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BEHAVIOURAL CHANGES IN EXPERIMENTAL MODELS ON LONG TERM EXPOSURE TO KAINIC ACID FOLLOWED BY NICOTINE – LOCOMOTOR ACTIVITY STUDY

***S.LOKANADHAM[1], USHA KOTHANDARAMAN[2] AND K.PRABHU[3]**

[1]Research Scholar, Department of Anatomy, Bharath University, Chennai, Tamilnadu, India*
[2]Professor and Head, Department of Anatomy, ESIC Medical College & PGIMSR, Chennai, Tamilnadu, India
[3]Associate Professor, Department of Anatomy, Sri Balaji Medical College, Chennai, Tamilnadu, India

ABSTRACT

Long term administration of Nicotine is capable to protect the excitotoxicity and neuronal degeneration induced by Kainic acid and it's analogues in rodents. 16 adult male albino rats of wistar strain weighing 135-150 grams were used for the present study. The rats were divided in to four groups each consists of 4 animals. The control group was given 0.9% saline as vehicle and the experimental groups (group-II with 1mg/kg Nicotine; group III- Kainic acid 1mg/kg; IV- Kainic acid followed by Nicotine 1mg/kg bodyweight) were given intraperitoneal injections respectively for a period of 28 days. All the animals were utilized on last day of the experiment by using digital photoactometer to study the locomotor activity. The mean and standard deviation for the control group was 396.4683±5.802298, for Nicotine treated group was 201.4441±12.91962, Kainic acid treated group was 163.7172679±3.774917218 and Kainic acid followed by Nicotine group was 256.3096±11.44552 calculated and recorded. There was a significant locomotor activity improvement in kainic acid followed by nicotine treated group compared to kainic acid and nicotine treated groups was observed. Our study helps to understand the neuroprotective effect of nicotine on kainic acid induced excitotoxicity.

KEY WORDS: locomotor, kainic acid, nicotine, photoactometer

S.LOKANADHAM
Research Scholar*, Department of Anatomy,
Bharath University, Chennai, Tamilnadu, India

***Corresponding author**

INTRODUCTION

Excitotoxicity is considered as an important mechanism involved in various neurodegenerative diseases of central nervous system. Kainic acid is an analogue of excitotoxic glutamate, can elicit selective neuronal death in the brain of rodents, of which the pathological changes partially mimic neurodegeneration in the Central Nervous System[1]. Nicotine acts on the nicotinic acetylcholine receptors, specifically the ganglion type nicotinic receptor and CNS nicotinic receptor. Ganglion type nicotinic receptors are present in adrenal medulla where as CNS nicotinic receptors were present in the central nervous system[2]. Small doses of nicotine have a stimulating action on the central nervous system whereas large doses depress[2,3]. Recent findings of nicotine effects on neuroprotection claimed it as a potential tool for the treatment of neurodegenerative disorders[4]. Neuroprotective effects of (-) – nicotine are observed in cortical or striatal cultured neurons against NMDA glutamate induced neurotoxicity[5].

MATERIALS AND METHODS

A total of 16 adult male albino rats of wistar strain weighing 135-150 grams were used for the present study. The animals were maintained under controlled conditions and in room temperature (23±2^0 C), humidity (50±5%) and a 12 h light and dark cycle. The animals were housed in sanitized polypropylene cages. The animals were fed with standard rat pellet diet commercially available manufactured by kamathenu Pvt Ltd., Bangalore and clean drinking water ad libitum. The rats were divided in to four groups each consists of 4 animals. The control group was given 0.9% saline as vehicle and the experimental groups (group-II with 1mg/kg Nicotine; group III- Kainic acid 1mg/kg; IV- Kainic acid followed by Nicotine 1mg/kg bodyweight) were given intraperitoneal injection respectively for a period of 28 days. Kainic aid was dissolved in (1:2) in Di methyl sulfoxide solution. All the animals were utilized to study the behavioral changes on long term administration of kainic acid followed by nicotine using Digital photoactometer (INCO, INDIA). Animals were maintained as per the national guidelines and protocols approved by an Institutional animal ethical committee of Sugen Life sciences (SLS/COM/IAEC/02/2013-2014).

RESULTS

Locomotor activity of the control group with an average count of 396.5 per 10 minutes was recorded.

Figure 1
Locomotor activity by using Digital photoactometer in experimental model (control group-saline treated)

An average count of 163.75 per 10 minutes was observed in 1 mg /kg Kainic acid treated experimental group.1 mg /kg Nicotine treated group animals shown an average count of 201.75 per 10 minutes.

Figure 2
Locomotor activity by using digital photoactometer in experimental models (1mg/kg nicotine treated)

Figure 3
Locomotor activity by using digital photoactometer in experimental models (1mg/kg kainic acid followed by nicotine treated)

In Kainic acid followed by Nicotine treated group; we have observed an average count of 256.5 per 10 minutes was observed [Table-1]

Table 1
Behavioral changes of experimental models by using Digital photoactometer

Group	Time	Animal-1 (counts)	Animal-2 (counts)	Animal-3 (counts)	Animal- 4 (counts)	Average
Control	600(Sec)	391	398	404	393	396.5
Nicotine 1mg/kg	600(Sec)	188	202	219	198	201.75
Kainic acid 1mg/kg	600(Sec)	163	165	168	159	163.75
KA+Nl (1mg/kg)	600(Sec)	244	252	271	259	256.5

The mean and standard deviation for all the groups were calculated and recorded. The mean and standard deviation for the control group was 396.4683±5.802298, for Nicotine treated group was 201.4441±12.91962, Kainic acid treated group was 163.7172679±3.774917218 and Kainic acid followed by Nicotine group was 256.3096±11.44552 calculated and recorded [Table-2].

Table 2
Statistical analysis

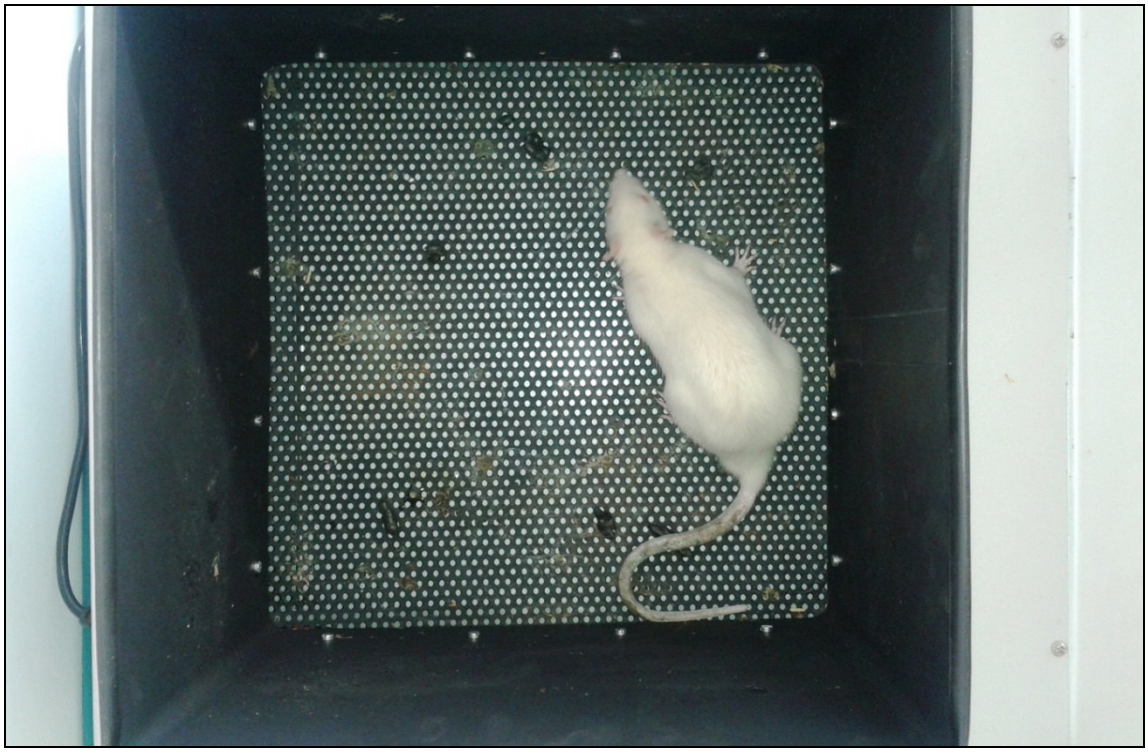
Group	Mean±Sd
Control	396.4683±5.802298
Nicotine 1mg/kg	201.4441±12.91962
Kainic acid 1mg/kg	163.7172679±3.774917218
KA+Nl (1mg/kg)	256.3096±11.44552

There was a significant locomotor activity improvement in kainic acid followed by nicotine treated group compared to individual kainic acid and nicotine treated groups was observed

DISCUSSION

Animals in the control group were shown significant locomotor activity compared to previous literatures [Figure-1&4].

Figure 4
Animal placed inside the photoactometer to observe the locomotor activity (Behavioral study)



We have observed hyperactivity followed by hypo activity in a span of 10 minutes1mg/kg nicotine treated group [Figure-2].Literatures stated that the initial hyper activity could be due to the initial increased levels of the excitatory neurotransmitters[6]. An increase in locomotor activity occurs consistently after nicotinic agonist administration followed by a subsequent challenge, a phenomenon known as behavioral sensitization[7]. Nicotine-induced increase in locomotor activity and changes in behavioral pattern depend on an intact dopaminergic system. Nicotinic AChRs contains α6 and β2 subunits are highly expressed in VTA dopamine neurons, and seem to be involved in both nicotine-induced locomotor activation[8]. Locomotor activity in kainic acid group animals was very poor compared to control and other experimental groups**.** Hypo activity could be due to striatal neuronal degeneration and energy impairment[9]. Kainic acid causes the degeneration of the striatal neurons expressing dopamine receptors, there by attenuate dopamine signalling and causing motor symptoms like altered locomotor, motor in coordination[5, 9]. In Kainic acid followed by Nicotine group; there was significant locomotor activity improvement when compared to Kainic acid group[Figure- 3], which may be due to role of Nicotine mediated antagonistic activity on Kainic acid induced toxicity through GABA mediated process[10,11].GABA agonists strongly inhibit both the behavioral and neurotoxic consequences of Kainic acid administration[12].Limited literature is available on locomotor activity of experimental models on long term administration of Kainic acid followed by Nicotine by using photoactometer in particular. Few studies on Nicotine and Kainic acid induced locomotor activity in experimental animals were available in the literature.

CONCLUSION

Due to limited literature available on locomotor activity in experimental animals on longterm administration of Kainic acid followed by Nicotine by using photoactometer. The present study helps to understand the protective role of Nicotine in neurodegenerative diseases.

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CONFLICT INTEREST: NIL

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