

# From grouping and cooperation to menstruation: Spiny mice (*Acomys cahirinus*) are an emerging mammalian model for sociality and beyond<sup>☆</sup>

Brandon A. Fricker, Aubrey M. Kelly<sup>\*</sup>

Department of Psychology, Emory University, 36 Eagle Row, Atlanta, GA 30322, United States of America



## ARTICLE INFO

**Keywords:**  
Social behavior  
Spiny mouse  
Cooperation  
Kinship  
Group interactions

## ABSTRACT

While spiny mice are primarily used as a model for Type II diabetes and for studying complex tissue regeneration, they are also an emerging model for a variety of studies examining hormones, behavior, and the brain. We began studying the spiny mouse to take advantage of their highly gregarious phenotype to examine how the brain facilitates large group-living. However, this unique rodent can be readily bred and maintained in the lab and can be used to ask a wide variety of scientific questions. In this brief communication we provide an overview of studies that have used spiny mice for exploring physiology and behavior. Additionally, we describe how the spiny mouse can serve as a useful model for researchers interested in studying precocial development, menstruation, cooperation, and various grouping behaviors. With increasingly available technological advancements for non-traditional organisms, spiny mice are well-positioned to become a valuable organism in the behavioral neuroscience community.

## 1. Introduction

Choosing an appropriate organism to answer specific scientific questions has been a valued approach in the hormones and behavior community for many decades. Indeed, scientists have not limited themselves to using only domesticated, laboratory rats and mice for experiments. To understand mechanisms underlying pairbonding, researchers began studying prairie voles (Young et al., 2011) and zebra finches (Adkins-Regan et al., 1997). To determine whether paternal care is modulated in similar or different ways than maternal care, researchers moved beyond studies of laboratory rats, and examined paternal behavior in species that evolved biparental care systems, such as prairie voles (Wang et al., 1994; Duclot et al., 2022), African striped mice (Rogers et al., 2023), and deer mice (Khadraoui et al., 2022). Striving to maintain ethological-relevance in experimental design can help us understand how species respond to varying environmental pressures, ultimately providing insight into how variation in social behavior arises.

While we know a fair amount about hormonal and neural mechanisms underlying flocking in birds (Goodson et al., 2012; Stevenson et al., 2020), and a few recent studies have begun to examine the neural mechanisms underlying grouping behavior in fish and insects (Tang et al., 2020; Messina et al., 2022; Homberg and Pfeiffer, 2023), we know

surprisingly little about how the brain modulates mammalian grouping behavior. This deficit is likely due to issues concerning the feasibility of housing large groups of mammals in a lab. Unfortunately, we cannot bring elephants and wildebeests into the lab for invasive studies. However, there are small mammals that evolved to live in groups and are amenable to lab settings. Researchers have been studying peer relationships in meadow voles, which aggregate in groups in the winter, with females forming multiple attachments to same-sex conspecifics that are both kin and non-kin (Beery et al., 2009). Naked mole-rats are used for examining neuroendocrine regulation of pubertal suppression in colonies (Peragine et al., 2017; Faykoo-Martinez et al., 2021), as well as cultural transmission of vocal dialect in groups (Barker et al., 2021). Further, studies in vampire bats are exploring how the brain represents individuals within groups (Rose et al., 2021). To expand upon the mammalian organisms available for studies examining mechanisms of grouping behavior, we began studying the spiny mouse (*Acomys cahirinus*) – a highly gregarious rodent that can be readily bred and maintained in the lab. In this brief communication we describe how the spiny mouse can serve as a useful model for a variety of studies examining hormones, behavior, and the brain.

<sup>☆</sup> This paper is part of the Virtual Special Issue, Non-model Contributions.

<sup>\*</sup> Corresponding author.

E-mail addresses: [brandon.alexander.fricker@emory.edu](mailto:brandon.alexander.fricker@emory.edu) (B.A. Fricker), [aubrey.kelly@emory.edu](mailto:aubrey.kelly@emory.edu) (A.M. Kelly).

## 2. The spiny mouse

Spiny mice are a communally breeding rodent native to Africa, the Middle East, and southern Asia (Nowak, 1999; Deacon, 2009; Frynta et al., 2011). Historically, spiny mice have been used for studying obesity due to their propensity to overeat in a lab setting and develop Type II diabetes (Gonet et al., 1966; Shafrir, 2000). However, in the last decade they have emerged as a model for studying complex tissue regeneration, and are the only mammal known to date that can regenerate entire suites of tissue (Seifert et al., 2012; Gawriluk et al., 2016). Spiny mice are precocial, and pups are born with fur and eyes and ears opened; additionally, pups are ambulatory on the day of birth and can eat dry food on postnatal day 2 (D'Udine et al., 1980; Haughton et al., 2016). Due to their long gestation (average 38–45 days), spiny mice have been used as a neurodevelopmental model, with studies revealing that rates of neural maturation can be quite different between precocial and altricial rodents (Brunjes, 1985; Tessitore and Brunjes, 1988; Brunjes et al., 1989). More recently, spiny mice have been used as a model for human-like reproductive biology given that they exhibit a menstrual cycle, and thus far, are the only rodent known to do so (Bellofiore et al., 2017; Bellofiore et al., 2018).

Unfortunately, there is currently a lack of field studies examining the behavioral ecology of spiny mice. However, telemetric field studies investigating temperature rhythms in spiny mice, along with observations from research groups that live-trapped spiny mice to bring into the lab, have found that spiny mice concentrate in rocky outcroppings (Elvert et al., 1999; Degen et al., 2002; Haughton et al., 2016). Spiny mice do not burrow in the wild or in the lab (Deacon, 2009), potentially resulting in greater exposure to predators, such as snakes and birds.

Increased risk of predation could be a driver for grouping behavior in spiny mice, as has been shown for other rodents (Zhou et al., 2023). Additionally, due to the harsh, natural environment (i.e., desert) of spiny mice and their lack of burrowing, they have evolved mechanisms of defense including skin-shedding and tail sheathing (Seifert et al., 2012), as well as osteoderms (i.e., bony plates) in their tails (a unique phenomenon in rodents) to facilitate escaping (Maden et al., 2023). Not only does the weak skin of spiny mice require modified handling methods in lab settings, but spiny mice should be group-housed in conditions with warmer temperatures that include igloos for sheltering rather than nesting material for burrowing (Shkolnik and Borut, 1969; Haughton et al., 2016).

Adult spiny mice (Fig. 1) are, on average, 30–50 g and can be housed in adult groups of ~30 adults (Haughton et al., 2016), allowing for the study of various grouping behaviors. Spiny mouse social behavior was first explored in the 1980s; these early studies found that lactating females will indiscriminately nurse neonates, regardless of genetic relation (Porter et al., 1980), and that spiny mice rely on odor cues associated with nursing to identify kin (Porter et al., 1983; Porter, 1988). Spiny mice also exhibit food sharing with related and unrelated conspecifics, but exhibit more food sharing with kin (Porter et al., 1981). Initial studies from our lab show that spiny mice exhibit a preference to affiliate with large over small groups of conspecifics, are highly affiliative, and exhibit little aggression in multiple social contexts (Fricker et al., 2021; Gonzalez Abreu et al., 2022). This high degree of sociality was also demonstrated in a study that found established spiny mouse breeding groups will not only display low levels of aggression toward unrelated newcomers, but will also accept newcomers into the group (Cizkova et al., 2011). Together, these studies demonstrate that spiny



**Fig. 1.** A group of male and female adult spiny mice huddling.  
Photo credit: Aubrey M. Kelly.

mice are a useful organism for answering an array of scientific questions. Below we describe how they may be of particular interest for researchers in the hormones and behavior community.

### 3. Spiny mouse performance in behavioral tests that generalize across rodents

Although spiny mice are an unusual rodent (e.g., they are precocial, regenerate their tissue, and exhibit a menstrual cycle), studies have demonstrated that spiny mice can readily be tested in standardized behavior tests that generalize across rodents. In an open field test, juvenile and adult male and female spiny mice spend roughly 10–15 % of the time in the central zone (Ratnayake et al., 2014). For comparison with other commonly used rodents in research, adult male Sprague Dawley rats spend 4–6 % (Schmitt and Hiemke, 1998), adult male and female C57BL/6 mice spend roughly 0.5–2 % and DBA/2 mice spend 3–6 % (Podhorna and Brown, 2002), and adult male and female prairie voles spend about 8–10 % of the test time in the central zone of an open field assay (Kelly et al., 2020). Together, these studies suggest that spiny mice may be a fairly bold rodent in novel, open environments, which could be a result of their behavioral ecology – spiny mice do not burrow and live in rocky outcroppings (Shkolnik and Borut, 1969) so may have an evolutionary history that entails being more accustomed to roaming in open and exposed spaces.

Juvenile and adult spiny mice demonstrate high levels of balance and dexterity in a rotarod test. While adult (PND 70–84) C57BL/6 mice remain on the rotarod for an average of 120 s, spiny mice of a similar age (PND 80–85) remain aboard for the full 300 second test (McIlwain et al., 2001; Ratnayake et al., 2014). In an elevated plus maze, similar to other rodent species, spiny mice spend more time in the closed arms compared to the open arms (Ratnayake et al., 2014). Further, while prepulse inhibition testing for measuring sensorimotor gating and novel object recognition tasks can be used for spiny mice, this species cannot be tested in a Morris Water Maze test due to the expression of excessive fear once in contact with water and subsequent inactivity and stress behaviors in the homecage (Ratnayake et al., 2014).

A variety of different social behavior tasks can be implemented for spiny mice, although we have found that they will quickly lose interest in restrained social stimuli (i.e., under a wire mesh container) if the openings on the stimulus container to gain nose/paw access are small. Spiny mice rapidly approach any type of conspecific (i.e., same-sex, opposite-sex, novel, familiar) in a standard social approach test. Using the same testing chamber, and thus providing animals with the same distance to travel to the stimulus container, we have found that spiny mice approach novel, same-sex conspecifics in an average of 7 s, whereas Mongolian gerbils take an average of 29 s and prairie voles an average of 82 s (Kelly et al., 2020; Fricker et al., 2021). In dyadic social interaction tests where animals are allowed to freely interact, spiny mice exhibit little to no aggression and high levels of prosociality regardless of conspecific type (Fricker et al., 2021; Gonzalez Abreu et al., 2022). Further, similar to other rodents, they exhibit social recognition of novel individuals as evidenced in a habituation-dishabituation paradigm, however spiny mice do not exhibit a preference for affiliating with or investigating novel or familiar conspecifics in a choice test (Fricker et al., 2021). Together, these tests demonstrate that spiny mice are socially curious and highly prosocial in reproductive and nonreproductive contexts. Although in many ways spiny mice are an outlier in the rodent world, they readily perform in several standardized rodent behavioral tests, and thus results from some behavioral studies may be generalizable to other species.

### 4. The rodent that menstruates

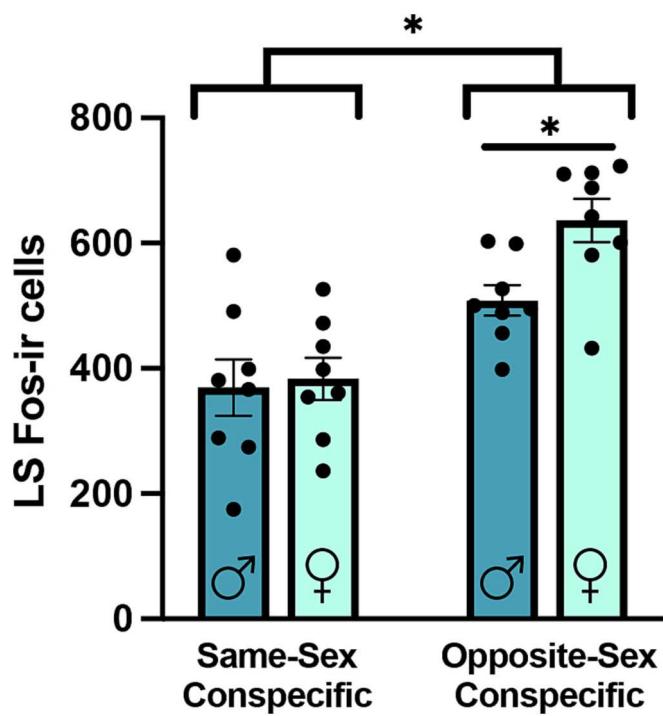
Until about 2016, menstruation was believed to be restricted to higher-order primates, a few species of bat, and elephant shrews. Then a research group in Australia observed that virgin female spiny mice

undergo cyclic endometrial shedding and blood in the vaginal canal concluding with each infertile cycle, demonstrating menstruation in a rodent for the first time (Bellofiore et al., 2017). Researchers are currently using spiny mice as a model for reproductive health in women and are examining physiology underlying abnormal uterine bleeding, amenorrhea, heavy menstrual bleeding, ovulatory disorders, pre-eclampsia, and menopause (Bellofiore et al., 2017; Bellofiore et al., 2018; Bellofiore et al., 2021a; Bellofiore et al., 2021b).

The menstrual cycle in spiny mice lasts an average of 9 days but ranges from 6 to 12 days in healthy, sexually mature females (Bellofiore et al., 2017; Bellofiore et al., 2021b). To our knowledge, only 1 study has examined behavioral changes associated with different stages in the spiny mouse menstrual cycle. In an open field test, females in the early menstrual phase travel less distance and at a lower velocity than females in the luteal phase; similarly, in an elevated plus maze, females in the early menstrual phase enter the open arms less than females in the luteal phase (Bellofiore et al., 2019). Further, females significantly increase food consumption during the early follicular and late luteal phases compared to the late follicular phase (Bellofiore et al., 2019). How social behaviors may change throughout the menstrual cycle remains an open question; future studies could explore how natural fluctuations in estrogen, progesterone, and DHEA influence female behavior, as well as male responses to females at different stages of the menstrual cycle. Further, spiny mice can serve as an excellent model for examining how the social environment (i.e., social isolation or being subjected to bullying) influences menarche and how social, sexual, and parental experience may influence menopausal transition. Together, there are many exciting future directions for research using spiny mice to better understand menstruation.

### 5. A gregarious phenotype

Most neuroscience studies examining affiliative social behaviors focus on bonding between two individuals in reproductive contexts, such as parent-offspring or mating bonds (Woolley et al., 2004; Young and Wang, 2004; Feldman, 2016). Yet, prior studies indicate that reproductive and nonreproductive contexts are differentially processed in the brain (Lee et al., 2019), and thus we cannot assume that neural circuits underlying reproductive bonding will similarly regulate nonreproductive affiliation. Further, because group living is not part of the life history of the most commonly used laboratory models, it is questionable whether the circuits that influence social interactions between two individuals in aggressive or reproductive contexts may generalize into an understanding of the complex mechanisms that modulate prosocial interactions with unrelated individuals in large groups. The ability to engage prosocially in both reproductive and nonreproductive interactions, particularly in group contexts, situates the spiny mouse as an ideal organism for examining how mechanisms underlying prosociality may differ depending on a wide variety of social contexts. Indeed, in an immediate early gene (IEG) study, we found that the lateral septum (LS), a brain region that is emerging as a hub for social information processing (Menon et al., 2022), is more responsive in male and female spiny mice to an opposite-sex conspecific than a same-sex conspecific, with greater effects in females (Fig. 2; see Supplemental materials). This sex difference in septal responsiveness specifically to an opposite-sex conspecific may reflect the preference of female spiny mice to affiliate with opposite-sex conspecifics, whereas males prefer affiliating with same-sex conspecifics (Fricker et al., 2021). Alternatively, it may be more important for females to respond more strongly to interactions in a reproductive context because the costs of breeding are greater for females than males (Simmons and Kvarnemo, 2006). Regardless, this finding highlights the importance of considering and examining reproductive and nonreproductive contexts in experiments that seek to understand how the brain processes the social environment and subsequently modulates behavior. Consistent with the finding that the LS is sensitive to distinct types of conspecifics, we recently showed that



**Fig. 2.** Male and female spiny mice that interacted with a novel opposite-sex conspecific exhibited greater neural responses in the lateral septum (LS) compared to those that interacted with a novel, same-sex conspecific ( $P < 0.01$ ), with stronger effects in females ( $P = 0.02$ ).

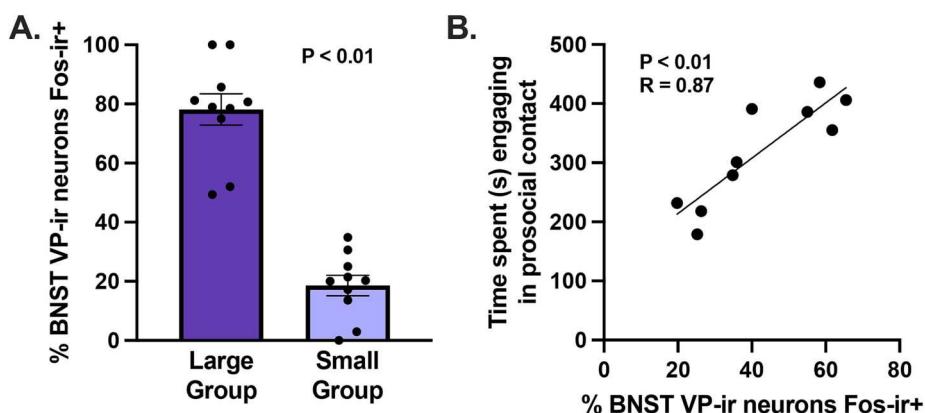
the LS is also differentially responsive to kinship status in male spiny mice, such that the LS exhibits a greater Fos response to dyadic interactions with novel kin compared to novel non-kin (Fricker et al., 2023). Together, these results suggest that the LS may play a particularly important role in social recognition in spiny mice. Similarly, the LS distinguishes kin from non-kin in rats (Clemens et al., 2020), suggesting that findings from spiny mice may be generalizable to other rodent species.

In behavioral ecology, gregariousness is a term used to describe species that affiliate with or live in groups (Miller, 1922; Treisman, 1975; Goodson and Kingsbury, 2011; Peterson and Weckerly, 2018). As group-living communal breeders, spiny mice exhibit a gregarious phenotype. Both males and females exhibit little aggression in numerous social contexts and if given a choice of affiliating with a small or a large group, spiny mice prefer to affiliate with the large group (Fricker et al.,

2021; Gonzalez Abreu et al., 2022). Early studies in our lab have sought to determine neural underpinnings of this preference to affiliate with large groups, specifically in nonreproductive contexts. For example, spiny mice exposed to a large group of novel, same-sex conspecifics exhibit greater Fos expression in vasopressin-producing neurons in the bed nucleus of the stria terminalis (BNST) compared to spiny mice exposed to a small group of novel, same-sex conspecifics (Fig. 3A; see Supplemental materials). Further, during dyadic social interactions with novel, same-sex conspecifics, BNST vasopressin neural responses positively relate to prosocial contact (Fig. 3B; see Supplemental materials), suggesting that this cell group may generally be involved in promoting prosocial behavior. Consistent with this possibility, previous research in the highly gregarious zebra finch demonstrated that the vasopressin cell group of the BNST directly facilitates the preference to affiliate with large groups (Kelly and Goodson, 2013). Together these findings suggest that the BNST vasopressin cell group may exhibit evolutionarily conserved functions across taxa and may contribute toward promoting the drive to affiliate in groups in a number of gregarious species. As mentioned earlier, a limited number of grouping mammals are available for laboratory studies. Yet, because of the relatively small size of spiny mice, it is feasible to maintain large groups in the lab, enabling researchers to ask a variety of questions related to grouping and sociality in mammals. Indeed, unlike most commonly used mammalian species in labs, spiny mice can allow us to examine mechanisms that facilitate complex societal living in groups comprised of individuals that are of mixed-sex and of mixed-genetic relation.

## 6. Communal breeding: a system ripe for exploring flexible group dynamics

Unlike many other species that are tractable for lab studies, spiny mice readily accept unrelated newcomers into same- and mixed- sex established groups (Cizkova et al., 2011; Haughton et al., 2016). This is likely a reflection of their communal breeding system. While field studies that systematically characterize the behavioral ecology of spiny mice are still needed, most communally breeding systems have high rates of male dispersal with females typically representing the philopatric sex. Notably, there is variation in dispersal and philopatry across species (Clutton-Brock and Lukas, 2011), and thus group composition of sex and kin may vary in spiny mice in the wild, however, field studies are needed to determine natural variation in group composition. Given that established same- and mixed- sex groups of spiny mice will accept unrelated newcomers in the lab (Cizkova et al., 2011), it is possible that both males and females of this species may disperse from the natal home, albeit likely at varying rates, and are likely to be subsequently welcomed into a new group in the wild. Although field studies are



**Fig. 3.** (A) Male and female spiny mice exposed to a large group of 8 novel, same-sex conspecifics exhibited a greater percentage of BNST VP-Fos colocalized neurons compared to spiny mice exposed to a small group of 2 novel, same-sex conspecifics. (B) The percentage of BNST VP-Fos colocalized cells positively correlated with time spent engaged in prosocial contact with a novel, same-sex conspecific during a social interaction in male and female spiny mice.

needed to confirm dispersal and philopatry patterns in spiny mice, the highly social nature of spiny mouse groups in the lab lends this system to the study of variation in group dynamics and social networks.

Spiny mice are an excellent organism for examining how behavior may vary when interacting with kin and non-kin. In novel group interactions, male spiny mice can discriminate between novel kin, novel non-kin, and familiar kin, as indicated by differential investigation (Fricker et al., 2023). Interestingly, males exhibit a preference to affiliate more with novel kin in novel groups comprised of all 3 conspecific types, suggesting that affiliation preferences upon forming a new group may be biased toward interacting with novel kin (Fricker et al., 2023). Further, in dyadic interactions with either novel kin or novel non-kin, male spiny mice behave more prosocially with and exhibit greater dorsal LS neural responses to novel kin (Fricker et al., 2023). These findings suggest that communally breeding species may have evolved specialized neural circuitry to facilitate a bias to be more affiliative with kin, regardless of whether they are novel or familiar, to enhance fitness and promote behaviors such as incest avoidance and nepotism. Although spiny mice behave prosocially toward kin and non-kin in resource abundant environments, future studies could investigate factors (i.e., resource scarcity) that may create tipping points that lead to overt kin-biased behavior and even group dissolution. Additional studies could explore the involvement of motivational systems in social recognition and preferences in complex groups.

While studies in CD1 mice allow for examination of social hierarchy changes upon the removal of a group member (Williamson et al., 2017), new adults cannot be added to established groups because the newcomer is likely to be the recipient of intense aggression. However, one could conduct studies in spiny mice in which a mouse is removed and/or added to determine how fluctuation in group members influences stability of dominance hierarchies as well as general cohesion of the group. An important aspect of group living is for group members to have the ability to rapidly learn when specific behaviors are appropriate or inappropriate. Exhibiting context-appropriate behavior (i.e., social competence) is crucial for an individual to gain acceptance into and thrive within a new group. Spiny mice are highly amenable for studies examining social competence and hormonal and neural mechanisms that enable animals to rapidly adapt to novel social environments, as well as studies that seek to map collective behavioral trajectories of groups upon social perturbation.

Communal breeding systems are characterized by shared care of offspring produced by more than one female (Riehl, 2021). Indeed, spiny mouse females exhibit indiscriminate parental care toward pups regardless of genetic relation (Porter et al., 1980), and we have observed the same for juvenile and adult males in our lab (Kelly et al., unpub obs). Thus, spiny mice can also be used for studies that seek to understand mechanisms of alloparental care, whether pups exhibit preferences for parental care specifically from kin, or how variation in the number of parents/adults present during early life influences development. Further, we recently found that female spiny mice in higher density cages give birth to fewer pups (Wallace et al., unpub obs), suggesting that spiny mice could potentially serve as a model for examining consequences of increasing, decreasing, or fluctuating population densities.

## 7. A rodent model for studying cooperative behaviors

The fields of biology and neuroscience have shown great interest in exploring cooperative behaviors, however few studies have been able to explore the neural underpinnings of cooperation. The most commonly studied cooperative behaviors include reciprocity, helping behavior, and coordinated cooperation.

Reciprocity is a behavior that occurs when individuals help or cooperate with non-kin, even at a cost to themselves, due to an expectation of receiving help in return at a later exchange (Trivers, 1971). Outside of studies examining human behavior, reciprocity has primarily been studied in non-human primates, such as wild vervet monkeys

(Seyfarth and Cheney, 1984; Borgeaud and Bshary, 2015). Unfortunately, there are a number of experimental limitations when working with non-human primates. Instead, some researchers have examined reciprocity in vampire bats, which are more amenable for invasive and/or laboratory-based analyses. Vampire bats regularly share blood meals in the absence of coercion, and primarily with unrelated conspecifics (Carter and Wilkinson, 2013; Carter et al., 2020). Vampire bats can be kept long-term in a lab setting, allowing for tracking instances of reciprocity over time. However, compared to other rodents, the neural toolkits for vampire bats are only beginning to materialize, with some of the first examples of electrophysiological recordings in behaving groups of bats occurring recently (Zhang and Yartsev, 2019). Whether spiny mice exhibit reciprocity is unknown but given that they peacefully live in groups with kin and non-kin and are highly prosocial in nonreproductive contexts, studies could seek to determine whether this species engages in reciprocity behaviors.

Unlike reciprocity, there are several examples of individuals providing aid to (i.e., helping) another conspecific in more traditional rodent models. For example, prairie voles will engage in consolatory allogrooming after observing foot shocks applied to both familiar, same-sex siblings and familiar, opposite-sex pairbond partners (Burkett et al., 2016). Prairie voles do not, however, console novel, same-sex conspecifics, suggesting a bias toward in-group members. Rats also appear to engage in in-group directed helping behavior. Both Sprague-Dawley and Long-Evans rats will free both trapped familiar and novel conspecifics of the same strain, but not novel individuals from a strain different to their own unless they are cross-fostered with the other strain from birth (Ben-Ami Bartal et al., 2014; Ben-Ami Bartal et al., 2021). While there is a wide array of tools for probing neural mechanisms of helping in rats and prairie voles, studies in these species may be limited to helping in contexts with in-group members and/or familiar individuals. Yet, helping behavior frequently occurs in human and non-human primates with novel, out-group members (Tan and Hare, 2013; Tan et al., 2017). The neural underpinnings of such xenophilic helping behaviors cannot easily be explored in rodent models that selectively help in-group members, leaving the mechanisms of an important type of helping behavior unclear. Given that spiny mice welcome new members to groups and behave in a highly prosocial manner toward novel conspecifics, this species may be particularly useful for studies examining similarities and differences in mechanisms underlying helping behavior in varying social contexts.

Coordinated cooperation can be defined as any behavior requiring coordinated or correlated responses between two or more individuals sharing the same goal or aligned interests. A classic example of such behavior comes from capuchin monkeys, which coordinate rope pulling to bring food closer (Mendres and De Walla, 2000). Notably, other non-primate species, like elephants, can also coordinate in a similar manner (Plotnik et al., 2011). Capuchins will even cooperate with a conspecific in more abstract tasks, such as an assurance game where they can choose to cooperate, despite not knowing if their partner will as well, or choose a guaranteed, but lower, payout (Robinson et al., 2021). To examine hormonal and neural mechanisms that facilitate coordinated cooperation, researchers could design game studies for rodents that are similar to the assurance game or prisoner's dilemma game (Wang and Kwan, 2023) or design operant cooperative tasks where multiple individuals must coordinate their movements to achieve a common goal (Avital et al., 2016). In large novel arenas, we have observed that spiny mice will sometimes explore in a collective group, suggesting that this species may exhibit coordinated cooperative movements. Ongoing studies in our lab are determining whether spiny mice will coordinate their movements to trigger the opening of a door that leads to an isolated pup – a stimulus that motivates a spiny mouse to action much more so than a food reward.

Some of the most complex forms of cooperative behaviors occur in species that live in large groups varying in relatedness and familiarity, like those driving successful human communities. The ease in which

spiny mice are bred and studied in a lab setting can allow researchers to take advantage of the preference of spiny mice to affiliate with large groups and behave prosocially with conspecifics that vary in sex, kinship status, and familiarity for the study of cooperative behaviors. Further, the neural toolkit for spiny mice is developing rapidly, and thus probing the neural mechanisms underlying these behaviors is increasingly feasible. Together, spiny mice could play a vital and informative role in understanding hormonal and neural mechanisms underlying cooperative behaviors.

## 8. Conclusions

Spiny mice are a useful organism for answering an array of scientific questions. In addition to being used as a model for Type II diabetes and for studying complex tissue regeneration, spiny mice are an excellent organism for examining mechanisms of behavior. Their precocial phenotype allows for the study of behavioral and physiological maturation on a unique developmental timescale. Researchers interested in the adaptive value and evolutionary history of unlearned knowledge may find the precocial spiny mouse as a use model organism. Additionally, spiny mouse reproductive physiology enables using female spiny mice as a model for human-like menstruation and menopause. While spiny mice can be used in standard rodent behavioral tests, because they are highly gregarious and readily affiliate with conspecifics in reproductive and nonreproductive contexts they are also ideal for studying hormonal and neural mechanisms underlying various grouping and cooperative behaviors. Spiny mice are a lab-tractable organism that researchers may find especially useful for answering numerous scientific questions within a single species.

## Data availability

The data presented here are available from the corresponding author upon request.

## Acknowledgements

We would like to thank Ashley W. Seifert (University of Kentucky) for helping us establish a spiny mouse breeding colony in our lab at Emory University. Additionally, we thank all members of the Kelly Lab for their contributions to getting a research program using spiny mice to examine the neural mechanisms underlying social behavior off the ground.

## Funding

This work was supported by the National Science Foundation (NSF IOS-2310626 to AMK). BAF was supported by the Department of Defense through the National Defense Science & Engineering Graduate (NDSEG) Fellowship Program.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yhbeh.2023.105462>.

## References

Adkins-Regan, E., Mansukhani, V., Thompson, R., Yang, S., 1997. Organizational actions of sex hormones on sexual partner preference. *Brain Res. Bull.* 44, 497–502.

Avital, A., Aga-Mizrahi, S., Zubedat, S., 2016. Evidence for social cooperation in rodents by automated maze. *Sci. Rep.* 6, 29517.

Barker, A.J., Veviurko, G., Bennett, N.C., Hart, D.W., Mograby, L., Lewin, G.R., 2021. Cultural transmission of vocal dialect in the naked mole-rat. *Science* 371, 503–507.

Beery, A.K., Routman, D.M., Zucker, I., 2009. Same-sex social behavior in meadow voles: multiple and rapid formation of attachments. *Physiol. Behav.* 97, 52–57.

Bellofiore, N., Ellery, S.J., Mamrot, J., Walker, D.W., Temple-Smith, P., Dickinson, H., 2017. First evidence of a menstruating rodent: the spiny mouse (*Acomys cahirinus*). *Am. J. Obstet. Gynecol.* 216, 40e1–40e11.

Bellofiore, N., Rana, S., Dickinson, H., Temple-Smith, P., Evans, J., 2018. Characterization of human-like menstruation in the spiny mouse: comparative studies with the human and induced mouse model. *Hum. Reprod.* 33, 1715–1726.

Bellofiore, N., Cousins, F., Temple-Smith, P., Evans, J., 2019. Altered exploratory behaviour and increased food intake in the spiny mouse before menstruation: a unique pre-clinical model for examining premenstrual syndrome. *Hum. Reprod.* 34, 308–322.

Bellofiore, N., George, E., Vollenhoven, B., Temple-Smith, P., 2021a. Reproductive aging and menopause-like transition in the menstruating spiny mouse (*Acomys cahirinus*). *Hum. Reprod.* 36, 3083–3094.

Bellofiore, N., McKenna, J., Ellery, S., Temple-Smith, P., 2021b. The spiny mouse—a menstruating rodent to build a bridge from bench to bedside. *Front. Reprod. Health* 3, 784578.

Ben-Ami Bartal, I., Rodgers, D.A., Bernardez Sarria, M.S., Decety, J., Mason, P., 2014. Pro-social behavior in rats is modulated by social experience. *Elife* 3, e01385.

Ben-Ami Bartal, I., Breton, J.M., Sheng, H., Long, K.L., Chen, S., Halliday, A., Kenney, J. W., Wheeler, A.L., Frankland, P., Shlyansky, C., Deisseroth, K., Keltner, D., Kaufer, D., 2021. Neural correlates of ingroup bias for prosociality in rats. *Elife* 10.

Borgeaud, C., Bshary, R., 2015. Wild vervet monkeys trade tolerance and specific coalitional support for grooming in experimentally induced conflicts. *Curr. Biol.* 25, 3011–3016.

Brunjes, P.C., 1985. A stereological study of neocortical maturation in the precocial mouse, *Acomys cahirinus*. *Brain Res.* 351, 279–287.

Brunjes, P.C., Korol, D.L., Stern, K.G., 1989. Prenatal neurogenesis in the telencephalon of the precocial mouse *Acomys cahirinus*. *Neurosci. Lett.* 107, 114–119.

Burkett, J.P., Andari, E., Johnson, Z.V., Curry, D.C., de Waal, F.B., Young, L.J., 2016. Oxytocin-dependent consolation behavior in rodents. *Science* 351, 375–378.

Carter, G.G., Wilkinson, G.S., 2013. Food sharing in vampire bats: reciprocal help predicts donations more than relatedness or harassment. *Proc. Biol. Sci.* 280, 20122573.

Carter, G.G., Farine, D.R., Crisp, R.J., Vrtilek, J.K., Ripperger, S.P., Page, R.A., 2020. Development of new food-sharing relationships in vampire bats. *Curr. Biol.* 30, 1275–1279 (e1273).

Cizkova, B., Sumbera, R., Frynta, D., 2011. A new member or an intruder: how do Sinai spiny mouse (*Acomys dimidiatus*) families respond to a male newcomer? *Behaviour* 148, 889–908.

Clemens, A.M., Wang, H., Brecht, M., 2020. The lateral septum mediates kinship behavior in the rat. *Nat. Commun.* 11, 3161.

Clutton-Brock, T.H., Lukas, D., 2011. The evolution of social philopatry and dispersal in female mammals. *Mol. Ecol.* 21, 472–492.

Deacon, R.M., 2009. Burrowing: a sensitive behavioural assay, tested in 5 species of laboratory rodents. *Behav. Brain Res.* 200, 128–133.

Degen, A.A., Khokhlova, I.S., Kam, M., Snider, I., 2002. Energy requirements during reproduction in female common spiny mice (*Acomys cahirinus*). *J. Mammal.* 83, 645–651.

Duclot, F., Liu, Y., Saland, S.K., Wang, Z., Kabbaj, M., 2022. Transcriptomic analysis of paternal behaviors in prairie voles. *BMC Genomics* 23, 679.

D'Udine, B., Gerosa, E., Drewett, R.F., 1980. Maternal behavior and the milk ejection reflex in a precocial murid (*Acomys cahirinus*). *Behav. Neural Biol.* 28.

Elvert, R., Kronfeld, N., Dayan, T., Haim, A., Zisapel, N., Heldmaier, G., 1999. Telemetric field studies of body temperature and activity rhythms of *Acomys russatus* and *A. cahirinus* in the Judean Desert of Israel. *Oecologia* 119, 484–492.

Faykoo-Martinez, M., Kalinowski, L.M., Holmes, M.M., 2021. Neuroendocrine regulation of pubertal suppression in the naked mole-rat: what we know and what comes next. *Mol. Cell. Endocrinol.* 534, 111360.

Feldman, R., 2016. The neurobiology of mammalian parenting and the biosocial context of human caregiving. *Horm. Behav.* 77, 3–17.

Fricker, B.A., Seifert, A.W., Kelly, A.M., 2021. Characterization of social behavior in the spiny mouse, *Acomys cahirinus*. *Ethology* 00, 1–15.

Fricker, B.A., Ho, D., Seifert, A.W., Kelly, A.M., 2023. Biased brain and behavioral responses towards kin in males of a communally breeding species. *Sci. Rep.* 13, 17040.

Frynta, D., Frankova, M., Cizkova, B., 2011. Social and life history correlates of litter size in captive colonies of precocial spiny mice (*Acomys*). *Acta Theriol.* 56, 289–295.

Gawriluk, T.R., Simkin, J., Thompson, K.L., Biswas, S.K., Clare-Salzler, Z., Kimani, J.M., Kiama, S.G., Smith, J.J., Ezenwa, V.O., Seifert, A.W., 2016. Comparative analysis of ear-hole closure identifies epimorphic regeneration as a discrete trait in mammals. *Nat. Commun.* 7, 11164.

Gonet, A.E., Stauffacher, W., Pictet, R., Renold, A.E., 1966. Obesity and diabetes mellitus with striking congenital hyperplasia of the islets of langerhans in spiny mice (*Acomys Cahirinus*): I. Histological findings and preliminary metabolic observations. *Diabetologia* 1, 162–171.

Gonzalez Abreu, J.A., Rosenberg, A.E., Fricker, B.A., Wallace, K.J., Seifert, A.W., Kelly, A.M., 2022. Species-typical group size differentially influences social reward neural circuitry during nonreproductive social interactions. *iScience*. <https://doi.org/10.1016/j.isci.2022.104230>.

Goodson, J.L., Kingsbury, M.A., 2011. Nonapeptides and the evolution of social group sizes in birds. *Front. Neuroanat.* 5, 13.

Goodson, J.L., Wilson, L.C., Schrock, S.E., 2012. To flock or fight: neurochemical signatures of divergent life histories in sparrows. *Proc. Natl. Acad. Sci. U. S. A.* 109 (Suppl. 1), 10685–10692.

Haughton, C.L., Gawriluk, T.R., Seifert, A.W., 2016. The biology and husbandry of the African Spiny Mouse (*Acomys cahirinus*) and the research uses of a laboratory colony. *J. Am. Assoc. Lab. Anim. Sci.* 55, 9–17.

Homberg, U., Pfeiffer, K., 2023. Correction to: unraveling the neural basis of spatial orientation in arthropods. *J. Comp. Physiol. A Neuroethol. Sens. Neural Behav. Physiol.* 209, 465.

Kelly, A.M., Goodson, J.L., 2013. Functional significance of a phylogenetically widespread sexual dimorphism in vasotocin/vasopressin production. *Horm. Behav.* 64, 840–846.

Kelly, A.M., Ong, J.Y., Witmer, R.A., Ophir, A.G., 2020. Paternal deprivation impairs social behavior putatively via epigenetic modification to lateral septum vasopressin receptor. *Sci. Adv.* 6.

Khadraoui, M., Merritt, J.R., Hoekstra, H.E., Bendesky, A., 2022. Post-mating parental behavior trajectories differ across four species of deer mice. *PLoS One* 17, e0276052.

Lee, N.S., Goodwin, N.L., Freitas, K.E., Beery, A.K., 2019. Affiliation, aggression, and selectivity of peer relationships in meadow and prairie voles. *Front. Behav. Neurosci.* 13, 52.

Maden, M., Polvadore, T., Polanco, A., Barbazuk, W.B., Stanley, E., 2023. Osteoderms in a mammal the spiny mouse *Acomys* and the independent evolution of dermal armor. *iScience* 26, 106779.

McIlwain, K.L., Merriweather, M.Y., Yuva-Paylor, L.A., Paylor, R., 2001. The use of behavioral test batteries: effects of training history. *Physiol. Behav.* 73, 705–717.

Mendes, K.A., De Walla, F.B.M., 2000. Capuchins do cooperate: the advantage of an intuitive task. *Anim. Behav.* 60, 523–529.

Menon, R., Suss, T., Oliveira, V.E.M., Neumann, I.D., Bludau, A., 2022. Neurobiology of the lateral septum: regulation of social behavior. *Trends Neurosci.* 45, 27–40.

Messina, A., Potrich, D., Perrino, M., Sheardown, E., Miletto Petrazzini, M.E., Luu, P., Nadtochiy, A., Truong, T.V., Sovrano, V.A., Fraser, S.E., Brennan, C.H., Vallortigara, G., 2022. Quantity as a fish views it: behavior and neurobiology. *Front. Neuroanat.* 16.

Miller, R.C., 1922. The significance of the gregarious habit. *Ecology* 3, 122–126.

Nowak, R.M., 1999. *Walker's Mammals of the World*. John Hopkins University Press, Baltimore (MD).

Peragine, D.E., Pokarowski, M., Mendoza-Viveros, L., Swift-Gallant, A., Cheng, H.M., Bentley, G.E., Holmes, M.M., 2017. RFamide-related peptide-3 (RFamide-3) suppresses sexual maturation in a eusocial mammal. *Proc. Natl. Acad. Sci. U. S. A.* 114, 1207–1212.

Peterson, L.M., Weckerly, F.W., 2018. Social behavior and changes in foraging behavior in a gregarious ungulate. *J. Mammal.* 99, 1422–1429.

Plotnik, J.M., Lair, R., Suphachoksahakun, W., de Waal, F.B., 2011. Elephants know when they need a helping trunk in a cooperative task. *Proc. Natl. Acad. Sci. U. S. A.* 108, 5116–5121.

Podhorna, J., Brown, R.E., 2002. Strain differences in activity and emotionality do not account for differences in learning and memory performance between C57BL/6 and DBA/2 mice. *Genes Brain Behav.* 1, 96–110.

Porter, R.H., 1988. The ontogeny of sibling recognition in rodents - superfamily Muroidea. *Behav. Genet.* 18, 483–494.

Porter, R.H., Cavallaro, S.A., Moore, J.D., 1980. Developmental parameters of mother-offspring interactions in *Acomys cahirinus*. *Z. Tierpsychol.* 53, 153–170.

Porter, R.H., Moore, J.D., White, D.M., 1981. Food sharing by sibling vs. nonsibling spiny mice (*Acomys cahirinus*). *Behav. Ecol. Sociobiol.* 8, 207–212.

Porter, R.H., Matochik, J.A., Makin, J.W., 1983. Evidence for phenotype matching in spiny mice (*Acomys cahirinus*). *Anim. Behav.* 31, 978–984.

Patnayake, U., Quinn, T., Daruwalla, K., Dickinson, H., Walker, D.W., 2014. Understanding the behavioural phenotype of the precocial spiny mouse. *Behav. Brain Res.* 275, 62–71.

Riehl, C., 2021. Evolutionary origins of cooperative and communal breeding: lessons from the crotaphagine cuckoos. *Ethology* 127, 827–836.

Robinson, L.M., Martinez, M., Leverett, K.L., Rossette, M.S., Wilson, B.J., Brosnan, S.F., 2021. Anything for a cheerio: brown capuchins (*Sapajus [Cebus] apella*) consistently coordinate in an Assurance Game for unequal payoffs. *Am. J. Primatol.* 83, e23321.

Rogers, F.D., Pena, C.J., Mallarino, R., 2023. African striped mice (*Rhabdomys pumilio*) as a neurobehavioral model for male parental care. *Horm. Behav.* 152, 105364.

Rose, M.C., Styr, B., Schmid, T.A., Elie, J.E., Yartsev, M.M., 2021. Cortical representation of group social communication in bats. *Science* 374, eaba9584.

Schmitt, U., Hiemke, C., 1998. Strain differences in open-field and elevated plus-maze behavior of rats without and with pretest handling. *Pharmacol. Biochem. Behav.* 59, 807–811.

Seifert, A.W., Kiama, S.G., Seifert, M.G., Goheen, J.R., Palmer, T.M., Maden, M., 2012. Skin shedding and tissue regeneration in African spiny mice (*Acomys*). *Nature* 489, 561–565.

Seyfarth, R.M., Cheney, D.L., 1984. Grooming, alliances and reciprocal altruism in vervet monkeys. *Nature* 308, 541–543.

Shafrir, E., 2000. Overnutrition in spiny mice (*Acomys cahirinus*): beta-cell expansion leading to rupture and overt diabetes on fat-rich diet and protective energy-wasting elevation in thyroid hormone on sucrose-rich diet. *Diabetes Metab. Res. Rev.* 16, 94–105.

Shkolnik, A., Borut, A., 1969. Temperature and water relations in 2 species of spiny mice (*Acomys*). *J. Mammal.* 50, 245–255.

Simmons, L.W., Kvarnemo, C., 2006. Costs of breeding and their effects on the direction of sexual selection. *Proc. Biol. Sci.* 273, 465–470.

Stevenson, S.A., Piepenburg, A., Spool, J.A., Angyal, C.S., Hahn, A.H., Zhao, C., Riters, L. V., 2020. Endogenous opioids facilitate intrinsically-rewarded birdsong. *Sci. Rep.* 10, 11083.

Tan, J., Hare, B., 2013. Bonobos share with strangers. *PLoS One* 8, e51922.

Tan, J., Ariely, D., Hare, B., 2017. Bonobos respond prosocially toward members of other groups. *Sci. Rep.* 7, 14733.

Tang, W., Davidson, J.D., Zhang, G., Conen, K.E., Fang, J., Serluca, F., Li, J., Xiong, X., Coble, M., Tsai, T., Molind, G., Fawcett, C.H., Sanchez, E., Zhu, P., Couzin, I.D., Fishman, M.C., 2020. Genetic control of collective behavior in zebrafish. *iScience* 23, 100942.

Tessitore, C., Brunjes, P.C., 1988. A comparative study of myelination in precocial and altricial murid rodents. *Brain Res.* 471, 139–147.

Treisman, M., 1975. Predation and the evolution of gregariousness. I. Models for concealment and evasion. *Anim. Behav.* 23, 779–800.

Trivers, R.L., 1971. The evolution of reciprocal altruism. *Q. Rev. Biol.* 46, 35–57.

Wang, H., Kwan, A.C., 2023. Competitive and cooperative games for probing the neural basis of social decision-making in animals. *Neurosci. Biobehav. Rev.* 149, 105158.

Wang, Z., Ferris, C.F., De Vries, G.J., 1994. Role of septal vasopressin innervation in paternal behavior in prairie voles (*Microtus ochrogaster*). *Proc. Natl. Acad. Sci. U. S. A.* 91, 400–404.

Williamson, C.M., Romeo, R.D., Curley, J.P., 2017. Dynamic changes in social dominance and mPOA GnRH expression in male mice following social opportunity. *Horm. Behav.* 87, 80–88.

Woolley, S.C., Sakata, J.T., Crews, D., 2004. Evolutionary insights into the regulation of courtship behavior in male amphibians and reptiles. *Physiol. Behav.* 83, 347–360.

Young, L.J., Wang, Z., 2004. The neurobiology of pair bonding. *Nat. Neurosci.* 7, 1048–1054.

Young, K.A., Gobrogge, K.L., Liu, Y., Wang, Z., 2011. The neurobiology of pair bonding: insights from a socially monogamous rodent. *Front. Neuroendocrinol.* 32, 53–69.

Zhang, W., Yartsev, M.M., 2019. Correlated neural activity across the brains of socially interacting bats. *Cell* 178 (413–428), e422.

Zhou, R., Hua, R., Tang, Z., Hua, L., 2023. Group-living decrease predation risk of individual: evidence from behavior, hormones and reproduction of plateau pika. *Front. Ecol. Evol.* 11, 1037377.