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The possible mechanisms involved in the anxiogenic effect on nicotine

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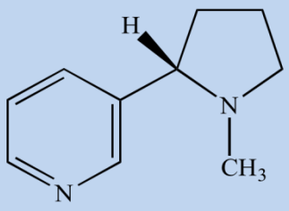


Introduction

Nicotine has been proven to exert anxiogenic effects in animals at specific doses [1,2]. One of its main sites through which it influences the central nervous system is by stimulating the release of dopamine in these structures.

Objective

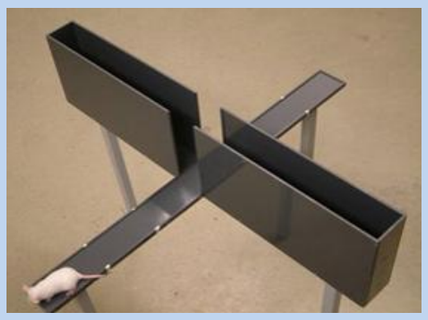
Considering its mechanism of action, the purpose of this study was to investigate if the dopamine system is involved in the anxiogenic effects of nicotine. To accomplish this, our study used haloperidol, a classic antipsychotic, and olanzapine, an atypical one, both dopamine antagonists.

Materials and methods

2 experiments (one for each antipsychotic):
the first one evaluating the interaction between nicotine and haloperidol
the second one evaluating the interaction between nicotine and olanzapine

Animals: 4 groups of 12 albino mice for each experiment:
Drugs: Normal saline solution inj. ip. 0.1ml/10gbw
Nicotine inj. sc. 0.1mg/kgbw
Haloperidol inj. ip. 0.02mg/kgbw
Nicotine inj. sc. 0.1mg/kgbw + Haloperidol inj. ip. 0.02 mg/kgbw
Olanzapine inj.ip. 0.5mg/kgbw
Nicotine inj. sc. 0.1mg/kgbw + Olanzapine inj.ip. 0.5mg/kgbw

• Elevated plus maze **test**



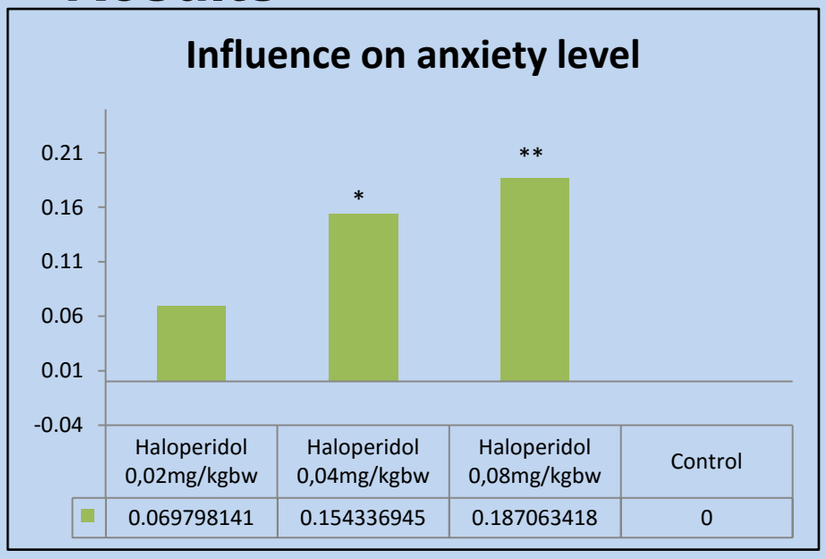
Parameters measured:

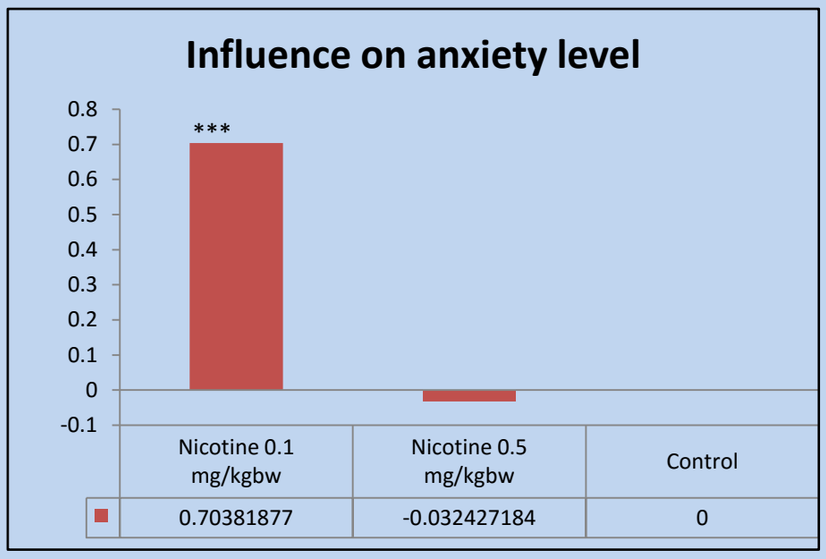
•Time spent in open arm
•Time spent in enclosed arm
•Number of visists in the open arm
•Number of visits in the enclosed arm

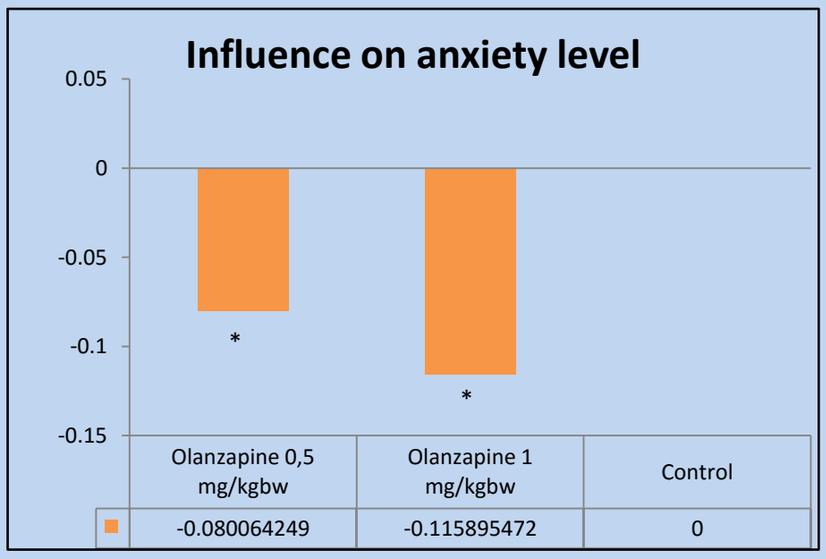
• Plasma level of corticosterone

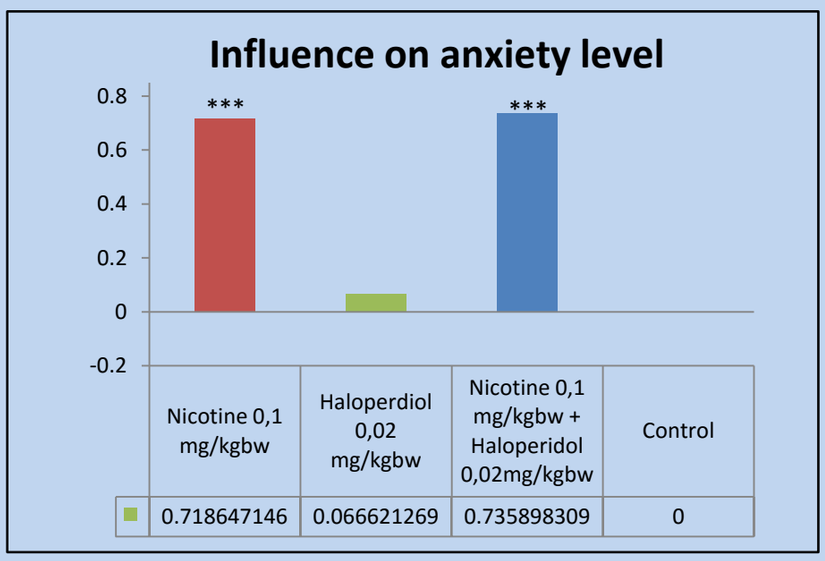
ANOVA method using SPSS

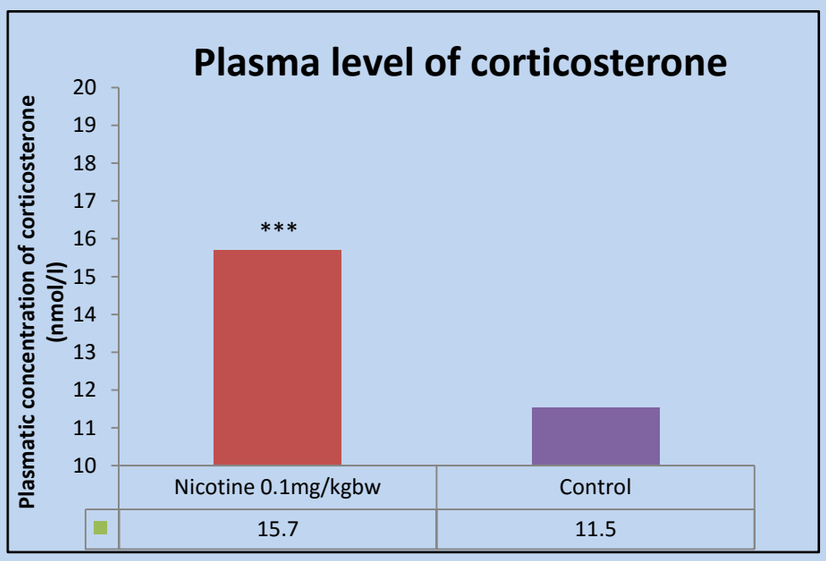
Results

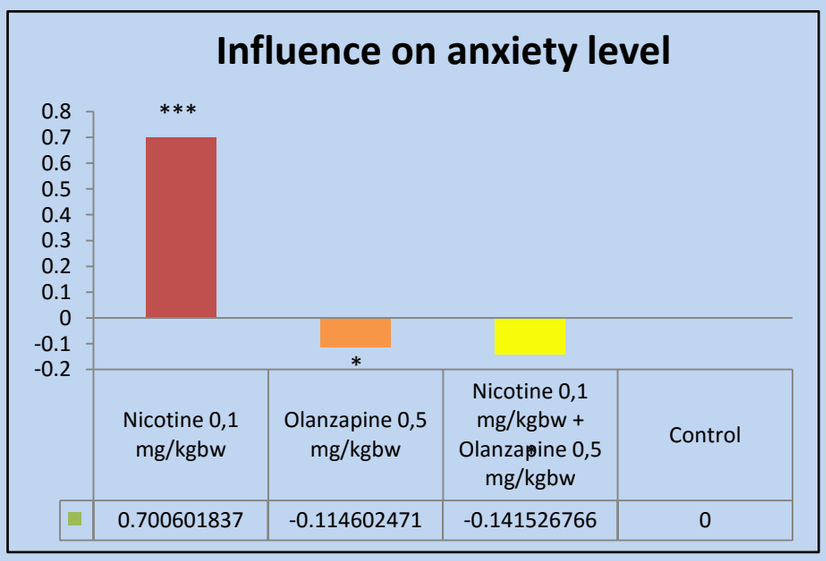












Discussion

Nicotine increased anxiety level by 72% ($p<0.05$), haloperidol by 7% and the nicotine-haloperidol association increased anxiety by 74% ($p<0.05$) as compared to the control batch. In the second experiment, nicotine increased the anxiety level by 70% ($p<0.05$), olanzapine decreased it by 11% ($p<0.05$) and the combination olanzapine-nicotine decreased the anxiety level by 14% ($p<0.05$). Corticosterone plasma level was increased by 38% in nicotine group as compared to the control group ($p<0.05$).

Conclusion

The two antipsychotics acted differently on the anxiogenic effects on nicotine: haloperidol had no influence, while olanzapine antagonized the anxiogenic effects of nicotine. Considering these results as well as the fact that olanzapine interacts with type 1 histaminergic and serotoninergic receptors, it is plausible that the anxiogenic effect of nicotine is produced via an interaction with either the serotoninergic or the histaminergic systems [3].

References
[1] Cheeta, S., Irvine, E., File, S.E., 2001. Social isolation modifies nicotine'seffects in animal tests of anxiety. Br J Pharmacol 132, 1389–1395.
[2] Trigo, J.M., Zimmer, A., Maldonado, R., 2009. Nicotine anxiogenic and rewarding effects are decreased in mice lacking beta-endorphin, Neuropharmacology 56(8), 1147-1153.
[3] Product Information: ZYPREXA 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, and 20 mg coated tablets, 2016. Eli Lilly Nederland BV.

No conflict of interest