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Nitric oxide modulates the antidepressant-like effect of acute lithium administration in the mouse forced swimming test

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Background

Lithium has largely met its initial promise as the first drug to be discovered in the modern era of psychopharmacology, yet no definitive mechanism for its effect has been established. In the present study we evaluated the involvement of L-arginine/nitric oxide (NO)/cGMP pathway in the antidepressant-like effects of acute lithium administration in the mouse forced swimming test (FST).

Materials and methods

Male NMRI mice weighting 23-30 g (Pasteur Institute) were used throughout the study. The FST was conducted using the method of Porsolt [1]. The locomotor activity was also evaluated by an open-field test.

Results

Lithium, at 30 and 100 mg/kg, significantly reduced the immobility times of mice in the FST, whereas at lower doses (0.5, 5 and 10 mg/kg) had no effect on the immobility time. The NO synthase (NOS) inhibitor NG-nitro-L-arginine methyl ester (L-NAME), at 10 and 30 mg/kg, and the selective neuronal NOS inhibitor Nω-propyl-L-arginine (L-NPA), at 5 and 15 mg/kg, had no significant effects on the FST, whereas they significantly decreased the immobility time at 100 and 30 mg/kg, respectively. Combination of non-effective dose of lithium (10 mg/kg) with low doses of L-NAME (30 mg/kg) or L-NPA (15 mg/kg) significantly reduced the immobility times in the FST. Moreover, the guanylyl cyclase inhibitor ODQ at 50 mg/kg significantly decreased the immobility time of mice, whereas it had not significant effects on the FST at 2, 10 and 20 mg/kg. Combination of lithium (10 mg/kg) with 20 mg/kg ODQ significantly decreased the immobility times in the FST. Non-effective doses of L-arginine (750 mg/kg) or sildenafil (5 mg/kg) significantly reversed the antidepressant-like effect of 30 mg/kg lithium in the FST. Neither of the drugs had effect on the locomotor activity.

Conclusions

These data indicate the involvement of L-arginine/NO/cGMP pathway in the antidepressant-like effect of lithium in the mouse FST and also might suggest the concurrent administration of NOS inhibitors and lithium as an appropriate strategy for treatment of depression.

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M Ghasemi will hopefully present this study.

References

1. Porsolt RD, Bertin A, Jalfre M: **Behavioural despair in mice: a primary screening test for antidepressants.** *Arch Int Pharmacodyn Ther* 1977, **229:**327-336.