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Brief report

Subordinate male mice show long-lasting differences in spatial learning that persist when housed alone

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Abstract

In the wild, house mice live in social groups, whereas in the laboratory male mice are often singly housed. Environmental enrichment such as that provided by social housing has been argued to improve the cognitive performance of laboratory animals in experimental tests. The aim of the present study was to test the cost of aggressive social interactions on learning in male CD-1 mice. We found that subordinate mice from more aggressive dyads showed spatial learning impairment, measured as alternation on a T-maze. Learning impairments in subordinates have hitherto been presumed attributable to the animals' exposure to, and relative standing within, the social group. By contrast, the impairment we observed could not have been the result of recent social defeat because it persisted weeks later when the mice were housed alone. Elevated urinary corticosterone predicted later subordination, though paradoxically these abnormally high levels were reduced by pair housing.

Keywords: CD-1 mouse; Social rank; Spatial learning; Corticosterone

Social housing provides a natural enrichment that should promote normal behaviour (Latham & Mason, 2004; Sherwin, 1998). However, the benefits of social housing are different for animals of different social rank. In the laboratory, subordinate animals can show higher levels of stress hormones such as glucocorticoids, suggesting that they suffer greater adverse effects of social stress than dominants (Creel, Creel, & Monfort, 1996). Such effects have been examined in relation to dysregulation of the hypothalamic–pituitary–adrenal axis (HPA) and possible glucocorticoid resistance (Avitsur, Stark, & Sheridan, 2001; Gariépy, Rodriguiz, & Jones, 2002; Preil et al., 2001). Consistent with the view that the HPA axis can become dysfunctional, the effects of social defeat and subordination include reduced food and water intake and decreased mating behaviour (Martinez, Calvo-Torrent, & Pico-Alfonso, 1998).

With respect to cognitive abilities, social status is known to affect learning in a number of species (Drea & Wallen, 1999; Nicol & Pope, 1999), including mice (Barnard & Luo, 2002), though evidence in particular learning contexts can be mixed (Barnard & Luo, 2002; Spritzer, Meikle, & Solomon, 2004). The relationship between spatial learning and dominance is of particular interest because both are likely to predict reproductive success in locating mates and subsequently repelling competitors. There is evidence in mice of a modulating effect of status in at least one widely used spatial paradigm, the radial maze (Barnard & Luo, 2002). Such effects have yet to be examined in relation to corticosterone. Corticosterone can be measured non-invasively in urine (Dahlborn, van Gils, van de Weerd, van Dijk, & Baumans, 1996; Fitchett, Collins, Mason, Barnard, & Cassaday, in press; Touma, Sachser, Möstl, & Palme, 2003), providing an

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integrated picture of systemic levels with good predictive validity. For example, rodent urinary corticosterone levels are reliably elevated after exposure to stressors (e.g., inescapable shock Brennan, Ottenweller, Seifu, Zhu, & Servatius, 2000). Conversely, reductions in urinary corticosterone provide evidence that the use of nesting material as environmental enrichment can promote welfare in mice (Van Loo et al., 2003).

In the present study, we tested pairs of male mice for learning differences mediated by social status on a T-maze spatial alternation task (Bertholet & Crusio, 1991; Gerlai, 1998). Subjects were 30 6-week old male mice (26–30 g) of the outbred albino strain CD-1 (Harlan, UK). Mice were maintained under a reversed 12:12-h light/dark cycle (lights on 20.30–8.30 h). All testing was carried out during the dark, active phase. Initially mice were singly housed in NPK M3 cages (48 × 15 × 13 cm). Mice were marked with black eyelash dye (Colorsport 30 Day Mascara, Brodie and Stone Plc, London, UK) for individual identification. After 2 weeks' single housing, the mice were housed in pairs, in clean NBK M3 cages, to provide 15 dyads. The timeline of the study is shown in Fig. 1.

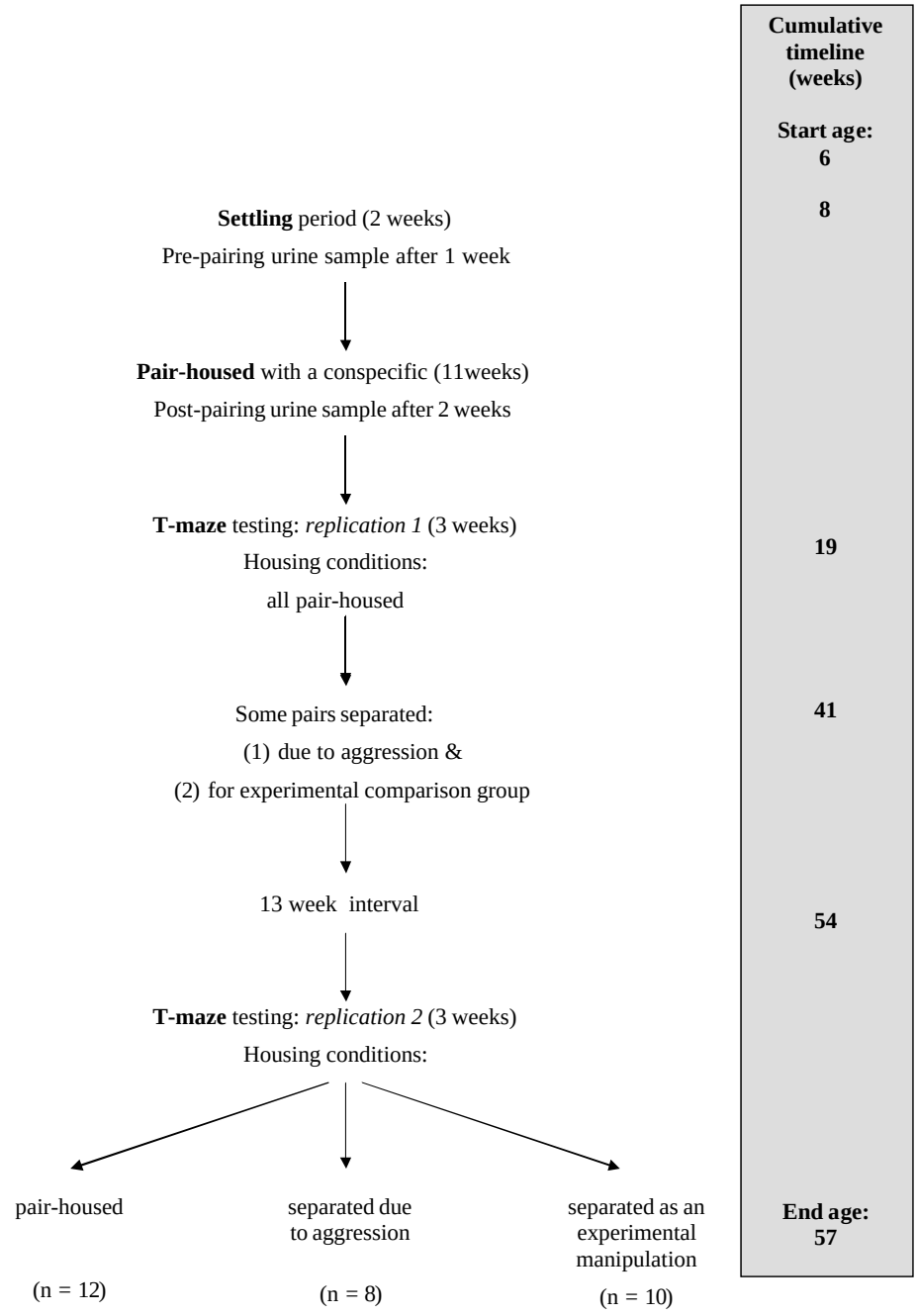

Fig. 1. The timeline of the study. The right-hand side panel gives the cumulative elapsed time in weeks.