Frontiers in Neuroendocrinology 30 (2009) 519–533

Contents lists available at ScienceDirect

Frontiers in Neuroendocrinology

journal homepage: www.elsevier.com/locate/yfrne

Neuroendocrinology and sexual differentiation in eusocial mammals

Melissa M. Holmes [a], Bruce D. Goldman [b], Sharry L. Goldman [b], Marianne L. Seney [a], Nancy G. Forger [a,*]

[a] Center for Neuroendocrine Studies and Department of Psychology, University of Massachusetts, Amherst, MA 01003, USA
[b] Department of Ecology and Evolutionary Biology, University of Connecticut, Storrs, CT 06269, USA

ARTICLE INFO

Article history
Available online 3 May 2009

Keywords:
Naked mole-rat
Damaraland mole-rat
Sex difference
Social status
Reproductive hierarchy
Eusociality
Social system

ABSTRACT

Sexual differentiation of the mammalian nervous system has been studied intensively for over 25 years. Most of what we know, however, comes from work on relatively non-social species in which direct reproduction (i.e., production of offspring) is virtually the only route to reproductive success. In social species, an individual's inclusive fitness may include contributions to the gene pool that are achieved by supporting the reproductive efforts of close relatives; this feature is most evident in eusocial organisms. Here, we review what is known about neuroendocrine mechanisms, sexual differentiation, and effects of social status on the brain and spinal cord in two eusocial mammals: the naked mole-rat and Damaraland mole-rat. These small rodents exhibit the most rigidly organized reproductive hierarchy among mammals, with reproduction suppressed in a majority of individuals. Our findings suggest that eusociality may be associated with a relative lack of sex differences and a reduced influence of gonadal hormones on some functions to which these hormones are usually tightly linked. We also identify neural changes accompanying a change in social and reproductive status, and discuss the implications of our findings for understanding the evolution of sex differences and the neuroendocrinology of reproductive suppression.

1. Introduction

Charles Darwin was intrigued by the type of social system seen in ants, termites and many bees and wasps where only a few individuals within a large colony engage in direct reproduction, while other members are sterile and act to support the reproductive efforts of the colony as a whole. Darwin pointed out that these "eusocial" societies, as they came to be called, posed a potential threat to his theory of evolution through natural selection, which emphasized the relative fitness of *individuals* in determining traits that would be transmitted across generations. It was difficult to understand how the trait of sterility could be transmitted to future generations. The dilemma has been resolved largely through the insights of Hamilton and others who analyzed the factors that contribute to *inclusive fitness*, emphasizing the fitness of individual *genes*. In short, genes that lead to sterility in some individuals can spread in a population if individuals carrying those genes support the reproductive efforts of their close relatives, who are likely to carry copies of the same genes [62].

While perhaps the most impressive degrees of sociality based on a reproductive hierarchy have been achieved in the numerous species of eusocial insects, a few mammals have similarly complex social structures. Eusociality occurs in at least two species of bathyergid rodents, naked mole-rats (*Heterocephalus glaber*) and Damaraland mole-rats (*Cryptomys damarensis*). In this review, we consider the evolution and neuroendocrine bases of the reproductive hierarchy associated with mammalian eusociality. We also describe our ongoing studies examining sexual differentiation and effects of social and reproductive status on the nervous systems of naked and Damaraland mole-rats. We review data showing that eusociality may be accompanied by a reduction of sex differences in behavior and in neural anatomy. Moreover, in the most social of mammals, neuroanatomy may be influenced more by an individual's breeding status than by its sex.

2. Cooperative breeding and eusociality

Cooperative breeding is defined as any social system in which members of a group assist in rearing young that are not their own. Cooperative breeders may exhibit plural breeding, where more than one adult female is actively reproducing within the cooperative group, or singular breeding, where only one female (at a given time) breeds within the social group despite the presence of other females of breeding age [57]. Cooperative breeding has been especially well studied in avians and is estimated to occur in about 3% of extant bird species. In mammals, cooperative breeding has been reported for 35 species in the order *Rodentia* [116] as well as for several species of callitrichid primates [57,117], canids [5,93] and in the dwarf mongoose and the meerkat [35].

Eusociality (literally, 'good sociality') is a term coined for the highest level of social organization based on reproductive castes

* Corresponding author. Fax: +1 413 545 0996.
E-mail address: nforger@psych.umass.edu (N.G. Forger).

0091-3022/$ - see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.yfrne.2009.04.010

[92] and can be understood as an extreme form of cooperative breeding. Eusociality probably evolves from cooperative breeding, and a survey of a variety of social species suggests a continuum from cooperative breeding to eusociality [83,113]. For a species to be considered eusocial, individuals must live in large groups including multiple adult generations in which only a few individuals participate in breeding, while other members are either sterile or do not reproduce for other reasons, such as behavioral inhibition. Some authors add the requirement of the existence of a caste system [37]. Eusociality has been a highly successful strategy within insects, with eusocial species constituting 75% of the insect biomass in some ecosystems [53]. Just two mammalian species are generally agreed to be eusocial.

2.1. Eusociality in mammals

The first claim of eusociality in a mammal was the description of the social/reproductive system observed in naked mole-rats [72], which are small (approximately 30–60 g), nearly hairless rodents native to Africa (Fig. 1A). Colonies of naked mole-rats collected in the field generally contain 60–80, and in one instance at least 295, individuals. There is typically just one breeding female (the queen) and 1–3 breeding males in each colony [11,82]. The reproductive hierarchy appears to be quite stable, and once an animal becomes a breeder, it generally remains so for life, which can be over 20 years in this species [22]. Reproductive animals are reported to be socially dominant to non-reproductive colony members [44,82].

Of five genera of the family *Bathyergidae*, or African mole-rats, naked mole-rats are the sole extant member of the genus *Heterocephalus*. Three of the bathyergid genera contain only solitary-living species, whereas the genus *Cryptomys* includes several species of varying sociality. At least one of these, the Damaraland mole-rat (*C. damarensis*), has also been claimed to be eusocial, although Damaraland mole-rats exhibit a smaller reproductive skew than do naked mole-rats, as each colony contains an average of about 16 animals with a single breeding pair (Fig. 1B).[1] All bathyergids are fossorial and are rarely observed above ground in the field [9]. Because the African mole-rats exhibit perhaps the widest range of sociality of any phylogenetically similar group of vertebrates, they offer a wonderful opportunity to test hypotheses regarding evolved associations between sociality, reproductive skew and particular aspects of physiology, anatomy and behavior.

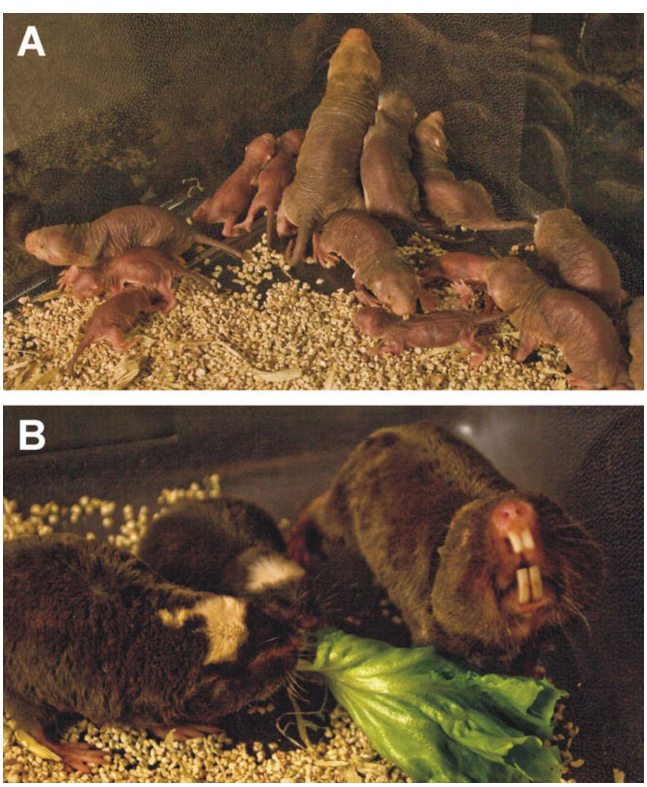

Fig. 1. Colonies of naked mole-rats (A) and Damaraland mole-rats. (B) The youngest naked mole-rats shown are 6 weeks old. In the foreground, one of these juveniles is about to be picked up by an older sibling. The breeding pair is not included in the photograph. Photography by Virge Kask.

2.2. Evolutionary origins of eusociality

In the Hymenoptera (ants, bees and wasps) eusociality appears to have originated independently approximately 12 times [129]. The preponderance of eusocial species may be related to haplodiploid sex determination in this group; that is, males possess a haploid chromosome number whereas females are diploid. One important consequence of haplodiploidy is that females are more closely related to their sisters (3/4 related, since all sisters share an identical set of chromosomes from their father) than they are to their daughters (1/2 related). This increases the value of helping sisters to reproduce. However, the existence of eusociality in termites and other diploid organisms, including certain species of aphids, thrips, beetles, and spiders raises doubts regarding the importance of haplodiploidy in the origins of hymenopteran eusociality [3,36,78,124].

Indeed, some have suggested that the multiple, independent origins of eusociality among hymenopterans may be related to the prior appearance in the group of a habit of selecting sheltered, enclosed nesting sites in which to deposit eggs and, in many cases, raise the young [1]. The protracted presence of a female and her offspring at a well protected nest site may set the stage for the origin of extended sociality, with a key step being delayed dispersal of offspring, perhaps because similarly protected sites are not readily available so that dispersal becomes relatively risky as compared to remaining at the natal site. In fact, before eusociality was known in any mammal, Alexander predicted that if a eusocial mammal did exist it would likely be a species of fossorial habit, living in a circumscribed and protected site [112].

Phylogenetic studies as well as comparative studies of colony dynamics suggest that eusociality evolved independently in naked mole-rats and Damaraland mole-rats [2,74]. Haplodiploidy cannot account for eusociality in these species, as both naked mole-rats and Damaraland mole-rats are strictly diploid. Instead, two hypotheses have been invoked to explain the evolution of cooperative breeding and eusociality in mole-rats, borrowing from ideas developed in the avian literature. First, the *ecological constraints hypothesis* suggests that ecological factors such as a shortage of suitable breeding territories, high mortality risk of dispersal, and low probability of finding a mate leads to delayed dispersal of young and, hence, overlapping generations of adults living in a single group [63]. Second, the *life history hypothesis* emphasizes the role of life history traits such as litter size and longevity in the origins of cooperative breeding. The two hypotheses are not mutually exclusive [63].

In support of the ecological constraints hypothesis, a major cost associated with fossorial life is the extraordinary amount of energy required to move to new territory during foraging. This is particularly significant for fossorial species that inhabit environments where food is patchily distributed, as is the case for both naked

[1] Recent taxonomy studies suggest that Damaraland mole-rats might more properly be considered *Fukomys damarensis* [80,123]. We use *Cryptomys* here to be consistent with the majority of the existing literature on this species.