Journal of Positive School Psychology http://journalppw.com
2022, Vol. 6, No. 7, 1586-1601

Involvement Of Cholinergic Receptors In The Positive Effect Of Sodium Benzoate On Memory, Electrical Activity Of CA1 Pyramidal Neurons And Biochemical Factors In Male Parkinson's Disease Rats

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Abstract

Thinking and memory problems are among the most worrisome potential Parkinson's disease (PD) symptoms. Given their significant impact on function and quality of life, understanding and treating the range of cognitive changes in Parkinson's is a top priority for researchers. The main cause of Parkinson's disease is the destruction of dopaminergic neurons in Substantia Nigra Pars Compacta (SNc). Considering the positive effects of sodium benzoate (NAB) on the central nervous system, the present study was performed to investigate the possibility of interference of cholinergic receptors on the positive effects of this drug. This experimental study was performed in two sections: electrophysiological and behavioral studies. In each section, the groupings were similar: Control group, Rotenone group (2mg/kg/19days/48h as IP), Solvent rotenone group, Rotenone group + Sodium benzoate (100 mg/kg/7days orally), Rotenone group + Sodium benzoate + Scopolamine (125nmol as Intracerebral injection), Rotenone group + Scopolamine + Sodium benzoate. (The number of animals in each group will be 8). At the beginning of the study, a Parkinson's disease-like model was developed by rotenone injection, and the model was confirmed through motor behavior and histological studies. Animal memory was assessed using step-through, then a single-unit recording method was used using an electro module and eProbe software to evaluate the electrical activity of pyramidal neurons in the CA1 region of the hippocampus. Finally, cytokines TNFα and IL-1, BDNF expression, and ROS levels were measured in the animal hippocampus. This study showed that in both parts, sodium benzoate was able to significantly improve the destructive effects of rotenone ($P \leq 0.05$). The use of scopolamine before applying NAB in electrophysiological and memory assessments could effectively reduce the positive effects of sodium benzoate ($P \leq 0.05$). But in biochemical studies, only when scopolamine was used before NAB prevented the positive effects of NAB ($P \leq 0.05$) and after NAB injection did not affect the results. The present study results showed that NAB could be at least partially a suitable option for treating rotenone-induced symptoms in male rats. This positive effect of rotenone appears to be partly due to the intervention of cholinergic receptors, as the use of scopolamine as a muscarinic receptor antagonist prevents the positive effects of NAB.

Keywords: Cholinergic receptors, Parkinson's disease, Scopolamine, Rotenone.

Significance of the findings:

sodium benzoate was able to significantly improve the destructive effects of rotenone. The use of scopolamine before applying NAB in electrophysiological and memory assessments could effectively reduce the positive effects of sodium benzoate. using scopolamine before NAB injection prevented the positive effects of NAB but after NAB injection did not affect the results.

1-Introduction

Parkinson's is often thought of as a disease that involves only movement. However, many people with Parkinson's complain of slowness of thinking, memory loss, decreased concentration, and difficulty finding words. Dementia refers to problems in memory and thinking that are advanced and interfere with daily activities and quality of life. Parkinson's dementia is diagnosed if the onset of dementia occurs one year or more after the beginning of motor symptoms. If signs of dementia appear before or simultaneously with Parkinson's symptoms, it is called dementia with Louis objects [1].

Memory and thinking problems in Parkinson's are caused by changes in the structure and chemistry of the brain. Dementia describes a set of symptoms caused by a significant loss in brain function. Researchers are still studying exactly how the brain becomes damaged, leading to dementia. Dementia is a hallmark of Alzheimer's, whereas dementia may or may not occur in people with Parkinson's. However, dementia produces a greater impact on social and occupational functioning in people with Parkinson's than in people with Alzheimer's due to the combination of motor AND cognitive impairments [2].

It is increasingly recognized that brain functions, from executive and motor function to memory and emotional responses, are highly regulated by integrating multiple interconnected neural circuits, providing clinical evidence for Parkinson's and Alzheimer's diseases. Neurological disorders have been presented with various causes, possibly as a result of the complex interaction of multisystem degenerations that go beyond the loss of dopaminergic neurons in Parkinson's disease and cholinergic denervation in Alzheimer's [3].

Studies show that even with moderate striatal dopamine depletion, cholinergic interneuronal reactivity may show measured cognitive and emotional cues in injured mice. Therefore, reducing their activity locally in the striatum may serve as an alternative therapeutic goal to reduce early immobility symptoms and lower movement disorders in the later stages of Parkinson's disease. Therefore, it can be said that optogenetic inhibition of striatal cholinergic interneurons reduces motor and non-motor defects in the early and late stages of Parkinson's rodent models. Thus, the optogenetic modulation of striatal cholinergic interneurons may provide a new tool for treating motor and cognitive symptoms in Parkinson's patients [4].

Significant loss of Mainert basal cell nucleus (NBM) cholinergic neurons has been reported in Parkinson's brains. One study found that NBM neuronal loss in the brains of Parkinson's patients was greater than that of Alzheimer's patients, suggesting that cholinergic loss in Parkinson's disease could be more prominent [5]. Dysfunction of the anterior brain basal cholinergic system is associated with persistent loss of presynaptic cholinergic markers in the cerebral cortex, sometimes accompanied by loss of muscarinic receptor binding sites. For

example, muscarinic binding and choline acetyltransferase (ChAT) activity are reduced in the dense part of the substantia nigra, hippocampus, and especially in the neocortex in Parkinson's patients [6].

Significant loss of cholinergic neurons in the nucleus accumbens nucleus has been reported in Parkinson's brains. Dysfunction of the anterior brain basal cholinergic system is associated with persistent loss of presynaptic cholinergic markers in the cerebral cortex, sometimes accompanied by loss of muscarinic receptor binding sites. For example, muscarinic binding and ChAT activity are reduced in the dense segment of the substantia nigra, hippocampus, and especially in the neocortex in Parkinson's patients [6].

Pharmacological studies showed that anticholinergic drugs had adverse effects on concentration and executive processes in people with Parkinson's disease with mild cognitive symptoms. Dubois et al. reported that anticholinergic drugs in patients with Parkinson's disease lead to severe impairment in attention and performance tests. Administration of anticholinergic drugs caused a symptomatic syndrome in patients with Parkinson's disease compared with the control group, indicating a specific anticholinergic vulnerability in Parkinson's disease [6]. Anticholinergic hypersensitivity may indicate cholinergic denervation in Parkinson's disease. In addition to the known dopaminergic reductions, destruction of the cholinergic apparatus is also an early feature of Parkinson's disease and worsens with the onset of dementia. For example, significant loss of cholinergic precursor neurons in Parkinson's brains has been reported. These findings support the hypothesis that the cholinergic apparatus's degeneration and/or dysfunction is an important factor in cognitive impairment in Parkinson's disease. This cholinergic component is likely to exacerbate cognitive deficits due to dopaminergic changes in the forehead in Parkinson's disease [5].

Scopolamine, a muscarinic receptor antagonist, blocks the activity of muscarinic acetylcholine receptors while causing transient cognitive forgetfulness and electrophysiological changes similar to those seen in Alzheimer's disease. In fact, to date, several studies have examined the neurophysiological changes associated with scopolamine injection observed in Alzheimer's and Parkinson's disease. Because different drugs have been used to treat Parkinson's disease, but the definitive treatment for this disease is unknown, experts are looking to evaluate other drugs [7].

Sodium benzoate is one of the most widely used compounds in the food industry, which is also one of the metabolites of cinnamon, easily crosses the blood-brain barrier and can have different effects on the central nervous system. Considering the protective effects of sodium benzoate on genes such as Parkin and DJ-1, cinnamon metabolites appear to play an important role in neuroprotection [8]. Glial cell activation and pathogenesis-related neuroinflammation are implicated in several neurological disorders, including Parkinson's disease. Studies have shown that NAB can inhibit the expression of proinflammatory molecules in the culture medium of astrocytes and Microglia. NAB is mediated to inhibit the expression of NF-KB and nitric oxide synthase (iNOS) by 3-hydroxy-3-methyl coenzyme A malonate and farnesyl pyrophosphate in activated astrocytes. This study suggests that NAB has anti-inflammatory effects by inhibiting cholesterol biosynthesis [9]. Other studies have shown that oral consumption of cinnamon powder reduces the expression of glial acid filamentous proteins (GFAP) as a specific astroglial marker, which is also

reminiscent of the anti-inflammatory effects of cinnamon in the brain [10]. Due to the properties of sodium benzoate, it is possible that this compound can have positive impacts on the central nervous system and its diseases.

Given that current studies have shown that different neurotransmitter devices are involved in neurological disorders, an attempt is made to investigate the possible path of sodium benzoate through cholinergic and dopaminergic pathways. For this purpose, in the present study, after creating an experimental model of Parkinson's disease in animals, we will first investigate the effect of sodium benzoate on memory and motor activity in Parkinson-like rats. The effect of cholinergic antagonist will be investigated in order to evaluate the positive effect of sodium benzoate through each of these receptors in reducing memory disorders, motor activity and electrophysiology of hippocampal CA1 in Parkinson-like mice.

2-Materials and Methods

2-1 Experimental animals

In this experimental study, 96 male Wistar rats (250 to 300 g) were used, and the ethics committee approved all laboratory protocols of Shahid Chamran University of Ahvaz (Ahvaz, Iran) and according to NIH guidelines for the care and use of animals Was tested in the laboratory)International Health Institute Publications No. 23-80; Revised in 1978). Animals were exposed to controlled humidity (50 ± 5%) and good light conditions (12 hours light/dark cycle, light) in standard and controlled environments. The room temperature was set at 23 ± 2 °C, and freely available food and water were available. The animals were placed in the laboratory for one week to get used to the conditions, then divided into two study sections with similar groupings (n = 8 in each group): control group (CO), rotenone group (2 mg/kg / 19Day/48h as IP) (RO), Solvent rotenone group (SRO), rotenone group + sodium benzoate (100 mg/kg/7days orally) (RO.NAB), rotenone group + sodium benzoate + scopolamine (125 Nanomol by intracerebral injection (RO.NAB.SCP), Rotenone + Scopolamine + Sodium benzoate (R0.SCP.NAB).

2-2 Experimental processes

The present experimental study was performed in two parts: memory study and electrophysiological studies. The grouping was completely similar in the two sections (mentioned above), and 48 male rats were used in each section.

Parkinson's disease-like model: To induce a model similar to Parkinson's disease, animals received rotenone (Sigma Aldrich, USA) at a 2 mg/kg dose for 19 days at 48-hour intervals. At the end of the injection period, disease-like modeling was performed through histological studies (assessment of the black body status of the animal's brain) and behavioral studies (using a rotarod, open field and bar test).

2-3 Memory Assessment

Animal memory was assessed using a step-through device. The step-through device consists of two chambers, light and dark, which are applied in a dark chamber. Evaluation of memory with the step-through includes 3 stages of training, testing and acquisition or reminder. In the first stage of training: the animal gets acquainted only with the device (without applying electric shock). In the second stage of the experiment: 24 hours after training, an electric shock with a certain current intensity (frequency 50 Hz, intensity 0.5 mA and for 2 seconds) enters the animal's legs in a dark room. The third stage of acquisition: To

evaluate memory and long-term memory, 24 hours after training, the animal is placed in the bright part of the device and the delay time in entering the dark part and the time spent in the dark compartment as long-term avoidance memory indicators Will be measured [11].

2-4 Histological confirmation

At the end of the study, the animals' brains were isolated and fixed in a 10% neutral buffer. After preparing the block, 20-micron sections were removed from near the electrode, and components were stained with hematoxylin and eosin (H&E). Then, a microscope (Japan; Olympus EX51) was used to confirm the destruction of the substantia nigra and to locate the CA1 region of the hippocampus.

2-5 Biochemical studies

At the end of the study, rats were anesthetized with ketamine hydrochloride/xylazine to assess hippocampal-derived growth factor levels. The heads of the animals were then removed, and their brains were completely removed; after washing with saline, they were placed on special ice and transported to a biochemistry laboratory to use special kits for brain-derived growth factors (BDNF), Inflammatory TNFα, IL-1 and ROS levels in the hippocampus should be evaluated [11].

2-6 Electrophysiological studies:

To evaluate the electrical activity of dopaminergic neurons in region A of the hippocampus, the animal was placed in the laboratory for at least 30 minutes the day after the last injection. Due to the effect of anesthetics such as ketamine/xylazine on memory function and learning, in this method, animals are anesthetized by intraperitoneal injection of urethane at a rate of 1.5 g/kg body weight. The advantage of this drug is the creation of stable and complete anesthesia, and we will not need to re-inject the drug during the test. Corneal reflexes and painful stimulation of the animal's toes ensure complete anesthesia. However, urethane increases fluid secretion into the airways and makes it difficult for the animal to breathe, which ultimately increases the noise when recording electrophysiology, so intubation will be done to counteract this.

For intubation, the mouse is placed in the back position, and the hair on the front of the neck is shaved, making an incision parallel to the trachea in the skin of the neck. The muscles and smooth tissue of the neck are then removed near the trachea to see the trachea. A small incision is made in the trachea, and a polyethylene tube is placed at the bottom of the trachea and sutured, after which the animal's normal breathing is checked.

The scalp of mice is removed to reveal the surface of the skull, and bregma is designated as the stereotactic reference point. A 2 mm diameter hole is made above the hippocampus's CA1 region (AP -3.8mm, ML ± 2.2mm, DV -2.4mm). The body temperature is maintained with a heating pad at 36-37 °C for the whole experiment.

A single-unit recording method will be used to assess the electrical activity of hippocampal neurons. In neuroscience, single-unit recordings provide a way to measure the electrical responses of individual nerve cells using a microelectrode device. When a nerve cell has the action potential, electrical waves are propagated in the nerve cells as a current passes through the excitatory membrane regions in the soma and axons. The inserted microelectrode can record the amount of voltage change over time. These microelectrodes must have a low resistance to pass high currents. In this

study, tungsten microelectrode (coated parylene with a diameter of 127 µm and tip resistance of 5 µm ohm) was used. Also, an electro module device (Science Beam, Tehran, Iran) and eprobe software (Science Beam, Tehran, Iran) will be used to amplify, process, isolate and observe the waves.

In general, the general method of working with this device is that a precise protocol is defined for different electrophysiology models at a specific time, and then after placing the microelectrode in the specified area at an experimental time to identify particular neurons and Once diagnosed. During the defined period, the behavior of the detected neurons is examined. In the present study, the microelectrode used from the perforated area in the pyramidal layer of CA1 is located according to the specified coordinates. After removing the noise and identifying the pyramidal neurons (based on their frequency behavior), the behavior of the desired neurons is recorded for 2 hours. At the end of 2 hours, m values of the average frequency of neurons in this period are recorded as the desired data.

At the end of the second part, histological and biochemical studies were performed as in the first part for each group.

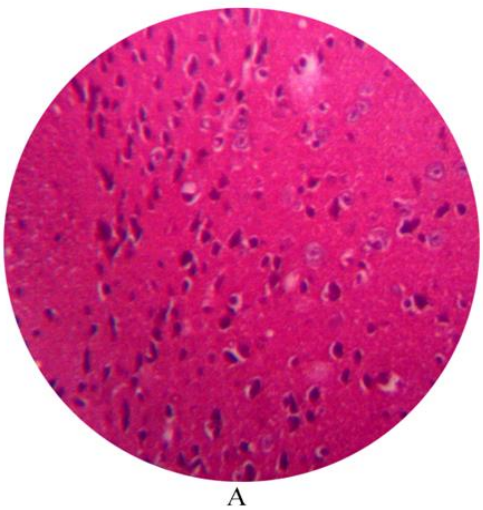
2-7 Statistical studies

All data were analyzed using ANOVA and Tukey post hoc test for multiple groups. All data were reported as mean standard error, and P <0.05 was considered statistically significant.

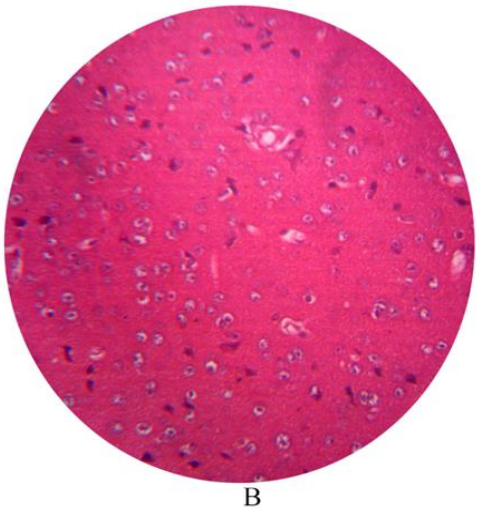
3- Results

3-1 Induction of Parkinson's disease model

Rotenone was injected intraperitoneally at a dose of 2 mg/kg/19 days at 48-hour intervals to induce Parkinson's disease model. Histological studies in substantia nigra (Figure 1) showed the destruction of dopaminergic neurons, as well as studies of motor behavior through rotarod, open field and test load, showing a decrease in balance power in the rotarod (Figure 2) (P <0.05), There was a decrease in mobility in the open field device (Figure 3) (P <0.05) and an increase in slowness in the onset of movements in the Bar test (Figure 4) (P <0.05).



A



B

Figure 1-Histological image of the cerebrospinal fluid region of rat treated with rotenone (B) compared with controls (A). The destruction of dopaminergic neurons is quite obvious compared to the image.

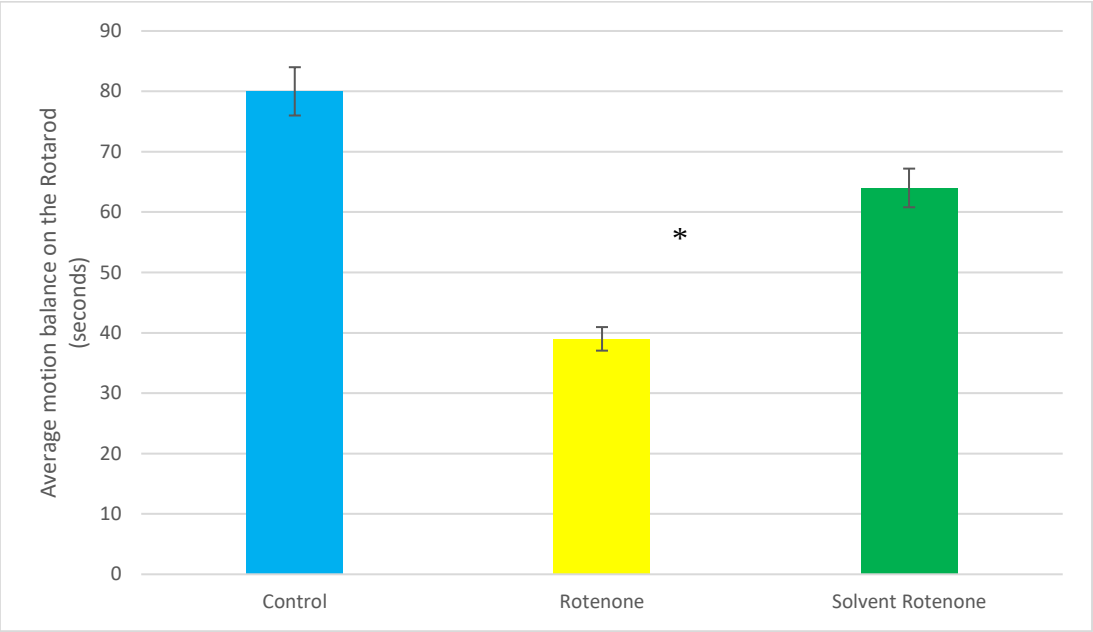


Figure 2- Comparison of motor balance in the rotarod device between rotenone group and control (*P<0.05, n=8, Mean±S.E.M)

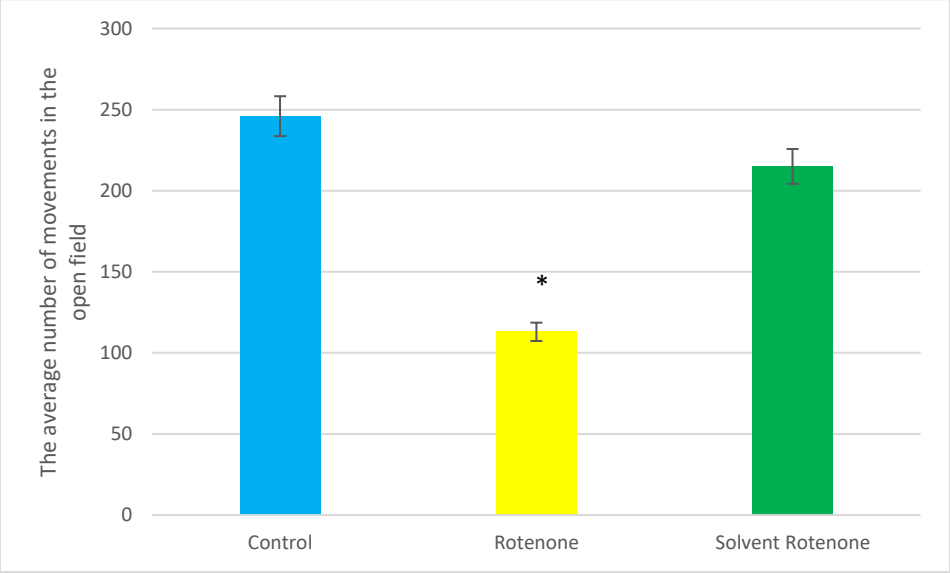


Figure 3-Comparison of motor activity in open field device between Rotenone group and control (*P<0.05, n=8, Mean±S.E.M)

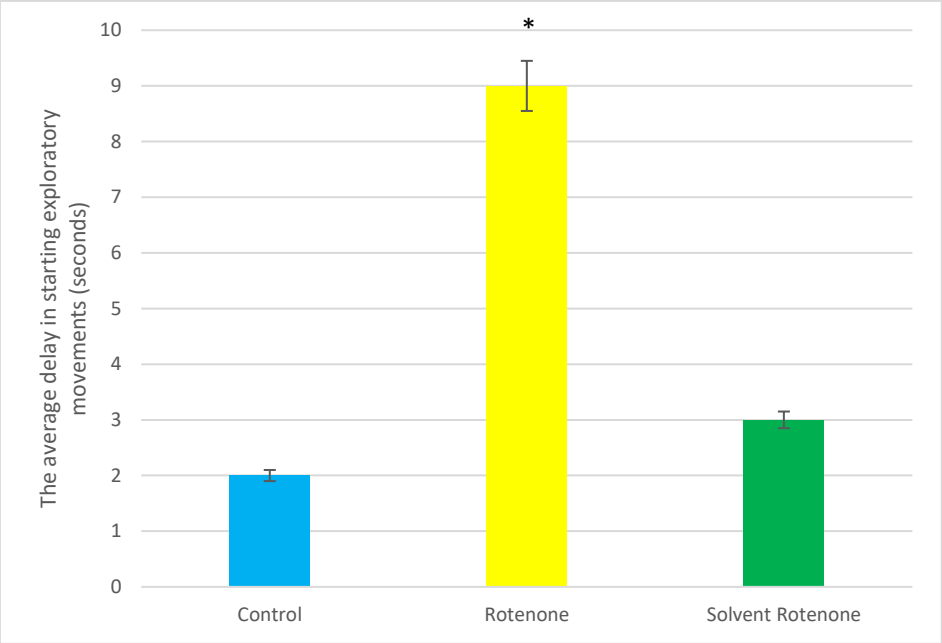


Figure 4-Comparison of mean delay in initiation of exploratory movements (seconds) between the control group and rotenone (*P<0.05, n=8, Mean±S.E.M)

3-2 Memory evaluation

The animals' memory was then assessed to evaluate the effects of the drugs. Figure 5 shows the effects of rotenone on postoperative or pre-test memory loss in the step-through device (P <0.01). One-way analysis of variance showed that sodium benzoate accelerates the entry into the dark chamber (P <0.05). The use of scopolamine as a cholinergic receptor antagonist before sodium benzoate significantly reduces the effects of sodium benzoate, and animals show more delay (P <0.05). However, the use of scopolamine after sodium benzoate impacts there are no positive effects on sodium benzoate (Figure 5).

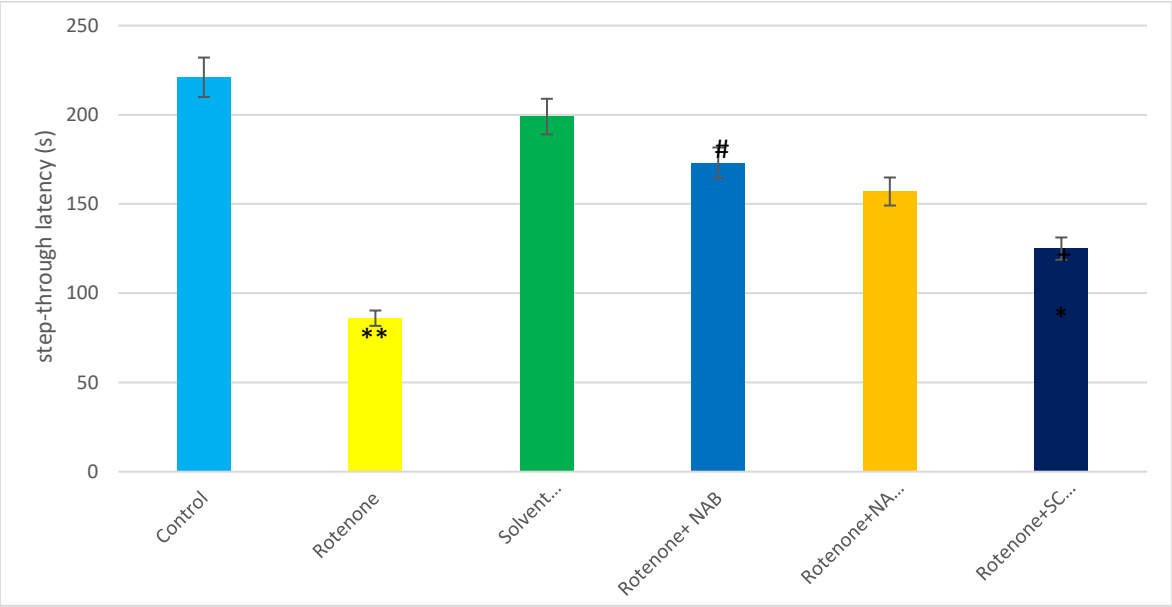


Figure 5- step-through apparatus indicates that animals in which recovery was impaired due to administration after rotenone training (rotenone-induced amnesia) improved recovery through sodium benzoate. However, the use of Scopolamine before sodium benzoate decreased memory recovery. (**P<0.01 Compared to controls, #P<0.05 Compared to the Rotenone group, +P<0.05 Compared to the Rotenone + NAB group, n=8, Mean±S.E.M)

3-3 Electrophysiological studies

To confirm the exact location of the electrode, the animals' brains were first subjected to histological and staining studies to ensure the exact location of the electrode to the desired coordinates (Figure 6). A single-unit recording technique evaluated the spontaneous activity of pyramidal neurons in the CA1 region of the hippocampus (Figure 7). This section showed that rotenone injection increased the mean spontaneous activity of pyramidal neurons in the CA1 region of the hippocampus compared to the control and solvent groups (P <0.01). The use of sodium benzoate was able to restore the frequency of neurons in the CA1 region of the hippocampus to normal (frequency below 8) (P <0.01). While the use of scopolamine before sodium benzoate was able to disrupt the positive effects of sodium benzoate on the spontaneous activity of neurons (P <0.05) (Figure 8).

Figure 6- Electrode entry site in the CA1 region of the hippocampus of adult male rats

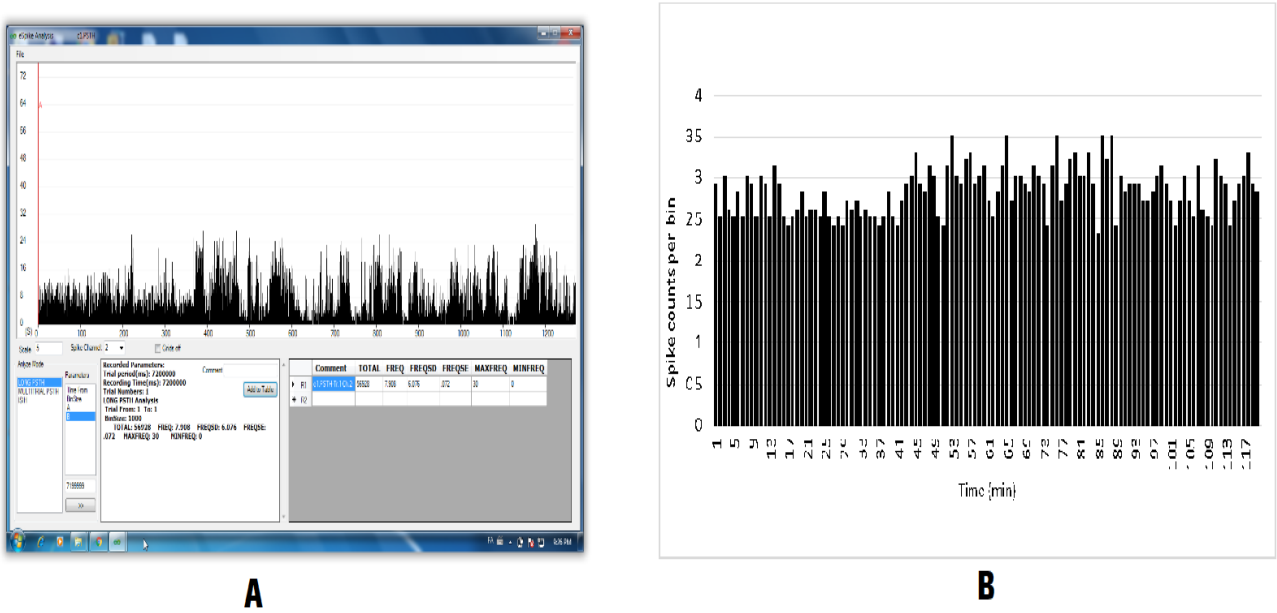


Figure 7- Single unit recording of spontaneous activity of pyramidal neurons in CA1 region of male rat hippocampus through the electro-module device and eprobe software. B- Electrical recording was continued for each mouse for 2 hours after neuronation; the mean frequency was obtained. In different groups, they were calculated and compared through software analysis.

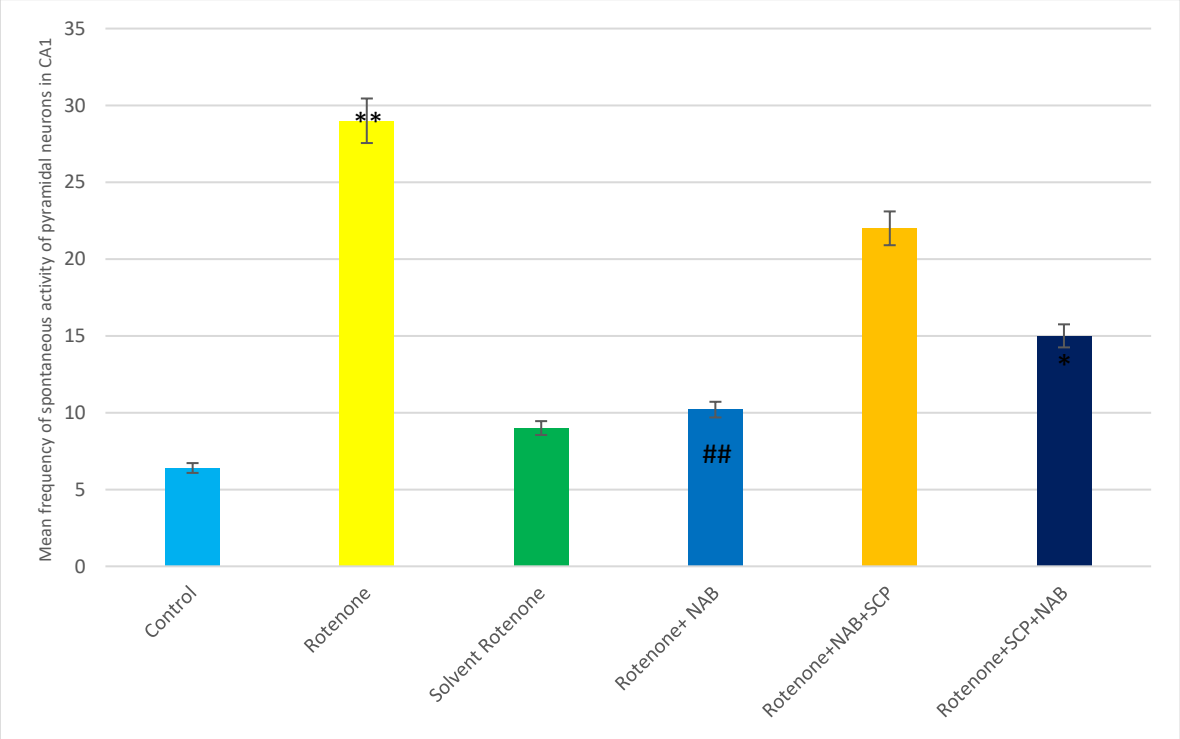


Figure 8- Mean frequency of spontaneous activity of pyramidal neurons in CA1 region, (**P<0.01 Compared to controls, ##P<0.01 Compared to the Rotenone group, *P<0.05 Compared to the Rotenone + NAB group, n=8, Mean±S.E.M)

3-4 Biochemical studies

Finally, biochemical factors from the animal hippocampus were evaluated. The evaluation results of BDNF levels showed that its level decreased in the rotenone group compared to the control group (P <0.01). However, the use of sodium benzoate increased it (P <0.05), and this increase decreased with the effect of scopolamine before and after sodium benzoate (P <0.05) (Figure 9). On the other hand, analysis of TNF-α and IL-1 levels showed that the level of these inflammatory factors in the rotenone group was significantly higher than in the control group (P <0.01). However, the use of sodium benzoate decreased them (P <0.05), and this decrease increased with the effect of scopolamine before and after sodium benzoate (P <0.05) (Figures 10 and 11). In parallel with these studies, examination of ROS levels showed that the amount of this free radical increased in the rotenone group compared to the control group (P <0.01). However, the use of sodium benzoate decreased them (P <0.05), and this decrease increased with the effect of scopolamine before sodium benzoate (P <0.05) (Figure 12).

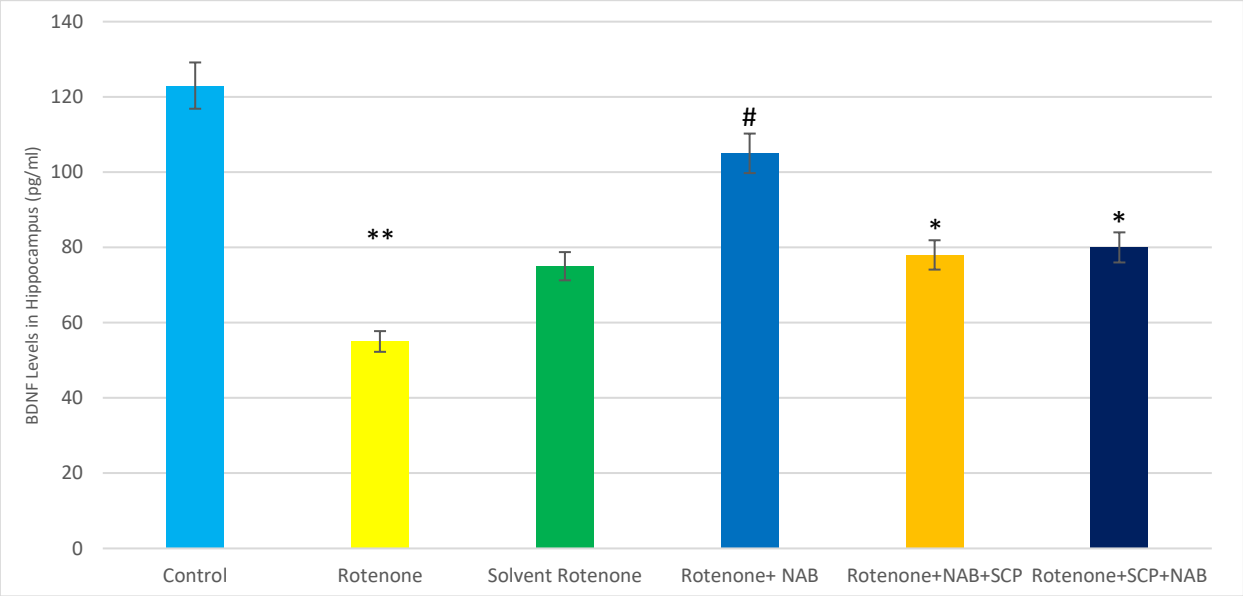


Figure 9- Mean BDNF Levels in Hippocampus (pg/ml), (**P<0.01 Compared to controls, #P<0.05 Compared to the Rotenone group, *P<0.05 Compared to the Rotenone + NAB group, n=8, Mean±S.E.M)

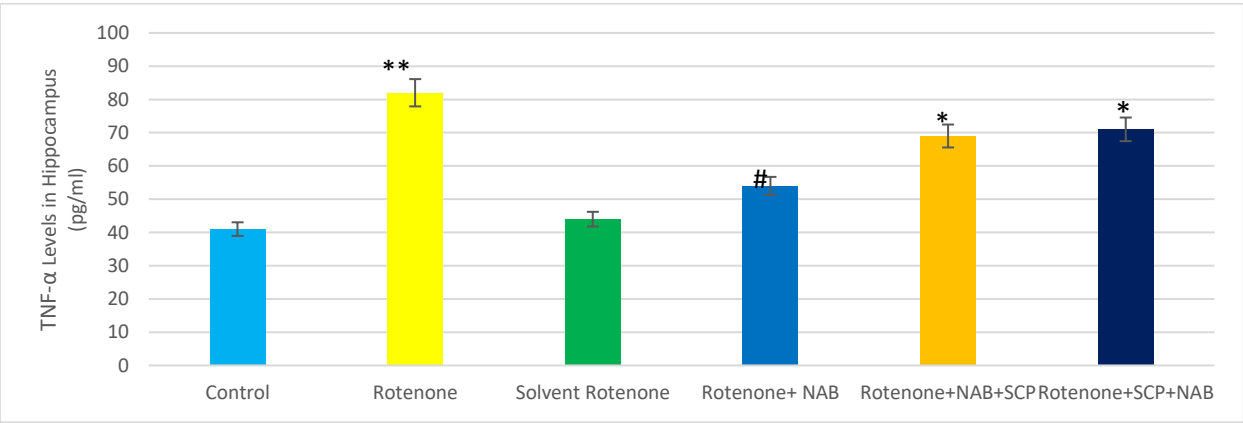


Figure 10- Mean TNF-α Levels in Hippocampus (pg/ml), (**P<0.01 Compared to controls, #P<0.05 Compared to the Rotenone group, *P<0.05 Compared to the Rotenone + NAB group, n=8, Mean±S.E.M)

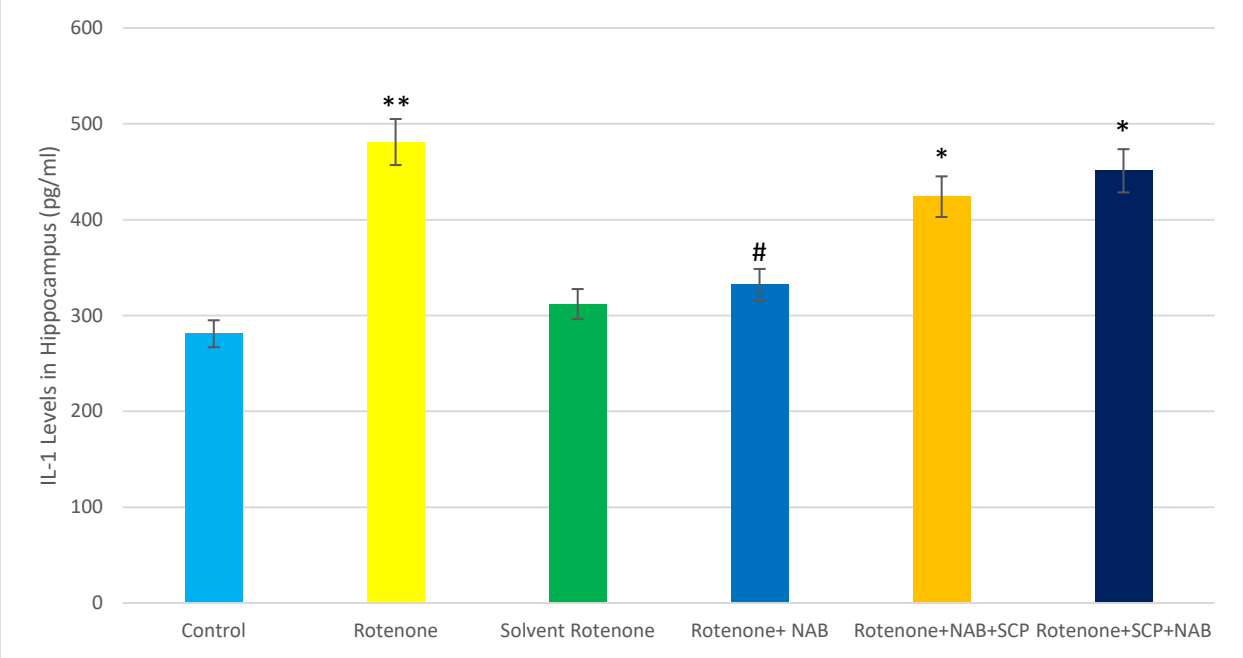


Figure 11- Mean IL-1 Levels in Hippocampus (pg/ml), (**P<0.01 Compared to controls, #P<0.05 Compared to the Rotenone group, *P<0.05 Compared to the Rotenone + NAB group, n=8, Mean±S.E.M)

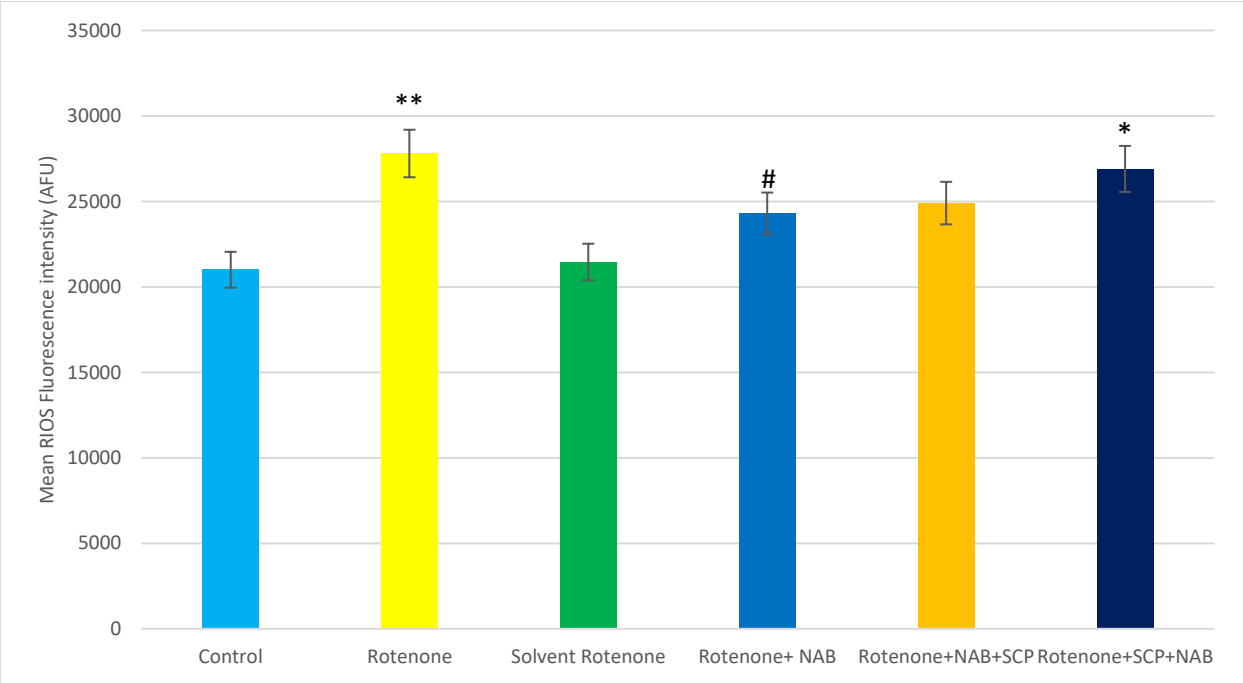


Figure 12- Mean Fluorescence intensity (AFU) related to ROS as an indicator of oxidative stress in homogenized hippocampal tissue in different groups. (**P<0.01 Compared to controls,

#P<0.05 Compared to the Rotenone group, *P<0.05 Compared to the Rotenone + NAB group, n=8, Mean±S.E.M)

4-Discussion

Memory impairment is one of the non-motor symptoms of Parkinson's disease that is usually seen in most patients in the advanced stages of the disease. In the present study, we were able to model Parkinson's disease by injecting rotenone. Studies have shown that the pathology of movement disorders caused by rotenone toxin is due to the hypersensitivity of the dopaminergic system to this toxin. Rotenone-induced apoptosis is associated with symptoms of Parkinson's disease. Due to its lipophilic nature, this compound can cross the blood-brain barrier. Rotenone induces apoptosis by inhibiting complex I mitochondrial electron transfer chains, increasing cell death and alpha-synuclein levels. This substance increases the production of mitochondrial oxygen free radicals and releases cytochrome C and the caspase-dependent apoptotic pathway. Rotenone will also cause Bad phosphorylation without altering its levels. By activating kinases, this toxin triggers stress on the endoplasmic reticulum and, like paraquat, activates microglial cells, which is a secondary source for ROS production. By subcutaneous injection, the brain can also induce an animal model that produces symptoms similar to Parkinson's disease [12].

Then, after creating a model of Parkinson's disease in animals by oral administration of sodium benzoate, an attempt was made to investigate the positive effects of this compound on Parkinson's disease. This study showed that NAB improved memory in the step-through test and improved the electrical activity of pyramidal neurons in the CA1 region of the hippocampus. Sodium benzoate also positively increased BDNF and decreased inflammatory cytokines and ROS in the hippocampus. Results show that sodium benzoate has been able to compensate for the negative effects of rotenone.

It was reported in a study that the use of sodium benzoate in Parkinson's patients can stimulate the production of dopamine by dopaminergic neurons, which indicates that it can be used as a suitable option for the treatment of Parkinson's disease [13].

Modi et al. (2016) reported that oral treatment with cinnamon and NaB improved learning in mice. Its function is that NaB activates CREB in hippocampal neurons through protein kinase A (PKA), which is responsible for rearranging molecules associated with synaptic flexibility [14].

Sodium benzoate, a widely used food preservative, has exhibited potent antioxidant stress properties. In addition, Thoth et al. Reported that NaB was highly safe, and the mice studied did not show any significant side effects, even though they received NaB (2%) for life. In addition, DJ-1 has been reported to be upregulated by NaB treatment, possibly by regulating the mevalonate pathway. One study also reported that NaB administration significantly increased DJ-1 expression and levels of NDUFS8 and ATP but decreased levels of ROS, cut caspase-3, and cut caspase-9. However, this protection provided by the DJ-1 high setting is dramatically offset by rotenone [15].

Then, scopolamine was used before and after sodium benzoate to investigate the possible pathways of positive effects of sodium benzoate through cholinergic receptors. The results showed that the use of scopolamine in many cases, especially when used before sodium benzoate, prevented the

positive effects of this compound. Pre-sodium injection of scopolamine prevented the positive impact of sodium benzoate on memory and electrical activity of pyramidal neurons. Intracerebral infusion of scopolamine before and after sodium benzoate prevented the reduction of inflammatory cytokines and ROS and increased BDNS by sodium benzoate. This suggests, however, that some of the positive effects of sodium benzoate may be due to the involvement of cholinergic receptors.

Simultaneously, and as shown by posthumous human brain histology, neurons expressing choline acetyltransferase (ChAT) are also degraded. Both cell death and decreased cholinergic markers are strongly associated with decreased cognitive ability, assessed through functional tests in patients with Parkinson's disease. For this reason, current therapies target both dopaminergic modulatory systems and acetylcholine. Rivastigmine, a cholinesterase inhibitor, has been shown to improve cognitive impairment [16].

Scopolamine is a nonspecific antagonist of mAChRs commonly used in cognitive studies. Blocking mAChRs with scopolamine has been shown to impair spatial memory encryption severely, but its effect on spatial memory recovery is less pronounced. Some studies show little or no effect of scopolamine on this issue, while others have reported the disorder [17].

Previous studies have hypothesized that Ach facilitates memory encoding by increasing the signal-to-noise ratio, improving theta rhythm modulation, increasing persistent spike, or enhancing afferent input. Pharmacological blockade of Ach transmission by atropine or scopolamine mAChR antagonists impairs new memory acquisition [18].

Sun et al. (2021) reported that scopolamine had quite significant effects on cellular and aggregate behavior in the CA1 region, disrupting the cellular character of the site [7]. Huang et al. (2011) documented memory impairment in mice treated with scopolamine in the Morris maze, consistent with this hypothesis [19].

5- Conclusion

The present study results showed that sodium benzoate could have positive effects on memory impairment induced by rotenone in Parkinson's mice. Given that scopolamine, as a cholinergic receptor antagonist, was able to prevent much of the positive effects of sodium benzoate, at least part of the positive effects of sodium benzoate is likely via cholinergic pathways.

6- References

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