Fluoxetine enhances the anticonvulsant effects of conventional antiepileptic drugs in maximal electroshock seizures in mice

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Abstract:
The present study was designed to investigate the effects of fluoxetine (FXT), a selective serotonin reuptake inhibitor, on the effect of antiepileptic drugs (AEDs) in the maximal electroshock seizure (MES) model in mice. FXT at the doses of 25, 20 and 15 mg/kg significantly increased the electroconvulsive threshold. The antidepressant applied at the lower doses (10, 5 and 2.5 mg/kg) did not influence the threshold. Moreover, FXT (at the highest subprotective dose of 10 mg/kg) increased the anticonvulsive potential of carbamazepine (CBZ), diphenylhydantoin (DPH), valproate (VPA) and phenobarbital (PB), producing a dose-related decrease in their ED₃₀ values against MES. Nevertheless, pharmacokinetic events may be involved in the interaction between FXT and PB or CBZ, since the antidepressant raised the total brain concentration of the two antiepileptics. FXT in combination with AEDs did not influence the motor performance in the chimney test and long-term memory. In conclusion, the data suggest that FXT modulates seizure processes in the brain and may be advantageous in the treatment of epilepsy in depressed patients, improving the seizure control in epilepsy.

Key words:
fluoxetine, antiepileptic drugs, epilepsy, depression, antidepressant, 5-HT reuptake inhibition