

AN ETHOEXPERIMENTAL ANALYSIS OF THE AGONISTIC INTERACTIONS IN ISOLATED MALE MICE: COMPARISON BETWEEN OF.1 AND NMRI STRAINS

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The aim of this study was to compare the agonistic interactions of intact rodents toward anosmic conspecific adults in two different strains of mice (OF.1 and NMRI), using an animal model of isolation-induced aggression. Individually housed male mice were exposed to anosmic 'standard opponents' and the encounters were videotaped and evaluated using an ethologically based analysis which facilitated estimation of time allocated to ten broad behavioural categories: 1. Body care; 2. Digging; 3. Non-social exploration; 4. Exploration from a distance; 5. Social investigation; 6. Threat; 7. Attack; 8. Avoidance/flee; 9. Defense/submission; 10. Immobility. The results showed that both strains of mice exhibited a very similar behavioural profile of agonistic interactions. It is concluded that both strains of mice can be appropriately used in psychopharmacological investigations in which an isolation-induced aggression model be employed.

Análisis etoexperimental de las interacciones agonísticas en ratones machos aislados: comparación entre las cepas OF.1 y NMRI. El objetivo de este trabajo fue comparar las interacciones agonísticas de ratones machos adultos en dos cepas diferentes de animales (OF.1 y NMRI), utilizando un modelo de agresión inducida por aislamiento. Así pues, ratones machos previamente aislados (durante 30 días) de cada una de las dos cepas fueron enfrentados a 'oponentes anósmicos', siendo dichos encuentros grabados en vídeo y posteriormente analizados mediante un programa de ordenador que facilitaba el tiempo acumulado que los animales pasaban en las siguientes categorías conductuales: 1. Cuidado corporal; 2. Escarbar; 3. Exploración no social; 4. Exploración desde una distancia; 5. Investigación social; 6. Amenaza; 7. Ataque; 8. Evitación/huída; 9. Defensa/sumisión, y 10. Inmovilidad. Los resultados mostraron que ambas cepas de ratones presentaban un perfil muy similar de interacciones agonísticas, lo que sugiere que tanto las cepas OF.1 como NMRI pueden ser de utilidad en investigaciones psicofarmacológicas en las que se emplee un modelo animal de agresión inducida por aislamiento.

The meeting of two unfamiliar conspecifics rodents is characterized by the display

of a number of species-typical behaviours. The term 'agonistic behaviour', introduced by Scott (1966), is defined as "a system of behaviour patterns having the common function of adaptation to situations involving physical conflict between members of the same species". Agonistic behaviour bet-

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ween adult male mice (intermale aggression) is actually one of the best-studied forms of male competitive aggression. Moreover, the study of agonistic behaviour in laboratory animals has evolved from the simple observation to the utilization of quantitative ethological techniques (Brain, Cerezo and Haug, 1992; Mitchell, 1993).

The purpose of the present study was to compare the agonistic interactions of intact rodents toward anosmic conspecific adults in two different strains of mice (OF.1 and NMRI), using an animal model of isolation-induced aggression.

Method

Animals

24 OF.1 and 24 NMRI strain albino male mice weighing 25-30 g were obtained from "Servicio de Animales de Laboratorio", Granada, Spain. Animals arrived in the laboratory at 42 days of age and were housed under standardised lighting conditions (light: 20:00-8:00), a constant temperature (21°C) and food and tap water available *ad libitum*, except during behavioural trials.

Upon arrival in the laboratory, the subjects were allocated to two different categories. Half of the animals were individually housed in transparent plastic cages (24 x 13.5 x 13 cm) as experimental animals. The remainder were housed in groups of six to be used as "standard opponents" and were temporally rendered anosmic by intranasal lavage with 4% zinc sulphate solution (Sigma Laboratories, Madrid, Spain) on both 1 and 3 days before testing. Fighting in mice, as in most rodents, is closely related to olfaction. This type of opponent was employed because it elicits attack but never initiates such behaviour (Brain, Benton, Childs and Parmigiani, 1981). Such animals rarely direct spontaneous attacks toward the test

animal. Therefore, fighting is always unidirectional, being easily quantified. All the experimental animals underwent an isolation period of 30 days before the behavioural test.

Behavioural test

An isolated animal and a "standard opponent" were confronted in a neutral arena for 10 min. This neutral cage consisted of an all-glass area, measuring 50 x 26 x 30 cm, with a fresh sawdust substrate. While separated by means of a plastic barrier, the animals were allowed 1 min of adaptation to the neutral cage before the encounter. The social encounters were videotaped using a Sony-V8 camera. Tests were carried out under white lighting between the second and sixth hours of the dark phase of the artificial cycle of the animals.

The tapes were analysed using a micro-processor and a custom-developed programme (Brain, McAllister and Walmsey, 1989) which facilitated estimation of time allocated to ten broad behavioural categories. Each category included a collection of different behavioural postures and elements, namely:

1. Body care (abbreviated groom, self-groom, wash, shake, scratch).
2. Digging (dig, kick dig, push dig).
3. Non-social exploration (explore, rear, supported rear, scan).
4. Explore from a distance (approach, attend, circle, head orient, stretched attention).
5. Social investigation (crawl over, crawl under, follow, groom, head groom, investigate, nose sniff, sniff, push past, walk around).
6. Threat (aggressive groom, sideways offensive, upright offensive, tail rattle).
7. Attack (charge, lunge, attack, chase).

8. Avoidance/flee (evade, flinch, retreat, ricochet; wheel, startle, jump, leave, wall clutch).
9. Defense/submission (upright defensive, upright submissive, sideways defensive).
10. Immobility (squat, cringe).

A detailed description of all elements can be found in Martínez, Castaño, Simón and Brain (1986) and Brain et al. (1989; 1992).

The use of videotape techniques assisted by computers has been strongly advocated by many workers investigating the impact of psychoactive drugs on social behaviour. This ethoexperimental procedure allows a complete quantification of the behavioural elements shown by the subject during the social encounters. Only the behaviour of the experimental animals was assessed. This analysis was performed by a trained experimenter who was "blind" as to the strain that each animal belonged.

Statistical analysis

The medians for times allocated to each broad behavioural category were determined. As statistical analysis, a non-parametric Mann-Whitney U-test was used to contrast the behaviour in the two strains of mice.

Results and Discussion

Table 1 illustrates medians (with ranges) of accumulated times allocated to the broad categories of behaviour described above.

In this study, the agonistic interactions in two strains of mice were compared because studies on several strains of rodents have revealed marked differences in the levels of aggression. As can be observed in Table 1, no significant differences were found in the offensive behaviours (threat and attack) toward the 'anosmic opponents' in OF.1 and NMRI animals. Similarly, there were no differences

between both strains of mice in the behavioural categories of body care, digging, non-social exploration, explore from a distance, social investigation, immobility, avoidance/flee and defense/submission. However, as indicated by ranges, there was a considerable individual variation among subjects on most of behavioural categories examined.

Isolated male mice can exhibit fierce attacks after weeks of isolation when confronted with an opponent intruder mouse in a short test. This isolation-induced aggression model is one of the most widely used aggression paradigms in psychopharmaco-

Table 1
Times (in seconds) allocated to broad behavioural categories in male mice of the OF.1 and NMRI strains (medians with ranges in brackets)

Behavioural categories	OF.1 (n=12)	NMRI (n=12)
Body care	6.71 (0.6 - 16.3)	6.95 (0 - 24.5)
Digging	28.81 (1.39 - 61.17)	53.29 (0 - 112.24)
Non-social exploration	370.45 (223.9 - 531.9)	329.48 (247.8 - 421.48)
Exploration from a distance	30.19 (11.38 - 89.43)	3.03 (1.36 - 77.5)
Social investigation	80.12 (5.5 - 257)	76.76 (2.01 - 154.05)
Threat	63.31 (0 - 158.87)	58.28 (0 - 89.89)
Attack	46.06 (0 - 162.29)	54.79 (0 - 197.39)
Avoidance/flee	0 (0 - 0)	0 (0 - 0)
Defense/submission	0 (0 - 0)	0 (0 - 0)
Immobility	0 (0 - 3.8)	0 (0 - 6)

logy. In this model, offensive and defensive aspects of agonistic behaviour are present, and they can be appropriately used to differentiate between several drugs that affect agonist behaviour. Likewise, this model can be especially useful to test the possible behavioural specificity of a given compound. In fact, isolation-induced aggression in mice has been recently used as a screening methodology for a wide range of drugs, including typical and atypical neuroleptics (Navarro, Miñarro and Simón, 1992; 1993; Navarro, Martín-López and Puigcerver,

1994; Martín-López, Caño and Navarro, 1996; Puigcerver, Navarro and Simón, 1996), benzodiazepines (Martín-López and Navarro, 1996), cyclopyrrolones (Martín-López, Caño and Navarro, 1994), antidepressants (Borrás, Salvador and Simón, 1994) or opiates (Espert, Navarro, Salvador and Simón, 1993).

In conclusion, both strains of mice exhibit a very similar behavioural profile and can be appropriately used in psychopharmacological investigations in which an isolation-induced aggression model be employed.

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