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Mini Review

Ethology of Swiss Webster Mice in House Facilities: A Narrative Review

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Abstract

Laboratory animal science focuses on achieving animal welfare in the laboratory environment. Achieving animal welfare is linked to understanding the behaviour and natural habits of the species used in laboratory settings. The most widely used species for scientific and educational purposes is the mouse. Among mouse strains, the Swiss Webster outbred stock is one of the most commonly used. The ethology of these mice under space restriction and environmental control in animal facilities identifies their main behaviours as: i) exploring the environment; ii) searching for food; iii) grooming; and iv) resting. Their sexual behaviour occurs predominantly during the early morning hours and includes: i) attempted coitus; ii) coitus; iii) grooming; and iv) resting. They display a maternal care behaviour pattern and high variability in paternal behaviours. Regrouping adult males creates social stress, leading to increased aggression among individuals in the group. Hierarchy is determined by the presence of a dominant individual, subordinates or those disputing dominance, and neutral individuals (those who neither attack nor are attacked). We believe that knowledge of the ethology of mice in animal facilities can improve efforts to promote the welfare of animals used for scientific purposes.

Keywords: Mouse, Swiss Webster, Etology and Animal Welfare

Introduction

Despite detailed studies on the genus Mus, particularly the Mus musculus species, as well as their genealogy, phylogeny, and the historical origins of lineages currently used in laboratories, including classical inbred strains, the lack of documentation and scientific reports makes it difficult to determine precisely which species or subspecies gave rise to the numerous mouse lineages now used in house facilities. It is known that the first laboratory-developed lineage was DBA. Among outbred stock mice (non-isogenic), the Swiss and CD-1 lineages are the best-known colonies. Interestingly, their origin is linked to 200 mice from the Pasteur Institute (France) provided by Amédée Borrel, who received them from an unknown individual. These animals were supplied to André de Coulon of the Anticancereux Romand Centre in Lausanne, Switzerland [1,2].

In 1926, Clara J. Lynch, an oncological researcher interested in genetics who worked at the Rockefeller Institute (now Rockefeller University) in New York, imported two male and seven female mice from André de Coulon. In the laboratory, all animals derived from these mice were known as the "Swiss", a nickname used by Lynch in her laboratory. Lynch also collaborated with and gave some of her "Swiss" mice to other researchers, both internally and to other institutions [1,2,3].

In 1932, one of the researchers who received the "Swiss" was Leslie Webster, who conducted susceptibility experiments to viral

infection and distributed the animals to academics and commercial breeders, including Carworth Farms in the USA, which produced what is now called Swiss Webster [1,2,3].

In conclusion, our animal model is a complex and highly interesting species, even when kept in a house facilities with space restriction. Knowledge of this animal, both regarding its wild behaviour and its management in teaching and research facilities, is essential for promoting animal welfare and recognising signs of discomfort and suffering. According to legislation and ethical principles, it is imperative to understand the biology, physiology, and behaviour of these animals in order to replicate their natural conditions in animal facilities [4]. Furthermore, as we have already demonstrated, knowledge of the behavioural characteristics of these animals, especially when they resemble those of humans, fosters empathy between handlers and animals, which greatly enhances the maintenance of their quality of life [4].

Swiss Webster Ethology

The Swiss Webster mouse is a highly docile and easy-to-handle animal. It is a non-isogenic, outbred stock with the characteristic of being albino. The estrous cycle lasts four days, with the estrus (fertile phase) lasting only four hours, followed by a gestation period of 21 days and a lactation period of 21 days [3,5]. At three to four weeks of age, these animals are considered infants, exhibiting predominantly resting behaviour and significant weight gain, approximately 50% of their body weight in one week [5]. They reach juvenile age between five and six weeks, during which there is a 40 to 60% increase in sex hormones, progesterone and testosterone, which stabilise in adulthood at eight weeks of age, when there is still a slight gain in body weight [6,7]. We performed an ethogram of these animals at each age and in different groups of male and female Swiss Webster mice. The most frequently observed behaviour was environmental exploration, in which the animal demonstrates vertical movement, either leaning against the cage wall or not. This exploratory activity is prominent in mice and occurs mainly after changing the bedding. During this exploration, olfactory and ultrasonic communication occurs between individuals in the group, sharing information about the new environment. Following environmental exploration, another frequently observed behaviour in mice kept in space restriction in a laboratory environment is searching for food. This search for food is characterised by the muzzle poking the floor or bedding provided to these animals, especially when changing bedding and when the floor or bedding allows for this activity, such as wood shavings. Another significant activity in the ethogram of Swiss Webster mice is self-grooming. This activity depends on the dynamics of each group, with some groups practising this activity more than others, forming a group habit and possibly mimicking individuals within the same group. Resting is closely linked to another activity: physical contact [6]. The mouse, as an extremely social animal, engages in physical contact during interactions, either through olfactory contact (sniffing) or body contact during rest.

As previously mentioned, rest and physical contact are the predominant activities of mice during infancy (3 weeks of age). This predominance is due to their position at the base of the food chain, where they are preyed upon by many animals. These activities promote lower energy expenditure and provide protection through resting behaviour at this age, resulting in high weight gain during infancy. Another notable observation is the absence of playful activity among individuals in the group. This lack of play may be related to conserving energy reserves and avoiding exposure to predators. In other species, playful activity increases the risk of predation and leads to higher energy expenditure. Understanding the predominant activities at each age is important for selecting appropriate flooring or bedding and environmental enrichment materials that encourage physical contact and rest during infancy, such as wood shavings and paper towels (nesting material) [7].

During the juvenile stage, environmental exploration and social interaction become the predominant activities, so flooring, bedding, and enrichment should be chosen to encourage these behaviours, such as using metal trapezes suspended in the cage. In adulthood, individuals are less active compared to juveniles, with shelters being the most preferred form of environmental enrichment. Therefore, shelter categories (igloos) are the preferred enrichment objects for adults [8].

Regarding preferences, these animals clearly show a preference for various types of flooring or bedding materials, feed and water processing methods, and environmental enrichment. As infants, they prefer wood shavings at the pine flakes and nesting material to support their predominant activities of rest and physical contact. At a slightly older age, their preference remains for wood flooring or bedding, but with enrichment that encourages physical activity, such as a trapeze. In both ages, they prefer non-autoclaved feed, with irradiation being the recommended feed processing method. For water, there was no difference in consumption between autoclaved and filtered water at any age [8].

During infancy, individuals from different pairs can be grouped without causing social stress or aggression within the group. These animals seem to form a fraternal group that persists throughout life, without the visible presence of a dominant individual and subordinates. This hierarchy becomes apparent during the juvenile stage and adulthood. The hierarchy consists of a single dominant group, disputants or subordinates, and another class known as neutrals. Neutrals are individuals who are part of the group but neither attack nor are attacked when dominance aggression occurs [9]. Dominance aggression is very common when adult males are regrouped, leading to social stress and inducing aggression [9]. When two different groups of mice– that is, two groups originating from separate groups – are combined, dominance is established through aggression, but this aggression is directed towards members of the group other than those grouped together in infancy. In most groups of adult male mice, highly aggressive behaviour is present; however, we observed that 10% of groups regrouped in

adulthood establish their hierarchy or social dominance without aggression [10].

The sexual behaviour of Swiss Webster mice in housed facilities is determined by the female's acceptance of the male and their mating behaviour. In nature, these animals form herds, with a dominant male interacting with several females. This behaviour is replicated in laboratory conditions with space restriction. However, it is the female who, if able, chooses her partner and the timing of mating, regardless of the male's persistence. The female selects the most skilled and least aggressive male available, forming a monogamous pair. She is receptive to mating on the third day of the estrous cycle for only four hours, predominantly during the early morning, as these animals are nocturnal. During the estrous cycle, the male pursues the female until she reaches estrus, at which point they mate. Mating occurs repeatedly, always interspersed with the male's genital grooming behaviour. This succession of matings can be explained by the animal's need to ensure the perpetuation of its genetic code or reproductive success through fertilization of the female. Once the female is fertilized, there is a 21-day gestation period, and the birth of the pups also occurs during the early morning hours. The Swiss Webster mouse can have litters of 8 to 16 pups, with an average of 12 weaned pups. The birth of the pups elicits maternal behaviour in females, who from birth onwards are dedicated to protecting the nest and the pups. The main activity of females after giving birth is cleaning the nest of blood and placental remains. This likely occurs due to the need to keep the environment clean and avoid odours that could attract potential predators. Cleaning the nest and the pups may be shared by the male, but in every 10 matings, 10 different types of paternal behaviour have been observed, ranging from cooperative and affectionate fathers to males who attack the female and her offspring. In the case of the cooperative father, he cares for the pups, providing warmth and hygiene while the female feeds or explores the environment. However, the male's ability to clean the pups is inferior to that of the female [7].

Aggressive behaviour is common among both male and female Swiss Webster mice. In females, it is associated with protecting offspring and competing for mates [11]. In males, aggression is triggered by stressful situations, with the dominant mouse displaying high levels of aggression by biting the back, tail, and urogenital region of other males. Muricidal behaviour does not occur; moreover, the need for social interaction compels both the aggressor and the victim to maintain physical contact while resting [12]. In light and dark field boxes, when aggressors and victims are paired, these two hierarchical classes remain together in the dark area of the box for a longer period, with a higher incidence than observed in individuals that do not display aggression in their dominance. We believe that the stress caused by constant aggression leads the victim to enter a depressive-like state, preventing it from changing its pairing or coexisting separately from its aggressor. Heightened aggression appears to be related to certain genetic individuals' susceptibility to stressful situations, specifically the social stress of adult male regrouping. It also suggests a connection to trauma experienced during lactation or infancy. These factors produce a disorder similar to Post-Traumatic Stress Disorder [13], characterised by a lack of elevation in corticosterone levels even in stressful situations [14], elevated dopamine levels [15], and a prevalence of type II dopamine receptors in the frontal cortex of highly aggressive mice [16]. This aggressive state is not reversible, and no form of management is effective in minimising this type of aggression.

Conclusion

Understanding the behaviours prevalent in mice under space restriction in a laboratory environment encourages increased use of materials and objects that improve quality of life and animal welfare [17]. For example, juvenile mice show a higher prevalence of resting and nesting behaviours. This knowledge enables the provision of flooring or bedding that allows for comfortable resting and nesting materials, such as paper towels. Furthermore, understanding the behaviour of mice in the laboratory increases empathy between handlers and animals, consequently improving animal welfare.

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Conflict of Interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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