BIOLOGY LETTERS

rsbl.royalsocietypublishing.org

Research

**Cite this article:** Schradin C, Pillay N, Kondratyeva A, Yuen C-H, Schoepf I, Krackow S. 2015 Basal blood glucose concentration in free-living striped mice is influenced by food availability, ambient temperature and social tactic. *Biol. Lett.* **11**: 20150208. http://dx.doi.org/10.1098/rsbl.2015.0208

Received: 16 March 2015
Accepted: 27 April 2015

**Subject Areas:**
ecology, evolution, behaviour

**Keywords:**
homeostasis, allostasis, phenotypic flexibility, physiological adaptation

**Author for correspondence:**
Carsten Schradin
e-mail: carsten.schradin@iphc.cnrs.fr

Electronic supplementary material is available at http://dx.doi.org/10.1098/rsbl.2015.0208 or via http://rsbl.royalsocietypublishing.org.

THE ROYAL SOCIETY PUBLISHING

Physiology

# Basal blood glucose concentration in free-living striped mice is influenced by food availability, ambient temperature and social tactic

Carsten Schradin[1,2,3,4], Neville Pillay[3], Anna Kondratyeva[1,2], Chi-Hang Yuen[3], Ivana Schoepf[3,4] and Sven Krackow[5]

[1]University of Strasbourg Institute for Advanced Study (USIAS), Strasbourg, France
[2]CNRS, UMR7178, 67087 Strasbourg, France
[3]School of Animal, Plant and Environmental Sciences, University of the Witwatersrand, Johannesburg, South Africa
[4]Institute of Evolutionary Biology and Environmental Studies, University of Zurich, Zurich, Switzerland
[5]XBehavior GmbH, Bänk Dägerlen, Switzerland

Vertebrates obtain most of their energy through food, which they store mainly as body fat or glycogen, with glucose being the main energy source circulating in the blood. Basal blood glucose concentration (bBGC) is expected to remain in a narrow homeostatic range. We studied the extent to which bBGC in free-living African striped mice (*Rhabdomys pumilio*) is influenced by ecological factors with a bearing on energy regulation, i.e. food availability, abiotic environmental variation and social tactic. Striped mice typically form extended family groups that huddle together at night, reducing energetic costs of thermoregulation, but solitary individuals also occur in the population. We analysed 2827 blood samples from 1008 individuals of seven different social categories that experienced considerable variation in food supply and abiotic condition. Blood samples were taken from mice in the morning after the overnight fast and before foraging. bBGC increased significantly with food plant abundance and decreased significantly with minimum daily ambient temperature. Solitary striped mice had significantly higher bBGC than group-living striped mice. Our results suggest that adaptive responses of bBGC occur and we found large natural variation, indicating that bBGC spans a far greater homeostatic range than previously thought.

## 1. Introduction

Energy is the driver of life. Animals take up energy from food in the form of fat, proteins and carbohydrates, but glucose is the main fuel circulating in the blood [1]. Blood glucose concentrations are held constant homeostatically, keeping the basal concentration within a narrow range [2]. Regulation of basal blood glucose concentrations (bBGC), defined as the stable overnight concentration, has been studied intensively [1,3]: blood glucose homeostasis is achieved through a coordinated action of several organs and hormones, which in turn are regulated by the central nervous system. However, there is significant genetic variation in bBGC (e.g. between laboratory mouse strains [4]), suggesting that adaptive responses to environmental variation can be selected for.

In humans, low bBGC can impair physical and cognitive performance [5,6]. In wild animals, similar effects of low bBGC could have significant fitness consequences. A range of interacting factors may cause deviation of bBGC, but so far these factors have not been studied simultaneously. For instance, bBGC can be influenced by body mass [7], age [8], sex [9] and ambient temperature [10]. Moreover, bBGC decreases during fasting [11] and is typically lower at times of low

**Table 1.** ANOVA table for the fixed effects on bBGC (log[mM]) with Satterthwaite approximation for denominator degrees of freedom (DDF). Slopes (*b*) with s.e. are also given. Significant effects are marked in bold. NDF, nominator degrees of freedom.

| fixed effect | *b* (×100) | s.e. | *F* (DDF, NDF) | NDF | DDF | *p*-value |
|---|---|---|---|---|---|---|
| **abundance of food plants** | 0.324 | 0.109 | 8.79 | 1 | 758.21 | **0.003** |
| *Zygophyllum* fruits | −1.172 | 0.794 | 2.17 | 1 | 583.61 | 0.14 |
| seedlings | −0.015 | 0.021 | 0.51 | 1 | 421.86 | 0.48 |
| rain | 0.435 | 0.643 | 0.46 | 1 | 2522.30 | 0.50 |
| **minimum temperature** | −0.360 | 0.151 | 5.73 | 1 | 1091.13 | **0.02** |
| duration of overnight fast | 1.507 | 0.887 | 2.89 | 1 | 955.00 | 0.09 |
| **social category** | | | 2.59 | 6 | 2724.06 | **0.02** |

food availability [12,13]. However, a clear link between food availability and bBGC is lacking, since seasonal differences also include differences in temperature and rainfall, which would influence energetic regulation.

Our aim was to understand how seasonally varying ecological factors influence bBGC in a free-living mammal that can be group-living or solitary. We analysed 2827 measurements of bBGC in diurnal, free-ranging African striped mice (*Rhabdomys pumilio*), collected over 5 years under varying environmental conditions. Striped mice live in an environment with significant seasonal changes in food availability, which additionally varies among years. We tested the hypothesis that food availability, as a main determinant of energy flow, is correlated with bBGC. We considered three food types: annual plants, which have high glucose content and determine the duration of the breeding season [14]; seedlings, which are high in protein content [14]; fruits of the succulent shrub *Zygophyllum retrofractum* (expected to be high in glucose content), which is fruiting at the beginning of the dry season, and could thus act as a buffer against decreasing availability of annual food plants. As thermoregulation during nights is energetically expensive in this species [15], we tested for the effects of daily minimum temperature, precipitation and duration of the overnight fast. Striped mice show social flexibility, with solitary and group-living individuals occurring in the same population [16]. Hence, we predicted that social tactic might have an impact on bBGC, because huddling in groups reduces energy expenditure at night [15].

## 2. Material and methods

We conducted the study in the Succulent Karoo semi-desert of South Africa, which is characterized by moist winters, followed by high food abundance in spring and hot dry summers with low food abundance, and high seasonal variation among years. We collected data from April 2009 until May 2014 from 12 striped mice groups on a 10 ha field site. Groups consisted of one breeding male, one to four breeding females and their non-reproductive offspring of both sexes that remain in their natal group after reaching adulthood [16]. We designated non-breeding individuals as 'juveniles' when body mass was less than 30 g, and 'philopatrics' when adult. Solitary males were referred to as 'roamers'. We determined social tactics of striped mice by using a combination of trapping, behavioural observations and radio-tracking [16]. Striped mice feed mainly on plants (more than 99%) [14], and plant surveys have been conducted on the 15th of each month and additionally on the 1st of each month since 2013 in eight monitoring plots of 4 $m^2$ each, using the Braun–Blanquet method [17]. We recorded the percentage of the area covered by edible plant specimens of 27 different species, palatability of which was known from behavioural observations [14]. On the same days, we recorded the fruiting status from 10 *Zygophyllum retrofractum* shrubs, using four categories: 0: no fruit; 1: low abundance; 2: medium abundance; 3: high abundance of fruit. At the beginning of the dry season, striped mice at our field site feed on the fruit of these shrubs, which was thought to possibly buffer the decreasing availability of annual food plants.

We trapped striped mice early in the morning before they left their nest to forage, to obtain bBGC after the overnight fast and before onset of pronounced physical activity and foraging. As soon as a mouse entered a trap, it was removed, and anaesthetized with diethyl ether, and a drop of blood was obtained from a sub-lingual vein. bBGC was measured using the One Touch Ultra Glucometer (LifeScan, Inc., Milpitas, CA, USA). For validation, 13 individuals were measured twice the same morning ($r = 0.75$, $p = 0.003$; paired $t_{12} = 1.0652$, $p > 0.30$).

We applied a linear mixed model using the 'lme4' package of v. 3.1.1 of R [18] with log-transformed bBGC as the dependent variable. Fixed factors were minimum daily temperature, precipitation, average number of seedlings growing on the plot areas, fruiting status of *Zygophyllum retrofractum* shrubs and abundance of food plants (sum of percentage area covered by each of the 27 food plant, averaged over the eight plots). Values of nutritional variables were estimated by linear approximation between survey dates. We included a seven-level categorical variable called 'social category' separating adult male breeders, male philopatrics, roamers, female breeders and female philopatrics, as well as juvenile males and females. Time of day each animal was trapped was added as a covariate, because it reflects duration of overnight fasting (in winter, sunrise is later and mice spend up to 2 h more in the nest than in summer). Individual identity as a random factor was omitted from the main analysis, as its variance component was close to zero. We included the sampling event at any nest (all mice sampled the same day at the same nest representing one event) as a random factor. In total, 2883 blood glucose measurements from 751 nest sampling events were available, but four outlying values below 2 and 52 values above 12 mM were excluded from the main analysis, to reach normality of residuals in the statistical model (Shapiro–Wilk test, $p > 0.1$). Inclusion of all data yielded similar parameter estimates with identical significance level pattern (see the electronic supplementary material).

## 3. Results

Social tactic affected bBGC significantly (cf. table 1), with solitary roaming males exhibiting significantly higher bBGC than the other adult social categories ($p < 0.05$; figure 1), but

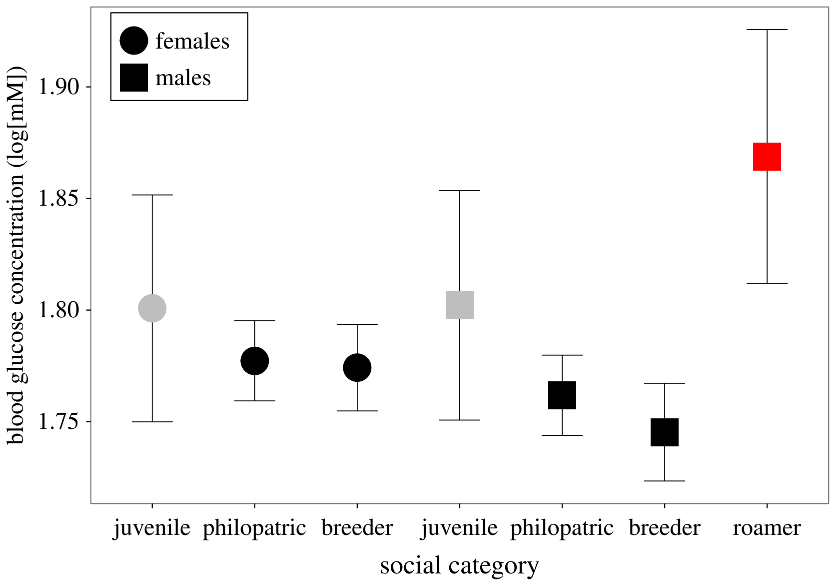


**Figure 1.** Basal blood glucose levels (least-squares means, 95% CI) for the social categories. Solitary roaming males had significantly higher levels than all other adult groups ($p < 0.05$) but not juveniles ($0.05 < p < 0.1$). (Online version in colour.)

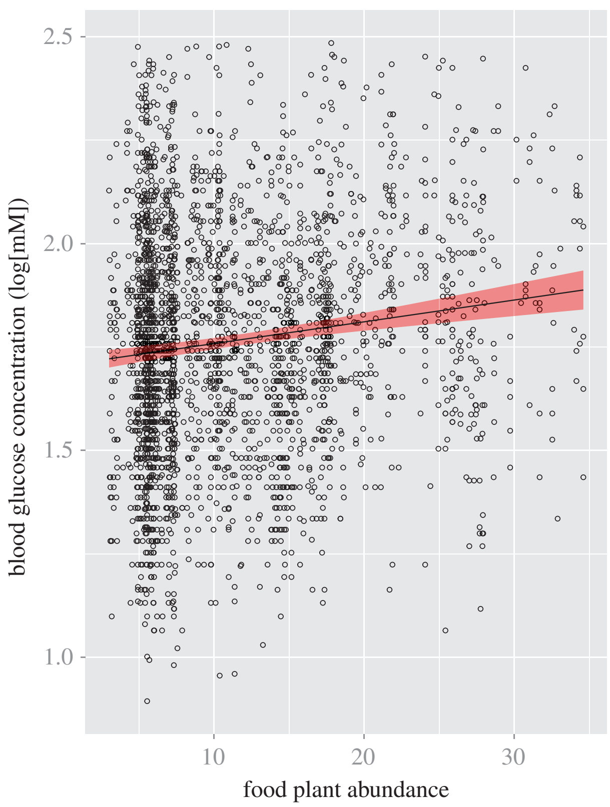


**Figure 2.** Basal blood glucose level increased significantly with increasing food plant abundance (linear regression line with 99% CI). (Online version in colour.)

non-significantly higher bBGC than juveniles ($0.1 > p > 0.05$). bBGC increased significantly with food plant availability (figure 2), in all study years (see figure in the electronic supplementary material). bBGC decreased significantly with daily minimum temperature, while the other factors did not reach significance (table 1).

## 4. Discussion

bBGC varies considerably between mammalian species, ranging from 3 to 28 mM [3], but is believed to be maintained within a narrow range within a single species [2]. Intraspecific variation in blood glucose concentration has been explained as being either non-basal or pathological [19]. By contrast, we found that ecological factors of food plant abundance and low temperatures have a significant influence on bBGC of free-ranging rodents after an overnight fast.

The abundance of food plants had the most significant effect on bBGC, while protein-rich seedlings did not correlate with bBGC, and the *Zygophyllum retrofractum* fruits did not act as a buffer against decreasing availability of annual food plants at the beginning of the dry season. Minimum ambient temperature was related to bBGC, but we found that neither rainfall nor duration of the overnight fast influenced bBGC. The colder it was in the morning, the higher the bBGC, which might be attributed to higher energy expenditure during colder nights. Striped mice reduce energy expenditure by sleeping in huddling groups [15]. The significantly higher bBGC measured in solitary roamers corroborates the supposition that higher energy expenditure increases bBGC, as living solitarily is energetically more expensive owing to the absence of overnight huddling. Moreover, roamers have larger home ranges and are exposed to territorial aggression on the part of the larger and stronger territorial males [16].

In conclusion, higher food availability, lower environmental temperature and social tactic were related to bBGC. Our findings point out that bBGC is much more variable than previously acknowledged, allowing for potentially adaptive responses to energetic constraints. Our study, which we believe is the first large-scale study on natural variation in bBCG in a free-ranging mammal, clearly shows that potentially adaptive responses to energetic constraints must be taken into account in order to understand the physiological regulation of blood glucose homeostasis, for example, the role of seasonal changes of glucocorticoids and thyroid hormones that, together with insulin, are at the basis of bBGC determination.

Ethics. Animal ethics clearance was provided by the University of the Witwatersrand (AESC 2007/10/01 and 2007/39/04).

Data Accessibility. The data are available as the electronic supplementary material.

Authors' Contributions. C.S. planned the study. C.S., C.H.Y., I.S. and N.P. coordinated the study. C.S., C.H.Y. and I.S. collected the data. C.S., A.K. and S.K. participated in data analysis. C.S., A.K. and S.K. wrote the manuscript, and C.H.Y., N.P. and I.S. commented repeatedly on it. All authors gave final approval for publication.

Competing Interests. We declare we have no competing interests.

Funding. Funding was provided by the Swiss National Science Foundation (31003A-135770/1 to C.S.), the University of the Witwatersrand, the University of Zurich, and the University of Strasbourg Institute for Advanced Study (to C.S.).

Acknowledgements. We thank Goegap Nature Reserve. We thank S. Blanc for valuable comments.

## References

1. Frayn NF. 2010 *Metabolic regulation: a human perspective*, 3rd edn. Oxford, UK: Wiley-Blackwell.
2. Bernard C. 1877 *Leçons sur le diabète et la glycogenèse animale*. Paris: Baillière.
3. Polakof S, Mommsen TP, Soengas JL. 2011 Glucosensing and glucose homeostasis: from fish to mammals. *Comp. Biochem. Physiol. B-Biochem. Mol. Biol.* **160**, 123–149. (doi:10.1016/j.cbpb.2011.07.006)
4. Svenson KL, Von Smith R, Magnani PA, Suetin HR, Paigen B, Naggert JK, Li R, Churchill GA, Peters LL. 2007 Multiple trait measurements in 43 inbred mouse strains capture the phenotypic diversity characteristic of human populations. *J. Appl. Physiol.* **102**, 2369–2378. (doi:10.1152/japplphysiol.01077.2006)
5. Rodriguez NR *et al*. 2009 Nutrition and athletic performance. *Med. Sci. Sports Exerc.* **41**, 709–731. (doi:10.1249/MSS.0b013e31890eb86)
6. Gilsenan MB, de Bruin EA, Dye L. 2009 The influence of carbohydrate on cognitive performance: a critical evaluation from the perspective of glycaemic load. *Brit. J. Nutr.* **101**, 941–949. (doi:10.1017/S0007114508199019)
7. Rosen ED, Spiegelman BM. 2006 Adipocytes as regulators of energy balance and glucose homeostasis. *Nature* **444**, 847–853. (doi:10.1038/nature05483)
8. McDonald RB. 1990 Effect of age and diet on glucose-tolerance in Sprague-Dawley rats. *J. Nutr.* **120**, 598–601.
9. Cetin N, Bekyurek T, Cetin E. 2009 Effects of sex, pregnancy and season on some haematological and biochemical blood values in angora rabbits. *Scand. J. Laborat. Anim. Sci.* **36**, 155–162.
10. Xue L, Liang HY, Jiang XF. 2012 Circannual temperature-related variation in hemoglobin a1c is unlikely to affect its use as a diagnostic test for type 2 diabetes. *Clin. Lab.* **58**, 481–488.
11. Harris SB, Gunion MW, Rosenthal MJ, Walford RL. 1994 Serum glucose, glucose-tolerance, corticosterone and free fatty-acids during aging in energy restricted mice. *Mechan. Ageing Develop.* **73**, 209–221. (doi:10.1016/0047-6374(94)90053-1)
12. Pambu-Gollah R, Cronje PB, Casey NH. 2000 An evaluation of the use of blood metabolite concentrations as indicators of nutritional status in free-ranging indigenous goats. *S. A. J. Anim. Sci.* **30**, 115–120. (doi:10.4315/sajas.v30i2.3859)
13. Larsen TS, Lagercrantz H, Riemersma RA, Blix AS. 1985 Seasonal changes in blood-lipids, adrenaline. noradrenaline, glucose and insulin in Norwegin reindeer. *Acta Physiol. Scand.* **124**, 53–59. (doi:10.1111/j.1748-1716.1985.tb07631.x)
14. Schradin C, Pillay N. 2006 Female striped mice (*Rhabdomys pumilio*) change their home ranges in response to seasonal variation in food availability. *Behav. Ecol.* **17**, 452–458. (doi:10.1093/beheco/arj047)
15. Scantlebury M, Bennett NC, Speakman JR, Pillay N, Schradin C. 2006 Huddling in groups leads to daily energy savings in free-living African four-striped grass mice, *Rhabdomys pumilio*. *Funct. Ecol.* **20**, 166–173. (doi:10.1111/j.1365-2435.2006.01074.x)
16. Schradin C, Lindholm AK, Johannesen J, Schoepf I, Yuen C-H, König B, Pillay N. 2012 Social flexibility and social evolution in mammals: a case study of the African striped mouse (*Rhabdomys pumilio*). *Mol. Ecol.* **21**, 541–553. (doi:10.1111/j.1365-294X.2011.05256.x)
17. Werger MJA. 1974 On concept and techniques applied in the Zürich-Montpellier method of vegetation survey. *Bothalia* **11**, 309–323.
18. R Core Team. 2014 *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. See http://www.R-project.org/.
19. Biddinger SB, Kahn CR. 2006 From mice to men: insights into the insulin resistance syndromes. *Ann. Rev. Physiol* **68**, 123–158. (doi:10.1146/annurev.physiol.68.040104.124723)