

Acute nicotine-induced anxiety: The function of central histaminergic capacities

Badgujar Girish Eknath^{1*}, Nikhil Singh², Ragini Bundela³, Ramakant Sharma², Karunakar Shukla⁴

¹ Department of Pharmacy, Dr. A.P.J. Abdul Kalam University, Indore, Madhya Pradesh, India

² Assistant Professor, Department of Pharmacy, Dr. A.P.J. Abdul Kalam University, Indore, Madhya Pradesh, India

³ Associate Professor, Department of Pharmacy, Dr. A.P.J. Abdul Kalam University, Indore, Madhya Pradesh, India

⁴ Professor and Principal, Department of Pharmacy, Dr. A.P.J. Abdul Kalam University, Indore, Madhya Pradesh, India

Abstract

Nicotine, a psychoactive component of tobacco products, may have varying impacts on anxiety levels depending on the individual. Some people believe that nicotine helps them relax and cope with stress better, while others find that it increases their anxiety and agitation. How much nicotine you use, how frequently you smoke, and whether you have any prior mental health issues are just a few of the many factors that might influence the association between the two. In an attempt to resolve the seemingly inconsistent results in the literature on the subject, this study aimed to examine the effects of different nicotine dosages on anxiety-like behavior in animals using a hole-board device and quantitative and qualitative analysis.

Keywords: Nicotine, Histaminergic, Anxiety, Diazepam, psychoactive

Introduction

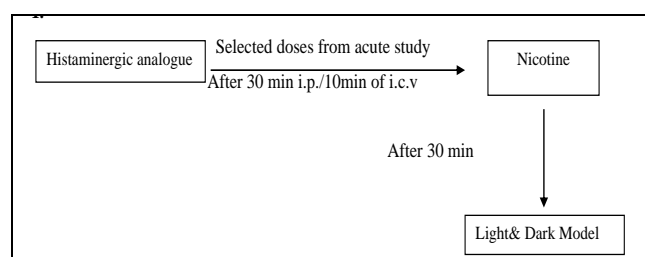
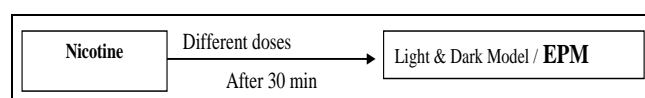
Nicotine, a naturally occurring alkaloid, is present in tobacco leaves belonging to the Solanaceae family and the cultivated plant *Nicotiana tabacum*. In liquid form, it tastes bitter, is colorless, soluble in water, and has a pH of 8.5, making it a weak basic. Nicotine should not be confused with nicotinic acid, also known as niacin, a fat-soluble vitamin B3. It is intriguing to investigate how nicotine affects behavior and how this could lead to continued tobacco use, which carries a significant risk to one's health. Nicotine binds as an agonist at nicotinic receptors, mimicking the effects of the endogenous neurotransmitter acetylcholine. While they are extensively dispersed throughout the brain, reward-related circuits are where they are most concentrated. Strong system neuron adaptations (signal transduction mechanisms) both within and between system neuron adaptations in the brain's motivational and stress systems account for a major portion of nicotine's addictive potential. This is said to be the main motivation behind tobacco product consumption. However, nicotine dependency is associated with mood liability, leading to heightened feelings of stress in many regular smokers and stress level has been shown to decline after smoking cessation. Whether smoking truly lowers stress is still up for debate. Numerous human studies have demonstrated that an increase in smoking among smokers when exposed to stress and such behavior is believed to reduce the subjective feeling of stress-related tension (Parrott, 1994; Todd, 2004). Nicotine can enter the body through the gastrointestinal tract, the lung, and the oral mucosa (GIT). Nicotine has a half-life of two hours. The kidneys, liver, and lungs metabolize between 80 and 90 percent of nicotine. Cytochrome-P450 2A6 (CYP2A6) is involved in the nicotine metabolism in liver. It's excreted in urine conjugated with glucuronic acid and in free form.

Materials and methodology

1. Materials

- L-Histidine
- Animals (Mice and rats)
- ICV (Intra Cerebro Ventricular)
- Models:
- Elevated Plus Maze (EPM):
- Light and Dark Model:
- Social interaction test (SIT):

2. Methodology



Results and discussion

Table 1: Effect of Nicotine on the mice and behavior after Nicotine induced anxiety:

Groups	Behavioral Parameters					
	Walking (Time in Sec)	Climbing (No. of Times)	Immobility Period (In Sec)	Paw Licking (No.)	Face Grooming (No.)	Rearing (No.)
I	160	20	25	15	12	18
II	70	10	45	9	9	15
III	50	7	78	7	8	12
IV	30	5	120	4	2	7

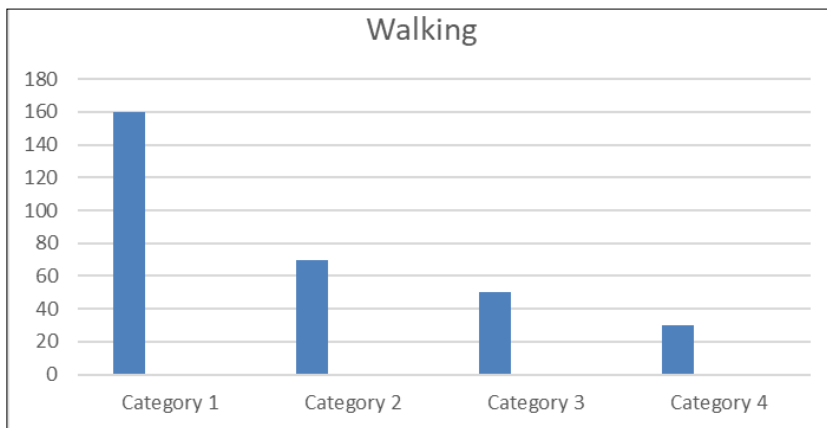


Fig 1: Graph of Behavioral Parameter of Walking

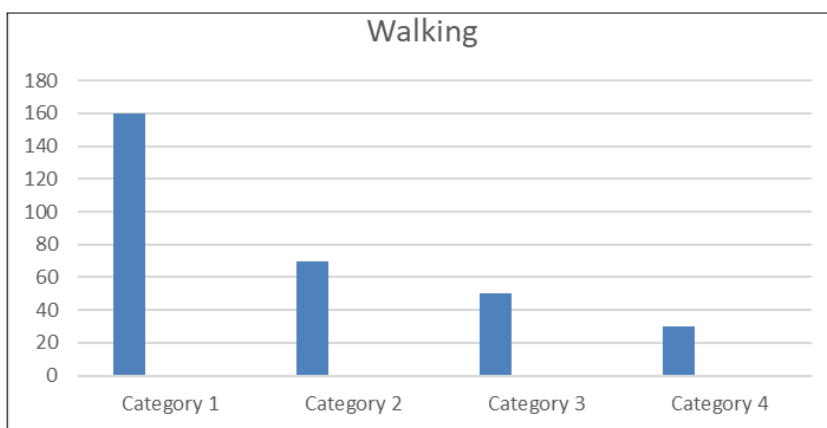


Fig 2: Graph of Behavioral Parameter of Climbing

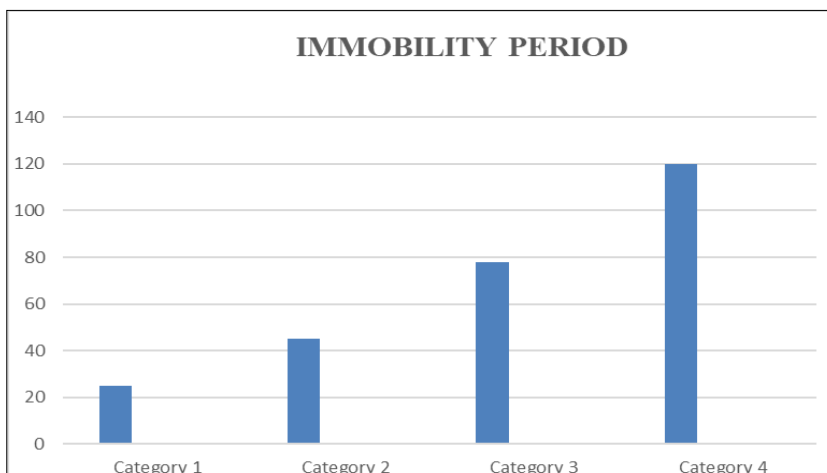


Fig 3: Graph of Behavioral Parameter of Immobility Period

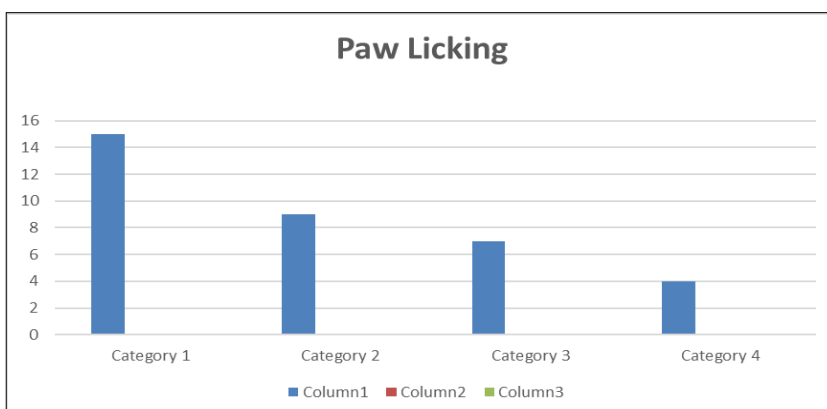


Fig 4: Graph of Behavioral Parameter of Paw Licking

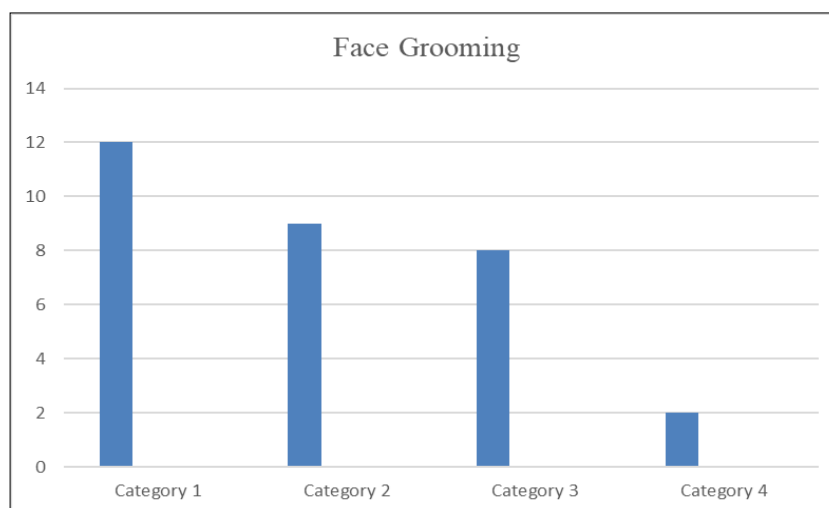


Fig 5: Graph of Behavioral Parameter of Face Grooming

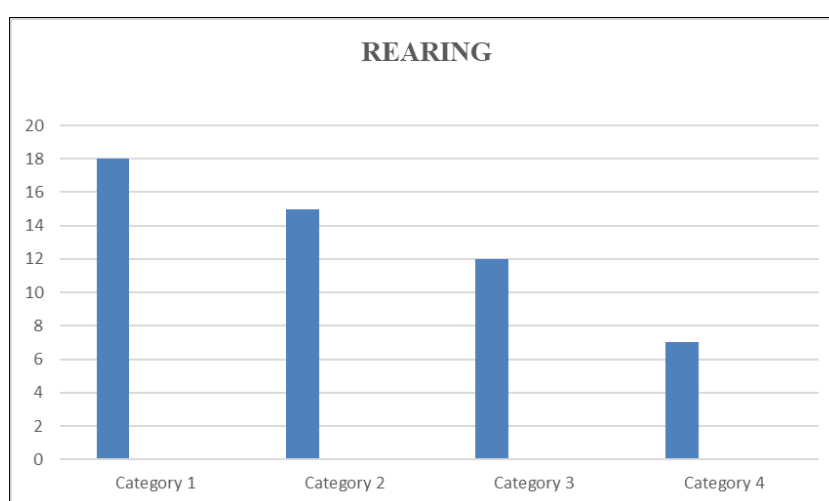


Fig 6: Graph of Behavioral Parameter of Rearing

Table 2: Antianxiety Activity of Histamine Analogues on Nicotine induced anxiety on mice by Light-dark Model.

Group	Treatment	Dose	No. of entries in light chamber	No. of entries in dark chamber	Time spent in light chamber (In Sec)	Time spent in dark chamber (In Sec)
I	Normal Saline	3 ml/kg	6.27±0.35	2.28±0.25	170±6.2	15±1.2
II	Negative Control	0.1 mg/kg	2.15±0.17	5.80±1.35	30±2.5	155±5.3
III	Diazepam	3 mg/kg	5.85±1.15	3.24±1.05	150±3.5	40±4.2
V	L-Histidine	15 mg/kg	4.35±0.90	2.85±0.50	125±3.2	68±2.8

All value is given in mean ± SEM, *P < 0.05, **P < 0.01 as compare with the control group (one way ANOVA followed by Dunnett's test).

Conclusion

L-Histidine (15mg/kg), two histamine analogues, demonstrated a robust antianxiety effect in the light-dark test. Two histamine analogues, L-Histidine (15 mg/kg), were evaluated for their anxiolytic effects using the light-dark anxiety model in this study. The inherent fear of heights and open spaces in rodents is capitalized upon in this concept. A dramatic increase in both the duration and frequency of light chamber use followed diazepam delivery, as expected. These results are in agreement with prior studies showing that diazepam and other benzodiazepines can generate anxiolytic effects, as shown in several anxiolytic screening techniques including the light dark model. Anxiolytic effects were observed in the light-dark model with histamine analogues (L-Histidine 15 mg/kg) by changing subjects' behavior such that they spent more time in the light chamber and entered it more often than in the

dark chamber. Diazepam had a similar effect, increasing the number of entries to the light chamber while decreasing the number of entries to the dark chamber.

Acknowledgments

Firstly, I would like to express my heartfelt gratitude to my project guide and co-guide Dr. Karunakar Shukla and Mr. Nikhil Singh, for guiding me throughout the course of the major project, extend my thanks all the teaching and non-teaching staff members so on.

References

1. Akhtar MS, Iqbal J. Evaluation of the hypoglycaemic effect of *Achyranthes aspera* in normal and alloxan-diabetic rabbits. *J Ethnopharmacol*, 1991;31(1):49-57.
2. Vogel HG, Vogel WH, Scholkens BA, Sandew J, Miller G, Vogel WF. *Drug Discovery and Evaluation*.

- 2nd ed. Berlin, New York: Springer, Verlag, 2002, 1103-6.
3. Schurr PE, Schultz JR, Parkinson TM. Triton induced hyperlipidemia in rats as an animal model for screening hypolipidemic drugs. *Lipids*,1971;7(1):68-73.
 4. Buccolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. *Clin Chem*,1973;19(5):476-82.
 5. Werner M, Gabrielson DG, Eastman J. Ultramicro determination of serum triglycerides by bioluminescent assay. *Clin Chem*,1981;27(21):268-71.