Anxiolytic-like effect of chronic treatment with 1MeTIQ measured in the EPM test in rats

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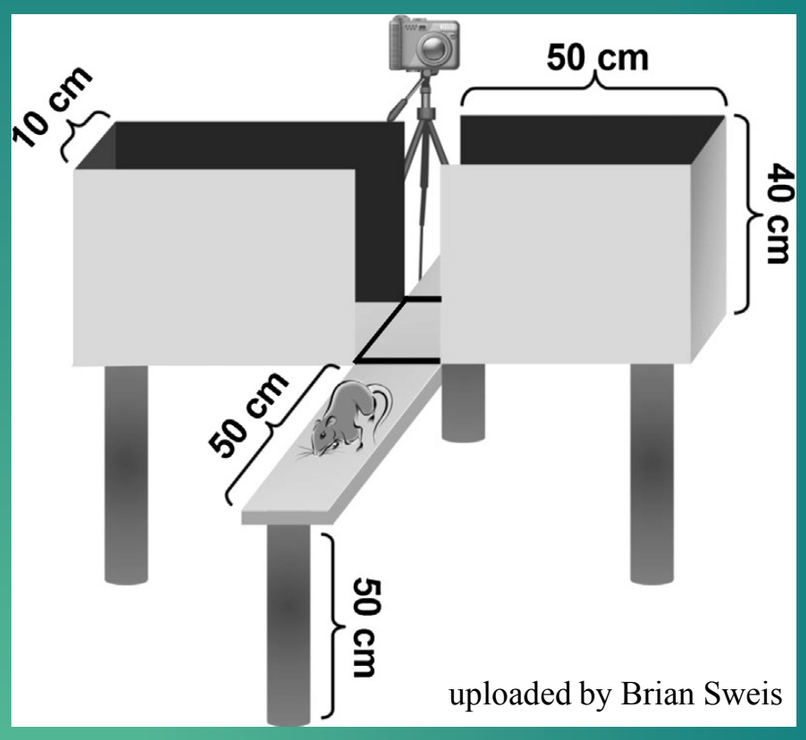
THE AIM

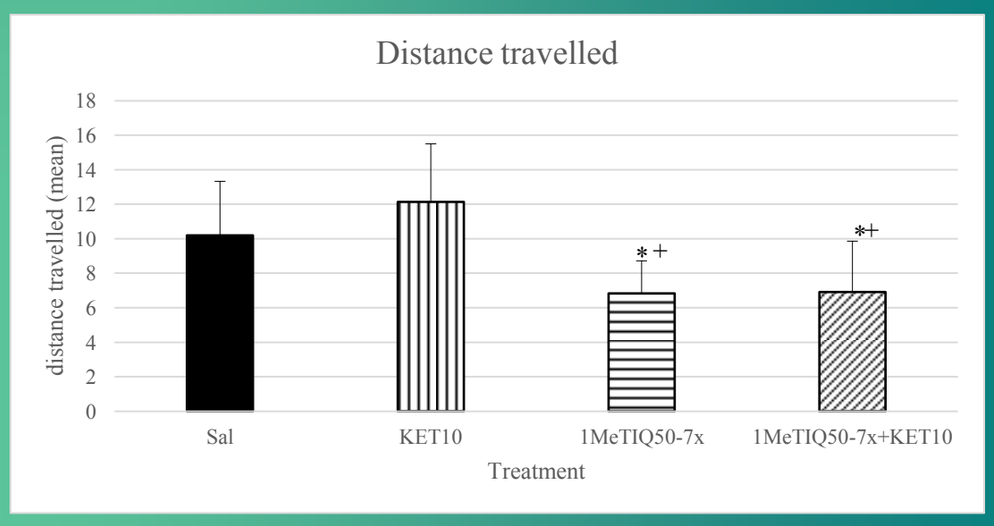
Anxiety is a one of the symptoms of schizophrenia. Ketamine, which acts as a noncompetitive antagonist of glutamatergic NMDA receptors by binding to the phencyclidine site, may induce schizophrenia-like symptoms and promote anxiogenic-like behaviour. The symptoms of anxiety in rodents can be measured by the elevated plus maze (EPM) test. 1-Methyl-1,2,3,4-tetrahydroisoquinoline (1MeTIQ), as a neuroprotective and antiaddictive substance, produces pharmacological effects by influencing monoaminergic and glutamatergic activity, as previously demonstrated by us[Wąsik et al. 2015]. The aim of the present study was to investigate the anxiolytic-like potential of 1MeTIQ after the administration of ketamine in the EPM test. In addition, the changes in the monoamine (DA, 5-HT, NA) concentration were measured in the rat hippocampus using HPLC methodology.

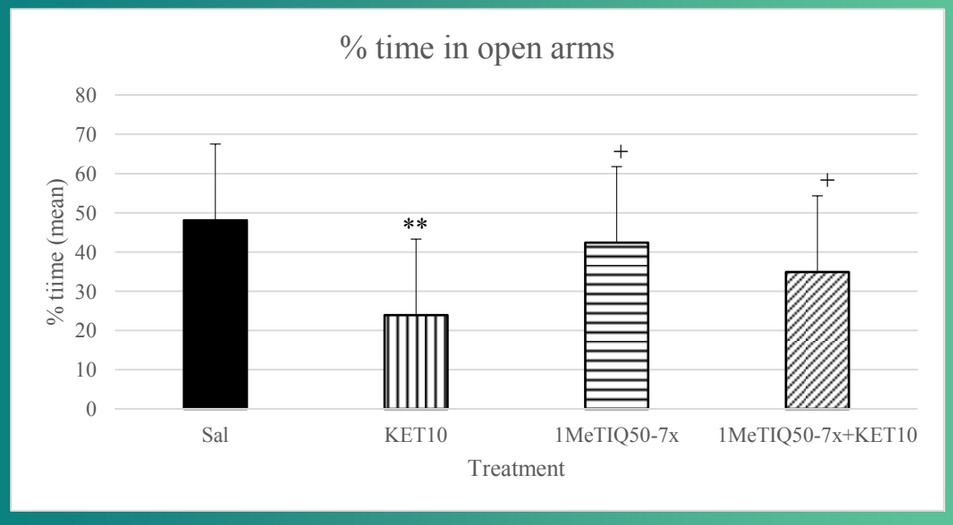


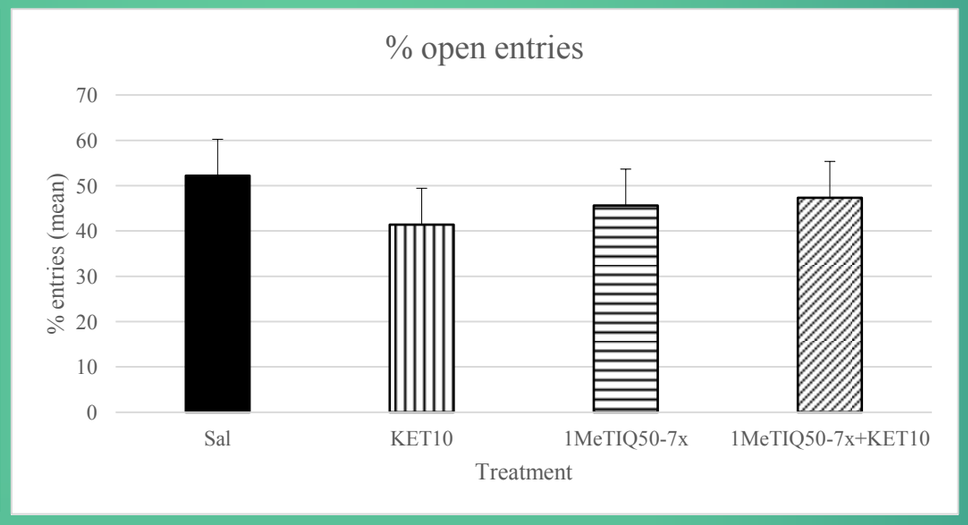
MATERIALS and METHODS

- The experiments were carried out on male Sprague - Dawley rats, weighing 300-340 g, kept under standard laboratory food and tap water, at room temperature of approximately 22°C, in a natural day-night cycle
- 1MeTIQ (50 mg/kg i.p.) was administered chronically (during 7 days) and ketamine (10 mg/kg i.p) was injected once, 20 minutes after last dose of 1MeTIQ.
- *Behavioral test* – the EPM test was performed to measured anxiety and locomotor activity
- *Ex vivo biochemical studies* – the changes in the monoamine (DA, 5-HT, NA) concentration were measured in the rat hippocampus using HPLC-ED methodology.

The effect of chronic treatment with 1MeTIQ on ketamine-induced changes in the EPM test







The influence of combined treatment with 1MeTIQ and ketamine on monoaminergic metabolism in the rat hippocampus

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Treatment	**N**	**DA**	**DOPAC**	**3-MT**	**HVA**	**NA**	**NM**	**5-HT**	**5-HIAA**
Saline/control	8	51±6	13±1,5	8±1	35±2	252±14	12±1	105±7	144±11
Ketamine10mg	8	69±24	19±5,6	11±1	30±5	279±27	11±1	135±20	183±22
1MeTIQ50mg – 7x	10	58±11	6±0,9	11±1	26±2	337±22*	45±4**	230±55*	178±15
1MeTIQ50mg -7x + Ketamine10mg	9	50±6	7±1,1^{++}	12±1*	31±3	307±25	47±3**$^{++}$	276±36**$^{+}$	177±11
F		*$F_{(3/31)}$=0,42 NS*	*$F_{(3/31)}$=4,64 P<0,008*	*$F_{(3/31)}$=2,11 NS*	*$F_{(3/30)}$=1,21 NS*	*$F_{(3/31)}$=2,56 NS*	*$F_{(3/31)}$=48,23 P<0,0000001*	*$F_{(3/31)}$=4,30 P<0,01*	*$F_{(3/31)}$=1,28 NS*

CONCLUSIONS

- A low dose of ketamine produces an anxiogenic effect in the EPM test.
- Chronic administration of 1MeTIQ (50 mg/kg) combined with ketamine showed anxiolytic-like effects in the EPM test.
- The anxiolytic-like effect of 1MeTIQ is related to its interaction with monoaminergic systems.

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DISCLOSURE
No confict of interest