

Thesis Title	Effects of Isolation Rearing on Behavioural Response to Antidepressant Drugs.
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Abstract

Isolation rearing after weaning may alter behaviour and neurochemistry in the mature animals and modifies the responsivity to psychoactive agents. The aims of the present studies were to investigate the effects of isolation rearing on rat forced swimming behaviour and locomotor activity, and to compare the effects of a tricyclic antidepressant, desipramine; an atypical antidepressant, mianserin; a selective 5-HT_{1A} receptor agonist, 8-OH-DPAT; and a selective α_2 -adrenoceptor antagonist, idazoxan on these behaviours in isolation and socially reared rats.

Male Wistar rats were obtained at 21 days of age (weaning) and were housed either singly (isolation rearing) or in groups of 5 rats/cage (social rearing). After 4 weeks, both isolation and socially reared rats were exposed to the forced swimming test (an animal model of depression) and an open field arena (an animal model of locomotor activity) either without drug pretreatment or following subchronic administration of drugs or vehicle 24, 5 and 1 h before testing.

The results demonstrate that isolation reared rats were more struggling, and had significantly less immobility time ($P < 0.01$) than socially reared rats in the forced swimming test. Moreover, the isolation reared rats showed hyperlocomotion, had significantly more number of rears but defecated on significantly fewer occasions whilst in the open field arena. The

results indicate that isolation rearing modified the behaviours of the adult rats. These effects may link to alterations of the central neurotransmission mechanisms.

Subchronic treatment (24, 5 and 1 h before a 5 min test) of the selective noradrenaline (NA) re-uptake inhibitor, desipramine (5, 10 and 20 mg/kg i.p.), the selective 5-HT_{1A} receptor agonist, 8-OH-DPAT (0.05, 0.1 and 0.5 mg/kg s.c.), and the selective α_2 -adrenoceptor antagonist, idazoxan (0.5, 1, 2 and 5 mg/kg i.p.) caused a dose-related decrease in the immobility time and increase in the struggling time in the forced swimming test, in both socially and isolation reared rats. These effects were more pronounced in isolation than socially reared rats. However, subchronic treatment of the 5-HT_{2C} receptor antagonist, mianserin (1, 3 and 15 mg/kg i.p.) produced a slight anti-immobility effect. The moderate dose of mianserin (3 mg/kg) significantly decreased immobility only in isolation reared rats, whereas, the highest dose (15 mg/kg) significantly decreased immobility in both groups ($P < 0.05$), and this effect was greater in the isolation reared rats.

For locomotor activity, subchronic treatment of all of the above drugs (at the same doses that used in the forced swimming test), the results show that desipramine significantly decreased locomotor activity, in a dose-dependent manner, whereas, 8-OH-DPAT and idazoxan did not significantly alter the locomotor activity in both socially and isolation reared rats. However, subchronic treatment of mianserin, at low dose (1 mg/kg i.p.) significantly increased locomotor activity in both socially and isolation reared rats, this effect was greater in isolation reared rats. At moderate dose of mianserin (3 mg/kg i.p.) significantly increased locomotor activity only in isolation reared rats, whereas, at highest dose (15 mg/kg i.p.) did not significantly alter the locomotor activity in either group. These results suggest that the antidepressant-like effects (decrease immobility and increase struggling) of the four drugs are not due to increase in locomotor activity.

All results indicate that isolation reared rats were more sensitive to the antidepressant-like effects of desipramine, mianserin, 8-OH-DPAT and idazoxan. Thus, rearing in isolation from the early stages of life may cause postsynaptic 5-HT_{1A}, 5-HT_{2C} receptors and presynaptic α_2 -adrenoceptor supersensitivities. Further studies will be required to determine whether there are alterations of the NA transporter sites in isolation reared rats.