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Social stress is unlikely to play a major role in reproductive suppression of female subordinate naked mole-rats and Damaraland mole-rats

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Medger [1] reviewed the mechanisms of reproductive suppression in two eusocial mole-rat species, the naked (*Heterocephalus glaber*) and Damaraland mole-rat (*Fukomys damarensis*) with a focus on the interplay of stress, glucocorticoids and reproductive activity in subordinate females. By referring to findings from other group-living mammals such as meerkats (*Suricata suricatta*) and olive baboons (*Papio anubi*), Medger [1] suggested that in these mole-rat species female subordinates (non-breeding colony members) are exposed to aggressive behaviours from dominant individuals, namely the queen (sole breeding female), causing elevated glucocorticoid levels, which lead to a block of reproduction. Medger [1] emphasizes the importance of environmental factors and colony stability in regulating stress in both species and extrapolates this to other social mole-rat species.

Medger [1] suggested that female subordinates of both species are exposed to substantial aggression by female breeders to prevent reproduction, leading to increased glucocorticoid levels. However, this conclusion is not supported by the literature, as to date, no study on unmanipulated and stable colonies of Damaraland mole-rats has observed apparent aggression between dominant breeding individuals and subordinates. Furthermore, previous observations on a small number of unmanipulated colonies of naked mole-rats showed that shoving (a proxy for aggression) by the queens was not more often directed toward high-ranking subordinate females, which are those that were to succeed them, than toward other colony members [2,3].

The studies cited by Medger [1] are all experimental in nature, as either the queen was removed from the colony, or unrelated males were introduced [4,5]. It is conceivable that such interference causes colony instability, which results in aggressive behaviours among colony members and possibly increased glucocorticoids. As pointed out by Medger [1], glucocorticoid levels do not differ between breeding and reproductively suppressed naked and Damaraland mole-rats [6,7]. The seasonal variations in glucocorticoids found in Damaraland mole-rats, particularly just after the rains [8], are likely the consequence of mobilization of carbohydrate reserves for the period of intense burrowing, as reported by Vulllioud *et al.* [9], rather than variation in reproductive suppression.

Medger [1] raises an essential point that the main mechanisms of reproductive suppression in subordinate females differ between the two eusocial mole-rat species. The difference in the suppressive mechanisms likely results from the two species possessing different ovulatory modes; however, this was not explored [10,11]. Naked mole-rats are spontaneous ovulators and reproductive suppression, found in the form of anovulation, results from suppression of

the onset of ovarian cyclicity in subordinate females, which therefore remain in a prepubertal stage [12]. By contrast, Damaraland mole-rats are induced ovulators, and anovulation in subordinate females occurs through a lack of copulation [11]. Consequently, such females remain in a prepubertal stage until virgin mating occurs, activating ovarian steroidogenesis, thereby priming the hypothalamic–pituitary–gonadal (HPG) axis and, consequently, inducing the onset of puberty [13]. These physiological differences explain why inbreeding avoidance, a major component of reproductive suppression [14], is effective in maintaining reproductive skew in Damaraland mole-rats, but not in naked mole-rats.

Medger [1] suggests that studies investigating the neuroendocrine mechanisms underlying reproduction can help understand the mechanism of reproductive suppression. However, Medger [1] fails to explore the differences between the two species. In spontaneously ovulating mammals, such as naked mole-rats, the positive feedback action of ovarian oestradiol leads to the release of gonadotropin-releasing hormone (GnRH), which stimulates the pre-ovulatory luteinizing hormone (LH) surge from the anterior pituitary. The neuropeptides, kisspeptin and RFamide-related peptide -3 (RFRP-3) are important regulators of gonadotropin release [15]. Zhou *et al.* [16] found that subordinate female naked mole-rats, which are anovulatory, possess significantly fewer kisspeptin-immunoreactive cells in the anterior hypothalamus compared to queens, suggesting that this neuron population is involved in the pre-ovulatory LH surge in naked mole-rats. Moreover, it implies that triggering the activation of these kisspeptin neurons is essential for the onset of reproductive activity. Peragine *et al.* [17] reported that RFRP-3 is crucial in suppressing puberty onset in naked mole-rats. Subordinate females show increased RFRP-3 expression in the dorsomedial hypothalamus compared to queens [17]. Further, treatment with exogenous RFRP-3 prevented puberty onset in subordinate females removed from their natal colony and allowed to enter puberty. Faykoo-Martinez *et al.* [18] identified several candidate genes, including those of the kisspeptin signalling pathway, which show a differential expression pattern in relation to reproductive status.

In induced ovulators, such as the Damaraland mole-rat, the mating stimulus activates kisspeptin neurons in the anterior hypothalamus, which leads to activation of GnRH neurons and, consequently, to ovulation [15,19]. Several

recent studies in female Damaraland mole-rats have identified differential hypothalamic gene expression patterns of neuropeptides involved in activating GnRH neurons according to the females' reproductive status. Queens have significantly more *Kiss1*-expressing cells, increased neurokinin B and decreased dynorphin gene expression in the arcuate nucleus of the hypothalamus compared to subordinate females [20–22]. Like naked mole-rat queens, Damaraland mole-rat queens have significantly fewer RFRP-3-expressing cells within the hypothalamus than subordinate females [20].

Medger [1] also alluded to the variation in the longevity between breeders and subordinates in social mole-rat species, which is a point of interest for many researchers [23–28]. Medger [1] suggested that the lower oxidative damage found in breeding females of the Damaraland mole-rat contributes to their longer lifespan [29] but does not mention that the opposite trend is seen in naked mole-rats [28]. Further, Medger [1] argues that high levels of glucocorticoids may contribute to the lower life expectancy of non-breeders. In the absence of empirical data, this remains pure speculation.

In conclusion, the existing body of research on naked and Damaraland mole-rats does not support the view that stress and an associated increase in glucocorticoids due to intra-sexual aggression plays a major role in reproductive suppression. In Damaraland mole-rats inbreeding avoidance plays a significant role in reproductive suppression, whereas in naked mole-rat elevated prolactin in subordinates of both sexes may bring about social suppression [14,30]. However, the importance of induced stress may play a significant role in reproductive suppression and colony stability in other social and eusocial mole-rat species [31–33].

Data accessibility. This article has no additional data.

Authors' contributions. D.W.H.: conceptualization, writing—original draft; N.C.B.: conceptualization, writing—original draft; C.V.: conceptualization, writing—original draft.

All authors gave final approval for publication and agreed to be held accountable for the work performed therein.

Conflict of interest declaration. We declare we have no competing interests.

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References

1. Medger K. 2022 Stress in an underground empire. *Biol. Lett.* **18**, 20220012. (doi:10.1098/rsbl.2022.0012)
2. Clarke FM, Faulkes CG. 2001 Intracolony aggression in the eusocial naked mole-rat, *Heterocephalus glaber*. *Anim. Behav.* **61**, 311–324. (doi:10.1006/anbe.2000.1573)
3. Medger K, Bennett NC, Ganswindt SB, Ganswindt A, Hart DW. 2019 Changes in prolactin, cortisol and testosterone concentrations during queen succession in a colony of naked mole-rats (*Heterocephalus glaber*): a case study. *Sci. Nat.* **106**, 1–7. (doi:10.1007/s00114-019-1621-1)
4. Clarke FM, Faulkes CG. 1997 Dominance and queen succession in captive colonies of the eusocial naked mole-rat, *Heterocephalus glaber*. *Proc. R. Soc. Lond. B* **264**, 993–1000. (doi:10.1098/rspb.1997.0137)
5. Cooney R, Bennett NC. 2000 Inbreeding avoidance and reproductive skew in a cooperative mammal. *Proc. R. Soc. Lond. B* **267**, 801–806. (doi:10.1098/rspb.2000.1074)
6. Edwards PD, Mooney SJ, Bosson CO, Toor I, Palme R, Holmes MM, Boonstra R. 2020 The stress of being alone: removal from the colony, but not social subordination, increases fecal cortisol metabolite levels in eusocial naked mole-rats. *Horm. Behav.* **121**, 104720. (doi:10.1016/j.yhbeh.2020.104720)
7. Medger K, Bennett NC, Lutermann H, Ganswindt A. 2018 Non-invasive assessment of glucocorticoid and androgen metabolite levels in cooperatively breeding Damaraland mole-rats (*Fukomys damarensis*). *Gen. Comp. Endocrinol.* **266**, 202–210. (doi:10.1016/j.ygcen.2018.05.018)
8. Young AJ, Oosthuizen MK, Lutermann H, Bennett NC. 2010 Physiological suppression eases in Damaraland mole-rat societies when ecological constraints on dispersal are relaxed.

- Horm. Behav.* **57**, 177–183. (doi:10.1016/j.yhbeh.2009.10.011)
9. Vulliamd P, Mendonça R, Glauser G, Bennett N, Zöttl M, Katlein N, Leal R, Fuerst R, Clutton-Brock T. 2021 Increases in glucocorticoids are sufficient but not necessary to increase cooperative burrowing in Damaraland mole-rats. *Horm. Behav.* **135**, 105034. (doi:10.1016/j.yhbeh.2021.105034)
 10. Faulkes CG, Abbott DH, Jarvis JUM. 1990 Social suppression of ovarian cyclicity in captive and wild colonies of naked mole-rats, *Heterocephalus glaber*. *J. Reprod. Fertil.* **88**, 559–568. (doi:10.1530/jrf.0.0880559)
 11. Voigt C, Medger K, Bennett NC. 2021 The oestrous cycle of the Damaraland mole-rat revisited: evidence for induced ovulation. *J. Zool.* **314**, 85–95. (doi:10.1111/jzo.12860)
 12. Faulkes CG, Abbott DH. 2009 The physiology of a reproductive dictatorship: regulation of male and female reproduction by a single breeding female in colonies of naked mole-rats. In *Cooperative breeding in mammals* (eds N Solomon & J French), pp. 302–334. Cambridge, UK: Cambridge University Press.
 13. Rissman EF. 1992 Mating induces puberty in the female musk shrew. *Biol. Reprod.* **47**, 473–477. (doi:10.1095/biolreprod47.3.473)
 14. Bennett NC, Faulkes CG, Molteno AJ. 1996 Reproductive suppression in subordinate, non-breeding female Damaraland mole-rats: two components to a lifetime of socially induced infertility. *Proc. R. Soc. B* **263**, 1599–1603. (doi:10.1098/rspb.1996.0234)
 15. Marques P, Skorupskaitė K, Rozario KS, Anderson RA, George JT. 2022 Physiology of GnRH and gonadotropin secretion. In *Endotext* (eds M Levy & M Korbonits). South Dartmouth, MA: MDText.com, Inc.
 16. Zhou S, Holmes MM, Forger NG, Goldman BD, Lovern MB, Caraty A, Kalló I, Faulkes CG, Coen CW. 2013 Socially regulated reproductive development: analysis of GnRH-1 and kisspeptin neuronal systems in cooperatively breeding naked mole-rats (*Heterocephalus glaber*). *J. Comp. Neurol.* **521**, 3003–3029. (doi:10.1002/cne.23327)
 17. Peragine DE, Pokarowski M, Mendoza-Viveros L, Swift-Gallant A, Cheng H-YM, Bentley GE, Holmes MM. 2017 RFamide-related peptide-3 (RFRP-3) suppresses sexual maturation in a eusocial mammal. *Proc. Natl Acad. Sci. USA* **114**, 1207–1212. (doi:10.1073/pnas.1616913114)
 18. Faykoo-Martinez M, Monks DA, Zovkic IB, Holmes MM. 2018 Sex- and brain region-specific patterns of gene expression associated with socially-mediated puberty in a eusocial mammal. *PLoS ONE* **13**, e0193417. (doi:10.1371/journal.pone.0193417)
 19. Bakker J, Baum MJ. 2000 Neuroendocrine regulation of GnRH release in induced ovulators. *Front. Neuroendocrinol.* **21**, 220–262.
 20. Voigt C, Bennett NC. 2018 Reproductive status-dependent kisspeptin and RF amide-related peptide (Rfrp) gene expression in female Damaraland mole-rats. *J. Neuroendocrinol.* **30**, e12571. (doi:10.1111/jne.12571)
 21. Voigt C, Bennett N. 2018 Reproductive status affects the expression of prolactin receptor mRNA in the brain of female Damaraland mole-rats. *J. Chem. Neuroanat.* **94**, 1–7. (doi:10.1016/j.jchemneu.2018.08.002)
 22. Voigt C, Bennett N. 2019 Reproductive status-dependent dynorphin and neurokinin B gene expression in female Damaraland mole-rats. *J. Chem. Neuroanat.* **102**, 101705. (doi:10.1016/j.jchemneu.2019.101705)
 23. Horvath S *et al.* 2022 DNA methylation clocks tick in naked mole rats but queens age more slowly than nonbreeders. *Nat. Aging* **2**, 46–59. (doi:10.1038/s43587-021-00152-1)
 24. Dammann P, Šumbera R, Maßmann C, Scherag A, Burda H. 2011 Extended longevity of reproductives appears to be common in *Fukomys* mole-rats (Rodentia, Bathyergidae). *PLoS ONE* **6**, 18757. (doi:10.1371/journal.pone.0018757)
 25. Schmidt CM, Jarvis JUM, Bennett NC. 2013 The long-lived queen: reproduction and longevity in female eusocial Damaraland mole-rats (*Fukomys damarensis*). *African Zool.* **48**, 193–196. (doi:10.3377/004.048.0116)
 26. Jacobs PJ, Hart DW, Suess T, Janse van Vuuren AK, Bennett NC. 2021 The cost of reproduction in a cooperatively breeding mammal: consequence of seasonal variation in rainfall, reproduction and reproductive suppression. *Front. Physiol.* **12**, 780490. (doi:10.3389/fphys.2021.780490)
 27. Jacobs P, Finn KT, van Vuuren AKJ, Suess T, Hart DW, Bennett NC. 2022 Defining the link between oxidative stress, behavioural reproductive suppression and heterothermy in the Natal mole-rat (*Cryptomys hottentotus natalensis*). *Comp. Biochem. Physiol. Part B Biochem. Mol. Biol.* **216**, 110753. (doi:10.1016/j.cbpb.2022.110753)
 28. Jacobs PJ, Hart DW, Bennett NC. 2021 Plasma oxidative stress in reproduction of two eusocial African mole-rat species, the naked mole-rat and the Damaraland mole-rat. *Front. Zool.* **18**, 1–9. (doi:10.1186/s12983-021-00430-z)
 29. Schmidt CM, Blount JD, Bennett NC. 2014 Reproduction is associated with a tissue-dependent reduction of oxidative stress in eusocial female Damaraland mole-rats (*Fukomys damarensis*). *PLoS ONE* **9**, 103286. (doi:10.1371/journal.pone.0103286)
 30. Bennett NC, Ganswindt A, Ganswindt S, Jarvis JUM, Zöttl M, Faulkes CG. 2018 Contrasting roles for prolactin in eusocial naked mole-rats, *Heterocephalus glaber* and Damaraland mole-rats *Fukomys damarensis*. *Biol. Lett.* **14**, 20180150. (doi:10.1098/rsbl.2018.0150)
 31. Sahn A *et al.* 2021 Increased longevity due to sexual activity in mole-rats is associated with transcriptional changes in the HPA stress axis. *Elife* **10**, 57843. (doi:10.7554/eLife.57843)
 32. Begall S, Nappé R, Hohrenk L, Schmidt TC, Burda H, Sahn A, Szafrański K, Dammann P, Henning Y. 2021 Life expectancy, family constellation and stress in giant mole-rats (*Fukomys mechowii*). *Phil. Trans. R. Soc. B* **376**, 20200207. (doi:10.1098/rstb.2020.0207)
 33. Hart DW, van Vuuren AJ, Erasmus A, Süess T, Hagenah N, Ganswindt A, Bennett NC. 2022 The endocrine control of reproductive suppression in an aseasonally breeding social subterranean rodent, the Mahali mole-rat (*Cryptomys hottentotus mahali*). *Horm. Behav.* **142**, 105155. (doi:10.1016/j.yhbeh.2022.105155)