied according to
473 environmental harshness. For striped mice, surviving the long pre-breeding season is
474 critical, but basal glucocorticoid levels were only related to survival in individuals of low
475 body mass. This result partially supports the cort-fitness hypothesis, while also adding to
476 the growing evidence that glucocorticoids might be important physiological mediators of
477 dispersal.

478

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493

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624 developing synthesis between endocrinology and evolutionary genetics. *Annu. Rev. Ecol.*
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626

627 **Tables and figures captions**

628

629 Table 1. Monthly food availability from January to June (mean number of food plant
630 species averaged over 8 monitoring plots of 4sqm), food availability during the pre-
631 breeding season (mean \pm sd over the 6-month period), population density (number of
632 striped mice per hectare) and predation pressure (percentage of predated striped mice
633 carrying transmitter, T) from 2009 to 2014.

634

635 Table 2. Cox proportional hazards model testing for the effects of baseline corticosterone,
636 body mass, food availability, population density, predation pressure, and the two-way
637 interactions of corticosterone with each of the other covariates, on striped mice
638 disappearance over the pre-breeding season (n = 331). All variables were standardized
639 (mean = 0 and sd = 1). Sex was included as a stratifying variable to correct for non-
640 proportional hazard and year was included as a frailty term since data were collected over
641 multiple years. Hazard ratios [exp(coef)] and their 95% confidence intervals (CI) are
642 presented. Significant effects are marked in bold.

643

644 Figure 1. Repeatability of baseline corticosterone at the onset of the pre-breeding season
645 in free-ranging striped mice (n = 66 paired measurements; black and grey circles indicate
646 males and females, respectively). Values on the x-axis are those used for the survival
647 analysis while values on the y-axis correspond to a second measurement for the same
648 individuals within less than 7 weeks.

649

650 Figure 2. The risk of disappearance from the population increased with elevated basal
651 corticosterone levels for light but not heavy individuals in free-ranging striped mice (Cox
652 proportional hazard model, n = 331, significant interaction baseline corticosterone x body
653 mass). The simulated marginal effects (line), 50% (dark blue shaded area) and 95% (light
654 blue shaded area) confidence intervals are shown.

655

656 Figure 3. Relationship between disappearance risk and food availability (a) and predation
657 pressure (b) during the pre-breeding season for free-ranging striped mice (Cox

658 proportional hazard model, $n = 331$). The simulated hazard ratio (line), 50% (dark blue
659 shaded area) and 95% (light blue shaded are) confidence intervals are shown.

660

661 Figure 4. Percentages of males (black boxes) and females (grey diamonds) that
662 disappeared from the population (solid lines; averaged over 6 years) and that immigrated
663 into the field site (dashed lines; averaged over 12 years) per month.

664

665 **Table 1**

Year	Monthly food availability						Food availability	Population density	Predation pressure
	(nb food plants averaged over 8 plots)						(mean \pm sd)	(mice/ha)	(% disappeared mice with T)
	<i>Jan</i>	<i>Feb</i>	<i>Mar</i>	<i>Apr</i>	<i>May</i>	<i>Jun</i>	<i>Pre-breeding season</i>		
2009	3.00	3.25	3.5	3.88	4.00	5.00	3.77 \pm 0.71	48.6	7.6
2010	2.25	2.13	3.13	2.75	2.88	3.63	2.79 \pm 0.56	28.3	17.5
2011	2.25	2.00	2.38	1.88	2.50	3.63	2.44 \pm 0.63	13.9	11.7
2012	2.00	1.75	1.63	1.00	1.38	2.13	1.65 \pm 0.41	30.3	7.5
2013	2.75	2.50	2.00	1.38	6.13	5.75	3.42 \pm 2.01	37.6	12.9
2014	2.25	2.25	1.75	1.63	3.00	3.00	2.31 \pm 0.59	39.8	18.8

666

667

668 **Table 2**

Variable	Coef	SE	Chisq	df	Hazard Ratio	95% CI	<i>p</i>
Baseline corticosterone	0.048	0.085	0.31	1	1.049	0.888–1.239	0.580
Body mass	0.026	0.083	0.10	1	1.027	0.873–1.208	0.750
Food availability	0.227	0.097	5.54	1	1.255	1.039–1.516	0.019
Population density	-0.003	0.089	0.00	1	0.997	0.837–1.189	0.980
Predation pressure	0.214	0.088	5.85	1	1.238	1.041–1.473	0.016
Corticosterone x Body mass	-0.246	0.087	8.06	1	0.782	0.660–0.927	0.005
Corticosterone x Food availability	-0.048	0.100	0.24	1	0.953	0.784–1.158	0.630
Corticosterone x Population density	-0.051	0.084	0.36	1	0.951	0.807–1.121	0.550
Corticosterone x Predation pressure	0.047	0.085	0.31	1	1.049	0.888–1.238	0.580

669