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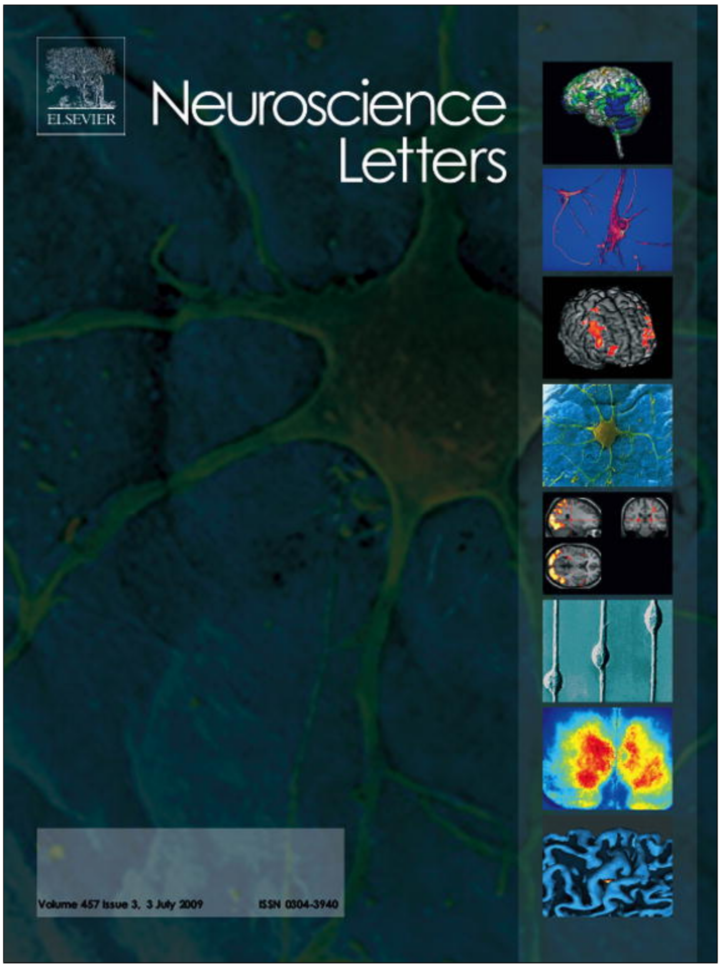

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Social dominance rank influences wheel running behavior in mice

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ABSTRACT

Dominance hierarchies within social groups determine resource distribution. Resources, such as food and access to mating partners, can act as reinforcers. The present study examined the effect of social rank on access to wheel running—a reinforcing behavior performed by laboratory animals. Mice were identified as dominant or subordinate and given access to a running wheel access under solitary or social conditions. In the solitary condition, subordinate and dominant mice spent equal amounts of time on the running wheel. In the social condition, when one wheel was present, subordinate mice spent less time on the wheel than did dominant mice. Conversely, when two wheels were present, subordinates spent more time on the wheel than did dominant mice. When mice were given 24 h access to one running wheel in the social condition, dominant mice ran more than subordinates during the dark cycle. Subordinate mice did not compensate for the lack of running wheel access by schedule shifting. These results suggest that social rank influences access to reinforcers by behavioral interference rather than by social inhibition.
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As in many other mammalian species, Balb/c mice in laboratory conditions establish social hierarchies that dictate the distribution of resources. These hierarchies are characterized by the emergence of a dominant individual who has priority access to resources such as food, water, resting places, and mating partners [14,19]. Such resources can act as reinforcers (e.g. [4,13]). Since there is evidence that wheel running is also a reinforcing behavior [15,21,25], it is feasible that dominant animals also have priority access to the running wheel [26].

A handful of published reports have indirectly examined the relationship between social stimuli and wheel running, and have returned conflicting results. Two studies suggested that social stimuli had no influence on wheel running access [6,8], whereas another implied that social stimuli did affect wheel running [19]. The first study that reported no effect of social stimuli on wheel running used both male and female hamsters [6]. It is possible that the social effects on wheel running access are gender- or species-dependent, or that wheel running is not reinforcing in hamsters. The second study used urine chemosignals from novel mice rather than direct mouse-to-mouse contact [8]. This suggests that any effect of social rank on wheel running behavior is dependent on a signal not present in mouse urine. Supporting this, mice had direct contact with one another in the study suggestive of an effect [19]. It therefore remains unresolved whether social rank influences running wheel access.

The present study explored whether running wheel access differed between social ranks. Animals were observed in both solitary and social conditions over short (1 h) and long (24 h) time periods to examine the role of hierarchy on wheel running. Social wheel running was further examined with two wheels to determine if observed differences in wheel running access between social ranks resulted from behavioral interference or social inhibition.

Subjects were seventy-eight 8–10-week-old male Balb/c mice (*Mus musculus*) weighing 30–35 g. Mice were housed in groups of 3 in 30 cm × 20 cm × 20 cm Plexiglas cages with a layer of wood shavings, and maintained on a 12 h light/dark cycle (lights on 19:00–07:00 h) at 22–24 °C. Water and food pellets were available *ad libitum*. Once a week, every mouse was weighed and marked or remarked on the rump with a distinctive stable color stain for easy individual recognition. Protocols were approved by the Animal Use and Care Committee at the Instituto de Neurobiología in accordance with NIH guidelines.

Behavioral recordings were performed daily from 1200 to 1300 h by an experienced independent observer on five triads at a time. Social rankings were done on the three cage mates. Triads were tested rather than pairs of mice since stronger social hierarchies are observed in larger groups [16]. Dominant mice were identified using a behavior sampling method that defined "winning" and "losing" individuals [7,17]. More specifically, the winning mouse bit and chased the losing mouse, while the losing mouse fled or adopted

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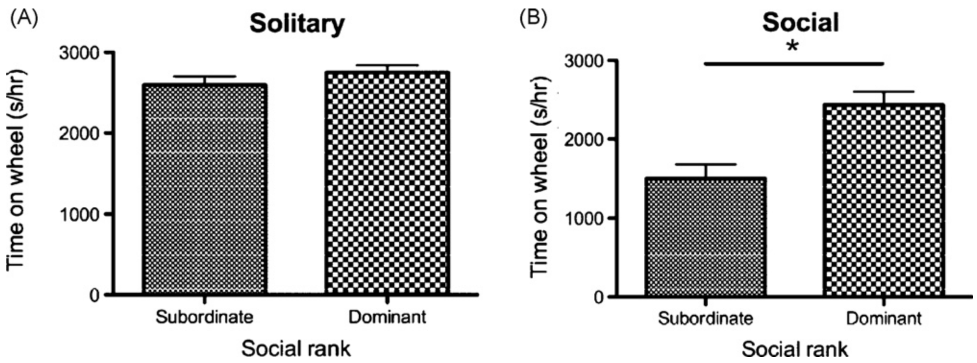

Fig. 1. *Social rank and wheel running use in solitary vs. social conditions*—1 h. In the solitary condition, subordinate and dominant mice do not differ in the amount of time spent on the running wheel ($^{*}p < 0.05$; A). Conversely, when tested as a group, dominant mice spend more time on the wheel than do subordinate mice ($^{*}p < 0.05$; B). Graphs show mean time ± SEM spent on the wheel for the hour session. In the social condition, dominant and subordinate mice sometimes occupied the running wheel at the same time.

characteristic submissive and defensive postures [7,12]. A dominant mouse was defined as a single mouse that was a consistent victor over the others and that received no attack for at least 5 consecutive days. The other two mice were classified as subordinates. With this method, the two subordinate mice are usually co-subordinates, but occasionally one shows dominance over the other. However, the situation in which two mice are co-dominants was not observed [7].

Before the social ranking tests, all mice were given 1 h access to a running wheel from 1200 to 1300 h each day for 7 consecutive days [9]. Wire running wheels were 20 cm in diameter, 10 cm wide, and housed in a glass cage (30 cm × 20 cm × 30 cm) with a wood shaving bed. The session was recorded by video camera (Sony Handycam Vision CCD-TRV46) and analyzed using Noldus Observer (Noldus Information Technology, The Netherlands). There were a total of five wheel apparatus/camera setups. For sessions during the dark cycle, infrared ray lighting (940 nm, 60 mW) was provided by the video camera recorder. In addition to running on the running wheel, mice can hang, climb or stay on or within the wheel [23]. Furthermore, when two mice are present on the wheel at the same time, it is not always possible to identify which animal is responsible for turning the wheel. The measure "time spent on the wheel" was therefore chosen as the dependent variable [24].

In all experiments, the same mice were observed in the solitary and social conditions. The order of presentation of the solitary and social conditions in all procedures was counterbalanced as fully as possible. Before the change between conditions, the social hierarchy was re-evaluated, and was found to be unchanged.

Thirty male mice were divided into 10 groups of 3. In the solitary condition, each mouse was placed alone in the experimental chamber for 60-min periods on 5 consecutive days. On the following 5 days, the three mice in each group were all placed in the wheel running chamber for 1 h. The total time spent by each mouse on the running wheel in both the solitary and social conditions was recorded. The mean time on the running wheel per hour was calculated for dominant and subordinate mice, and the difference analyzed by the Mann–Whitney U test.

Twenty-seven male mice were divided into 9 groups of 3. Each group had a well-defined social hierarchy. Mice were placed in the experimental chamber for 24 h on 5 consecutive days. The cages were recorded continuously for 24 h in both the solitary and social conditions. Total time on the running wheel was obtained for each mouse, as was time spent on the running wheel for the 12-h light and 12-h dark cycles. Data were analyzed by ANOVA followed by Fisher's post hoc test.

Twenty-one mice were divided into 7 groups of 3. For the solitary condition, each mouse was placed alone in the wheel running chamber for 1 h every day for 5 consecutive days. On the following 5 days, all 3 mice in each group were placed together in the wheel running chamber equipped with two wheels for 1 h. Total time spent on the running wheel by each mouse in both the solitary and social conditions was recorded. Data were analyzed by the Mann–Whitney U test.

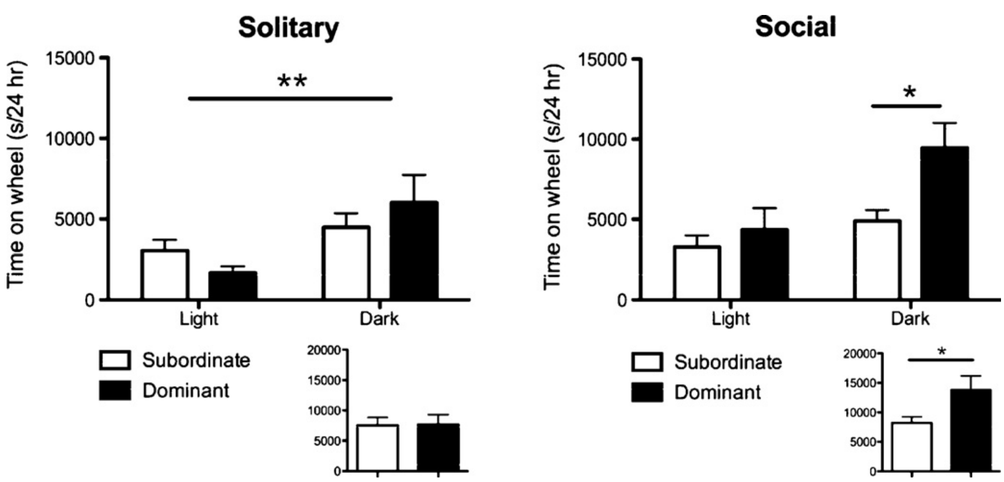

Fig. 2. *Social rank and wheel running use in solitary vs. social conditions*—24 h. In the solitary condition, no significant difference was observed in time spent on the running wheel between dominant and subordinate mice (A inset). All mice spent more time on the running wheel during the dark cycle than during the light cycle ($^{**}p < 0.01$; A). In the social condition, dominant mice spent more time on the running wheel both overall ($^{*}p < 0.05$; B inset) and during the dark cycle ($^{*}p < 0.05$; B). Graphs show mean time ± SEM spent on the wheel for the entire 24 h session.

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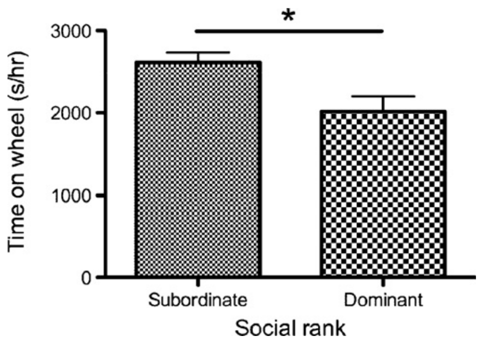

Fig. 3. *Social rank and wheel running use in the social condition with two running wheels.* Subordinate mice spent more time on the running wheel than did dominant mice (* $p < 0.05$). Graphs show mean time ± SEM spent on the wheel for the hour long session.

The mean time spent on the running wheel by dominant vs. subordinate mice in the solitary condition for a 1 h period is shown in Fig. 1A. There was no significant difference between the time that dominant vs. subordinate mice spent on the running wheel ($p > 0.05$).

The mean time spent on the running wheel by dominant and subordinate mice in the social one wheel condition is shown in Fig. 1B. Dominant mice use the running wheel for about the same amount of time as they did in the solitary condition, whereas subordinates use it for significantly less time than the dominant mice ($p < 0.05$).

The influence of dominance rank on wheel running over a 24-h period is shown in Fig. 2A and B. In the solitary condition, social rank had no overall effect on wheel running (Fig. 2A, inset). However, there was a significant difference between the dark and light periods [$F(1,28) = 11.41$, $p < 0.001$; Fig. 2A]. The light/dark cycle difference was observed in both the dominant and subordinate mice ($p < 0.01$), and there was no significant interaction between period and social dominance rank [$F(1,28) = 2.83$, $p > 0.05$].

In the social condition, there was a significant main effect of dominance rank [$F(1,25) = 6.28$, $p < 0.05$; Fig. 2B, inset] and of light–dark cycle time [$F(1,25) = 14.29$, $p < 0.001$] on time spent on the running wheel (Fig. 2B), but no significant interaction [$F(1,25) = 3.87$, $p = 0.061$]. More specifically, during the dark cycle, dominant mice spent significantly more time on the running wheel than did subordinates ($p < 0.05$; Fig. 2B).

Fig. 3 shows the mean time spent on the running wheel during an hour session in the social condition with two wheels. Dominant mice spent less time on the running wheel than subordinate mice ($p < 0.05$).

The present results demonstrate that social dominance rank influences running wheel access. When the running wheel is a limited resource, as in the one wheel social conditions, the dominant animal gets priority access, whereas subordinates are allocated less time on the wheel. This is not the result of a general reduction in wheel running behavior in subordinate mice, since subordinates spent as much time on the running wheel as their dominant counterparts in the solitary condition. Reduced running wheel access by subordinates was not a result of physical occlusion by dominant mice, for two reasons. First, when two running wheels are provided, the subordinate ran more than the dominant mouse. Second, subordinate and dominant mice often co-occupied the running wheel in the one wheel social condition (our unpublished observations). When given 24 h daily running wheel access, both subordinates and dominants run more during the dark cycle than the light cycle in the solitary condition. However, in the social condition, only the dominant mice run more during the dark cycle, suggesting that the subordinates are restricting running during the more desirable dark cycle and are not compensating by a schedule shift to the less desirable light cycle. Taken together, these results suggest that reduced time on the running wheel in subordinate mice is a result of the dominant animal's increased access to rewarding stimuli, as is seen with natural rewards such as food and sex, and that this is likely occurring because of behavioral inhibition of the subordinate mice when faced with a limited resource in the presence of the dominant mouse.

For the present study, mice were housed in groups of 3. Using our scoring method, the majority of social groups exhibited a clear dominant mouse with two subordinate mice who did not exhibit dominance over one another. However, in a minority of social groups, there was a clear linear hierarchy, with one mouse being dominant over the two others, the second being subordinate to the dominant mouse and dominant over the other mouse, and the third being subordinate to both other mice. However, in groups with linear hierarchies, the intermediate mouse acted like subordinate mice groups with one dominant and two equal subordinates. Therefore, these mice were treated as subordinates.

For the present study, we examined time on the running wheel as our dependent measure. However, mice exhibit a vast number of behaviors on the running wheel other than running. Mice also hang, climb or stay on or within the wheel [23]. Our results suggest that dominant mice have priority access to the running wheel in total time spent on the wheel. However, it is unclear if subordinate mice may compensate for reduced running wheel time by performing either different or more vigorous behaviors than their dominant counterparts.

Dominant mice did not physically exclude subordinates from the running wheel in the social condition. Rather, dominant and subordinate mice often occupied the wheel at the same time in the social situation. If the reduction in wheel running by the subordinate mouse was a result of physical interference by the dominant animal in the one wheel social condition, we would expect that the subordinates would spend a reduced amount of time on the running wheel in the two wheel social condition as well. In this way, it appears that social dominance rank is a critical determinant of access to the running wheel when it is a limited resource. Supporting this view, subordinate behavioral inhibition in the presence of a dominant animal has been previously observed in the case of intracranial self-stimulation [14,18].

Inducible differences in brain levels of molecules relevant to reward in dominant vs. submissive animals may explain the differential behavior of dominant and subordinate mice [10,11]. For example, dominant mice have much lower levels of brain encephalin than subordinates [7], and previous work from our lab demonstrated that wheel running behavior is modulated by endogenous opioids [25]. Another such change was observed in non-human primates. Dominant monkeys exhibited changes in dopamine D2 receptor levels in the brain during social but not solitary housing [20]. Furthermore, dominant monkeys housed socially did not self administer cocaine [20], which stands in contrast to individually housed primates, the vast majority of whom will self administer cocaine (e.g. [1,27]). This suggests that dominant animals reduce consumption of a reinforcer when in a social setting where the reinforcer is not in limited supply. This accords with the present study, in that solitary dominant mice spend as much time on the running wheel as do their subordinate counterparts, but under the two wheel social condition, when the reinforcer is not a limited resource, dominant mice spent less time on the running wheel than subordinates. It therefore seems likely that differences in transmission in pathways relevant to processing rewarding stimuli between dominant vs. subordinate mice may play an important role in access to the running wheel.

The 24 h observation revealed that both dominant and subordinate mice spent more time on the running wheel during the dark cycle in the solitary condition. In the 24 h social condition, however,

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only dominant mice exhibited this pattern of wheel running access. Surprisingly subordinate mice did not adopt a schedule-shifting strategy to compensate for reduced time on the running wheel during the dark. There are several possibilities why subordinate mice did not schedule shift. First, it is possible that mice are incapable of such a strategy. This seems unlikely, since rodents will change their circadian rhythms if a wheel is available only during the light cycle [3] Second, it is possible that wheel running is not strongly reinforcing enough for subordinates to develop a compensation strategy. However, previous evidence indicating that many species are highly motivated to use the running wheel [23] and that it serves as a rewarding stimulus [15,21,25]. Third, the presence at all times of a dominant animal may act as a stressful stimulus that causes physiological and behavioral reward changes in the subordinate animals [5,10,11,18]. Finally, subordinate mice may have a strategy of changing the method by which the wheel is used, for example possibly by running faster. Further observations are necessary to clarify why subordinate mice do not schedule shift.

Dominance hierarchies are characteristic of many groups of social animals, including humans. The changes in behavior of different social ranks in mouse model may prove useful to examine aspects of human dominance. For example, differences in DA transmission have been observed between different social ranks in both human [22] and mouse [2] hierarchies. Indeed, subordinate mice exposed repeatedly to novel dominant mice exhibit experience-dependent social aversion that is accompanied by changes in mesolimbic dopamine transmission [2]. This suggests that mouse models of behavioral changes in response to social rank may be useful to investigate the neural basis of bullying.

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