World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Boron attenuates anxiety-related behaviors in an MK-801-induced schizophrenia mouse model

Murat Sırrı Akosman [1,*], Ruhi Türkmen [2] and Hasan Hüseyin Demirel [3]

[1] *Department of Anatomy, Faculty of Veterinary Medicine, Afyon Kocatepe University, 03200, Afyon, Turkey.*
[2] *Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, Afyon Kocatepe University, 03200, Afyon, Turkey.*
[3] *Bayat Vocational School, Afyon Kocatepe University, 03200, Afyon, Turkey.*
Murat Sırrı Akosman, Orcid: 0000-0001-6675-8840
Ruhi Türkmen; Orcid: 0000-0003-4726-3900
Hasan Hüseyin Demirel Orcid: 0000-0002-4795-2266

World Journal of Advanced Research and Reviews, 2026, 29(02), 1098-1100

Publication history: Received on 06 January 2026; revised on 14 February 2026; accepted on 17 February 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.29.2.0372

Abstract

Schizophrenia is a chronic psychiatric disorder characterized by abnormal behavior and impaired brain function. MK-801, a noncompetitive NMDA receptor antagonist, is frequently used to induce schizophrenia-like symptoms in rodents, including locomotor hyperactivity and anxiety-related behaviors. Boron is a trace element with known antioxidant and neuroprotective effects, though the alkaline form of boron has not been studied in this context. This study aimed to investigate the protective effects of alkaline boron on behavioral alterations induced by MK-801 in mice. Twenty-four male BALB/c mice were randomly assigned to four groups (n=6): control, MK-801 (1 mg/kg, i.p.), boron + MK-801 (boron-100 mg/kg + MK-801-1 mg/kg, i.p.), and boron (100 mg/kg, i.p.). Injections were administered daily for 14 days. Thirty minutes after the final dose, animals underwent the open field test, where locomotor activity, time spent outside the center, grooming frequency and duration, and defecation count were recorded. Data were analyzed using Duncan's multiple range test. MK-801 administration induced locomotor hyperactivity, reduced grooming behavior, and suppressed defecation compared to controls ($p<0.05$). Boron treatment did not exert protective effects on locomotor activity, grooming, or defecation parameters ($p>0.05$). However, boron significantly attenuated the MK-801-induced reduction in time spent outside the center, suggesting an anxiolytic-like effect ($p<0.05$). Alkaline boron demonstrated partial protective effects in an MK-801-induced schizophrenia mouse model, specifically on anxiety-related behavior. These findings highlight the need for further research to elucidate the mechanisms underlying boron's neuroprotective potential and its relevance for schizophrenia-related behavioral deficits.

Keywords: Schizophrenia; MK-801; Boron; Open field test; Anxiety; Locomotor activity

1. Introduction

Schizophrenia is a chronic and severe mental disorder characterized by impaired social behavior and abnormal brain function, affecting approximately 1% of the global population. Although it is a widely observed condition worldwide, the etiopathogenesis of schizophrenia has not yet been fully clarified. According to reports by the World Health Organization, neurological diseases affecting motor functions rank second after cardiovascular diseases in terms of prevalence. However, the treatment of neurological diseases also poses a significant economic burden on countries [1,2]. MK-801, an NMDA receptor antagonist, is commonly used in animal models of schizophrenia as it induces various

* Corresponding author: Murat Sırrı Akosman

schizophrenia-like symptoms in experimental animals. Locomotor hyperactivity, considered a positive symptom of schizophrenia, is also observed in mice following MK-801 administration [3-5].

Boron is a very important micro-mineral found in nature as compounds and taken into the body with daily food and drink consumption. Boron is effective in various metabolic, nutritional, immune, hormonal and physiological processes in the body. In the healthcare field, it is used in osteoporosis and rheumatoid arthritis treatments, in the treatment of brain tumors with Boron Neutron Capture Therapy, and in the treatment of burns and wounds. In addition to these properties, boric acid also has antioxidant properties [6]. Boric acid has neuroprotective effect. However, its alkaline form has not been previously investigated.

This study is one of the first to examine the potential protective effects of the alkaline form of boron on schizophrenia-like symptoms induced by MK-801 in mice. Behavioral parameters such as the distance traveled, time spent outside the center, grooming duration and frequency, and the number of defecations were measured using the open field test. Upon reviewing previous studies conducted with MK-801, it was noted that behavioral evaluation has mostly focused on the distance traveled, often neglecting other exploratory and behavioral parameters. Therefore, this study also aims to draw attention to this gap.

2. Methods

The presented study was conducted on 24 male BALB/c mice. The animals were housed in the Experimental Animal Unit of Afyon Kocatepe University. This research was funded by Afyon Kocatepe University Scientific Research Projects Coordination Unit No.:17.VF.05. Ethical approval for the experimental procedures involving the animals was obtained from the Afyon Kocatepe University Local Ethics Committee for Animal Experiments (AKUHADYEK-208-17). Before the experiment, the animals were kept in a quarantine room for one week. All animals were housed in plexiglass cages under controlled conditions: room temperature of 20–22°C, a 12/12-hour light/dark cycle, and were fed ad libitum with commercial pellet feed and tap water.

The study was conducted using four groups, each consisting of six mice. The control group received 0.9% physiological saline solution (PSS) i.p. at a dose of 10 ml/kg, since the drugs were dissolved in PSS. The second group was administered MK-801 (Sigma, St. Louis, MO, USA)(1 mg/kg)-i.p.. The third group received both boron (Borax Decahydrate, $Na_2B_4O_7{\cdot}10H_2O$, Eti Mine Industrial Company General Management Kırka/TURKEY)(100 mg/kg)-i.p. and MK-801 (1 mg/kg,)-i.p.; in this group, boron was administered in the morning and MK-801 in the afternoon. The fourth group received only boron (100 mg/kg)-i.p.. Injections were continued for fourteen days, and thirty minutes after the last administration, the animals were subjected to the open field test.

The open field test apparatus used in the study has a square area with high surrounding walls, constructed from galvanized stainless steel, was built for this purpose. The base of the apparatus was divided into 36 equal squares. Animals were placed at the center of the apparatus, recorded by video for 10 minutes, and their movements and the number of squares they crossed were analyzed. The findings were analyzed using Duncan's multiple range test. The findings are expressed in the table below.

3. Results

Table 1 The behavioral analysis of the mice.

Measurements	Control	MK-801	Boron+MK-801	Boron	P value
Distance travelled	164±35[a]	447±172[b]	515±156[b]	127±61[a]	0.000*
Time spend outside the center	549±32 [a]	449±89 [b]	533±33 [a]	550±40 [a]	0.014*
Grooming count	5.5±1.2 [a]	1±0 [b]	1.5±0.8 [b]	8.2±5.9 [a]	0.001*
Grooming time	104±80 [a]	10±6 [b]	4±2 [b]	119±80 [a]	0.002*
Defecation count	2.7±0.8 [a]	0±0[c]	0±0[c]	1.8±0.8 [b]	0.000*

[a,b,c]In the same column, values with different letters show statistically significant differences ($p < 0.05$). Values were expressed as mean ± SD.

Upon evaluation of the presented data, it was observed that MK-801 induced schizophrenia symptoms in the animals. Administration of boron did not exert a protective effect in terms of the distance traveled, number and duration of groom, and defecation count ($p>0.05$). However, a protective effect was observed regarding the time spent outside the center ($p<0.05$) (Table 1).

4. Discussion

The open field test evaluates locomotor ability and exploratory behavior. On one hand, defecation and urination in the open field have been used as indicators of emotionality. On the other hand, the amount of time animals spend in specific zones of the open field is used to analyze anxiety levels. Since rodents tend to stay near corners or the periphery when exposed to a new environment, the time they spend in the center of the open field reflects their anxiety levels. The less time the animals spend in the center, the higher their level of anxiety is considered to be [7-9].

In the present study, although boron demonstrated a protective effect on the time spent in the center, an indicator of anxiety, it is difficult to determine exactly which brain region this protective effect is exerted upon, as no single area of the brain is solely responsible for this behavior. Because it is still unclear which specific brain regions mediate each distinct open field behavior; however, it is likely that multiple levels of the central nervous system are involved, including the olfactory cortex, limbic areas (emotion, fear), and higher neocortical regions (exploration, motor activity).

In summary, while boron failed to exert protective effects on locomotor hyperactivity, grooming, and defecation parameters, it demonstrated a significant protective effect on anxiety-related behavior in the open field test. These findings highlight the need for further research to clarify the neuroprotective potential of the alkaline form of boron in schizophrenia models.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Knapp M, Wong G. Economics and mental health: the current scenario. World Psychiatry. 2020;19(1):3-14.

[2] Zahra W, Rai SN, Birla H, Singh SS, Dilnashin H, Rathore SA, Singh SP. The global economic impact of neurodegenerative diseases: opportunities and challenges. In: Bioeconomy for Sustainable Development. Singapore: Springer; 2020. p. 85-100.

[3] Akıllıoğlu K, Köse KS, Dönmez KM. The effect of caffeine in a model of schizophrenia-like behavior induced by MK-801 in mice. Behav Brain Res. 2025;12,483:115468.

[4] Xiu Y, Kong XR, Zhang L, Qiu X, Chao FL, Peng C, Gao Y, Huang CX, Wang SR, Tang Y. White matter injuries induced by MK-801 in a mouse model of schizophrenia based on NMDA antagonism. Anat Rec (Hoboken). 2014;297(8):1498-507.

[5] Zhong Y, Wang W, Zhang M, Yao Y, Liu H, Zhang K. Efficacy and safety of prophylactic use of benzhexol after risperidone treatment in MK-801-induced mouse model of schizophrenia. Psychopharmacology. 2025;242:651-61.

[6] Kabu M, Akosman MS. Biological Effects of Boron. Rev Environ Contam Toxicol. 2013;225:57-75.

[7] Choleris E, Thomas AW, Kavaliers M, Prato FS. A detailed ethological analysis of the mouse open field test: effects of diazepam, chlordiazepoxide and an extremely low frequency pulsed magnetic field. Neurosci Biobehav Rev. 2001;25(3):235-60.

[8] Stafstrom CE. Behavioral and cognitive testing procedures in animal models of epilepsy. In: Models of Seizures and Epilepsy. Academic Press; 2006. p. 613-28.

[9] Sturman O, Germain PL, Bohacek J. Exploratory rearing: a context- and stress-sensitive behavior recorded in the open-field test. Stress. 2018;21(5):443-52.