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The effect of housing conditions on lipopolysaccharide-induced depressive-like behaviour in mice

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Inflammation is thought to play a key role in the pathology of depression. Acute administration of lipopolysaccharide (LPS) is often used to assess the role of inflammation in depressive-like behaviours, such as the forced swim test (FST), in mice (O'Connor et al. 2009. *Mol. Psychiatry*. 14(5), 511-522). We have previously shown that acute LPS failed to induce a depressive-like behaviour in the FST (Wickens et al. 2014. *J. Psychopharmacol.* 28(8), A107). Baseline depressive-like behaviour is influenced by environmental factors, including lighting and housing conditions (Bogdanova et al. 2013. *Physiol. Behav.* 118, 227-239). Here, we have investigated the influence of the light cycle and group/individual housing on LPS-induced depressive-like behaviour in mice.

Adult male C57BL/6J mice (10-14 weeks, Charles River) were randomly assigned to LPS or control groups (n=9-15/group). Mice were housed individually or in groups of 3-4 under a normal (lights on: 06:00) or reverse (lights on: 18:00) 12-hour light cycle. LPS (0.415 or 0.83mg/kg, i.p.) or saline was injected before being tested in the open field test (OFT) at +6 or +24 hours to assess sickness and the FST at +24 hours to assess depressive-like behaviour. Immobility in the FST was manually scored for 6 minutes. Distance travelled in the OFT was analyzed using automated video analysis. Data were analysed using one-way ANOVA followed by Dunnett posthoc test.

Reduced locomotion was seen 6 hours after LPS administration in all housing conditions, including 'group-housed/light-phase' ($F_{(2,33)}=49.82$, $P<0.001$), 'individual-housed/light-phase' ($F_{(2,27)}=70.48$, $P<0.001$), 'group-housed/dark-phase' ($F_{(2,40)}=78.56$, $P<0.001$) and 'individual-housed/dark-phase' ($F_{(2,33)}=97.65$, $P<0.001$). LPS had a significant effect on immobility 24 hours after LPS administration in 'group-housed/light-phase' mice ($F_{(2,29)}=5.582$, $P<0.0089$), with 0.415mg/kg LPS inducing a significant increase in immobility ($P<0.05$), but had no effect in all other housing and lighting conditions. Reduced locomotion was still present in the OFT at 24 hours after LPS ($F_{(2,49)}=8.621$, $P<0.001$).

Whilst sickness behaviour, as interpreted by reduced locomotion in the OFT, was observed in all LPS-treated groups, depressive-like behaviour in the FST was only observed in one group: group-housed/light-phase, 0.415mg/kg LPS. This finding suggests that the depressive response to LPS in the FST is sensitive to the housing conditions, along with the dose of LPS used. However, reduced locomotion was observed at 24 hours, indicating the presence of sickness, which is a confounding factor for depressive-like behaviour in the FST observed at 24 hours.

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