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SHORT COMMUNICATION

Social Isolation Induces Preference for Odours of Oestrous Females in Sexually Naive Male Staggerer Mutant Mice

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Abstract

The staggerer murine mutation induces olfactory deficits. Mutant males do not prefer oestrous odours to anoestrous ones. A period of social isolation after weaning induces such a preference in mutants.

The staggerer mutation affects the olivo-cerebellar circuitry (Sidman *et al.*, 1962; Hirano and Dembitzer, 1975; Crepel *et al.*, 1980; Mariani and Changeux, 1980; Zanjani *et al.*, 1990, 1994). Motor deficiencies which are evident in these mutants could at least partially explain some of their behavioural disturbances, e.g. their lack of reproduction. However, other effects of this mutation can cause this abnormality. Since mutant males behave in the same way when meeting sexually receptive and sexually unreceptive females (Baudoin *et al.*, 1991), olfactory deficits have been supposed. Studying the olfactory preferences of staggerer males for the odours of sexually receptive and unreceptive females, we showed that, contrary to non-mutant mice, these males are not attracted by the vaginal secretions of oestrous females although they are not anosmic (Féron and Baudoin, 1992). The olfactory behavioural deficits of staggerer mutants (Baudoin *et al.*, 1994) have been recently confirmed by electrophysiological studies of the main olfactory system (Math *et al.*, 1995). The histological study of the olfactory bulb demonstrates deficits at this level, i.e. a reduction in the size of the ol- factory glomeruli (unpublished results). Disorders of the accessory olfactory system have not been demonstrated.

Postpubertal social isolation, which improves sexual behaviour in male mice (deCatanzaro and Gorzalka, 1979), can also restore reproduction in staggerer mutant males (Féron and Baudoin, 1995). After 2 months of partial social isolation, 33% of these males demonstrate a reproductive capacity. When sexually experienced staggerer males are tested for their olfactory attraction to oestrous female smells they are clearly attracted by the vaginal secretions of oestrous females (Féron and Baudoin, 1993).

In order to separately analyse the effect due to sexual experience and the effect due to isolation on these olfactory preferences, we tested sexually naive staggerer males, partially isolated for 2 months, for their olfactory attraction to oestrous female odours.

Male staggerer mutant mice were produced in our stock with C57BL/6 mice heterozygous for the staggerer gene. To increase their chances for survival, young staggerer males were kept with their mother and siblings until they were 40 days old (Guastavino, 1978). Each mutant male was then placed in a Makrolon transparent cage (26 × 16 × 14 cm) for 50 days with a non-mutant female. Nine staggerer males were partially isolated from the age of 90 days to 150 days (experimental group). They had no direct physical contact with congeners of the breeding room. Eight staggerer males were reared with one non-mutant adult female during the same period (control group). This rearing condition is well tolerated by mutants and prevents intra-male differences resulting from hierarchical processes which develop in multi-male groups in mice (Sandnabba, 1986).

Two parameters were used to control for the lack of sexual experience of staggerer males: the absence of a vaginal plug in the female during their period of cohabitation with the staggerer male; and the absence of pregnancy detected in these females during and 20 days after the end of cohabitation.

Staggerer males 150 days old were tested for their olfactory choice for oestrous or anoestrous female odours. Males were introduced into the centre of a circular open

Table 1 Time spent by experimental and control staggerer males on each of the four sectors of the apparatus (mean ± SEM)

Female odours	Urine			Vaginal secretions		
	From sexually receptive females	From sexually unreceptive females	*P*	From sexually receptive females	From sexually unreceptive females	*P*
Experimental group	141.78 ± 21.96	189.56 ± 34.89	n.s.	187.22 ± 46.34	81.44 ± 15.36	<0.02
Control group	141.59 ± 11.21	165.50 ± 13.40	n.s.	148.56 ± 24.97	144.35 ± 16.56	n.s.

field, 40 cm in diameter, with rigid and opaque 20 cm high walls. The floor of the field was fitted with four microtubes (Ø 1 cm), containing cotton wool and odours, situated 5 cm from the outer edge of the field. Four different types of odours were presented in four adjacent sectors: the urine of oestrous females, the vaginal secretions of oestrous females, the urine of anoestrous females and the vaginal secretions of anoestrous females (Féron and Baudoin, 1992, 1993). Urine from female mice was immediately collected after introducing each female in a clean Plexiglas cage. Vaginal secretions were collected by washing the vagina with 0.1 ml of saline solution. In order to use identical sources of stimulation, each source of odours was prepared from a mixture of urine or vaginal secretions from five non-mutant females. The urine and vaginal secretions were then quickly frozen. They were thawed for ~30 min before the test. The mice could not lick these sources of odours. Testing occurred between 18.00 and 21.00 h, at the end of the photoperiod (L:D = 12:12). The time spent by each individual in each of the four sections of the open field was recorded and used as an index of 'relative olfactory preference' (Féron and Baudoin, 1992). The data were analysed for the first 10 min of testing. Statistically significant differences in the time spent in the sectors containing odours of receptive and unreceptive females were tested using the Wilcoxon test.

This analysis showed that isolated staggerer males spent significantly more time in the sector containing the vaginal secretions of sexually receptive females than in sectors containing the vaginal secretions of sexually unreceptive females. Control mutants showed no such difference (Table I).

When compared with control staggerer males, partially isolated mutants appeared to be more attracted by the odours of oestrous females than by odours of sexually unreceptive females. Despite their lack of sexual experience these males demonstrated olfactory preferences previously observed in both sexually experienced mutant males and sexually naive non-mutant males (Féron and Baudoin, 1992). This result leads to the hypothesis that the modification in olfactory preference is one of the mechanisms involved in the restoration of sexual behaviour induced by social isolation (Féron and Baudoin, 1995).

Social isolation reduces the behavioural olfactory deficits of staggerer mutant males. This social deprivation could decrease olfactory thresholds for an appropriate behavioural response to an odour and perhaps for its perception. Social isolation has been reported to affect the level of brain catecholamines and serotonin concentration in non-mutant mice (Garattini *et al.*, 1969; Welch and Welch, 1969a,b; Brain, 1975), and similar mechanisms could be implicated in the behavioural improvements of staggerer male olfactory preferences. An evaluation of the functional consequences of isolation should be made by conducting electrophysiological studies of the main olfactory system which would determine the implication of more peripheral versus more central changes in the olfactory improvement of socially isolated staggerer males. A complementary study will be made using pharmacological agents to change the concentration of neuromediators in the brain in order to reproduce the effects of social isolation on staggerer male olfactory behaviour.

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