

The Prospective Protective Effect of Selenium Against Chronic Restraint Stress-Induced Memory Impairment in Male Albino Rats

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Abstract

Background: Selenium (Se) had underscored many beneficial neuroprotective potentials, particularly with respect to learning and memory. However, the protective effect of Se in memory impairment associated with Chronic Restraint Stress (CRS) is not yet elucidated.

Aim of Study: The present study was carried out to examine the effect of Se treatment against CRS induced behavioral and biochemical abnormalities.

Material and Methods: The stress was induced by restraining the animals in well ventilated tubes (6h/d) for consecutive 21 days. Animals were randomly divided into 4 groups (8 rats each): Normal control, drug control, CRS and Se treated CRS groups. After 21 days of the experiment, memory function was evaluated by Passive Avoidance (PA), T-maze and object recognition tasks. Hippocampal oxidative stress markers, Brain Derived Neurotrophic Factor (BDNF), amyloid P (A β) protein, phosphorylated TAU (p-TAU) protein as well as glutamate and acetylcholinesterase activity (AChE) levels were assessed.

Results: This study revealed that the memory performance was markedly deteriorated in CRS group, accompanied by noticeable alterations in hippocampal oxidative stress markers, depleted levels of BDNF together with overproduction of A β , p-TAU and glutamate as well as, excessive activity of AChE enzyme. Meanwhile, these behavioral and biochemical deviations were alleviated under 21 days of Se co-treatment in CRS exposed rats.

Conclusion: This study proved the beneficial protective effects of Se in CRS-induced memory deficits and its associated pathological changes in rats, which may draw the attention to Se as a new therapeutic candidate for memory dysfunction associated with stress and its related disorders.

Key Words: Selenium – Chronic restraint stress – Memory impairment – Passive avoidance – T maze.

Introduction

STRESS is a physiological or psychological response evoked by adverse stimuli, which may

disturb the homeostasis of the body especially brain functions [1]. Chronic stress can trigger the activity of the hypothalamic-pituitary-adrenal axis, increasing the circulating levels of the stress hormones, Glucocorticoids (GC) [2]. One of the most vulnerable targets of stress is hippocampus, which is a limbic region important in learning and memory, and abundantly expresses GC receptors [3]. Stress activates hippocampal glucocorticoid receptors, increases neuronal metabolism, decreases cell survival and neurogenesis, triggers dendritic atrophy and causes long-term potentiation and cognitive deficits [4,5]. In addition, chronic stress was correlated with many age-related neurodegenerative diseases as Alzheimer's Disease (AD) [6].

Chronic restraint stress is a specific and common method used to induce psychological and physiological stress. It is well settled for its ability to impair cognitive hippocampus-dependent functions, particularly learning and memory [7,8]. Many studies demonstrated the possible underlying mechanisms for the pathophysiology of CRS induced memory impairment [9-12]. Nevertheless, few studies have investigated the effectiveness of therapeutic agents for the treatment of chronic stress-induced memory deficits [3].

Selenium has received a considerable attention as an essential trace element, having a pivotal role in maintaining physiological functions. Dietary selenium can exist as selenomethionine, selenocysteine, or selenite [13]. Selenoproteins, such as Glutathione Peroxidase (GPx) and Thioredoxin Reductase (TrxR) enzymes are of particular interest due to their integration in generating antioxidant defense, regulating gene expression, cell viability and proliferation [14]. In addition, Se is a vital mineral for the brain, involved in regulating vital neural antioxidant signaling pathways which

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mediate its beneficial effects against neurotoxicity and oxidative damage in various brain disorders [15,16]. A decreased blood selenium level and GPx activity were reported in patients with memory impairment [17,18]. Moreover, Se deficiency has been associated with an increased risk of AD [19].

A number of clinical trials recorded the beneficial role of Se in modulating learning and memory deficits in different neurological disorders including, Alzheimer's disease, scopolamine or lead induced cognitive deficits, [16,20,21] as well as after transient cerebral hypoxia-ischemia [22]. However, and up to our knowledge, the protective effect of Se on CRS-induced cognitive impairment had not been previously recorded.

Therefore, the present study was designated to investigate the possible neuroprotective effects of Se on CRS-induced cognitive deficits in rats, further dissecting its possible mechanisms involved.

Material and Methods

Selenium in the form of sodium selenite (Na_2SeO_3) was purchased from Sigma Chemical Co. (St. Louis, MO, USA), and was freshly dissolved in 0.9% NaCl. All other chemical reagents were obtained from Sigma. Co, unless described otherwise and are of high analytical grade.

Animals and experimental protocol:

This study was carried out from July 2018 to November 2018, and all procedures were performed in accordance with the guidelines for the animal experimental protocols of Tanta Faculty of Medicine.

Thirty two male adult albino rats weighing 200-250g, were maintained under standard laboratory conditions, kept on a 12-h light-dark cycle with free access to food and water and were acclimatized to these conditions for at least 1 week prior to the experiment.

Rats were randomly categorized into four equal groups, 8 rats each:

- *Group I:* Served as normal control group, which was not stressed and had free access to water and food.
- *Group-II:* Served as drug control group, which was not stressed and received oral Se in the form of sodium selenite dissolved in 0.9% NaCl at a dose of (0.35mg/kg/d) for 21 days [23,24].
- *Group III:* Served as CRS group which were exposed to CRS for 6h/day for 21 days.

- *Group IV:* Served as Se treated CRS group, which received oral sodium selenite at a dose of 0.35 mg/kg/d once daily, 60 minutes prior to exposure to CRS sessions for successive 21 days.

The control and stressed rats were given the same volume of saline.

Induction of chronic restraint stress:

Each rat was placed in a conical plastic tube (20 X 7cm) for 6 hours (from 10a.m. to 4p.m.) for successive 21 days. The tip of the restrainer has several small holes to allow sufficient breathing and the rats were unable to move within the tubes, this paradigm was proved to induce cognitive deficits in rats [1,3].

Behavioral memory tasks:

At the end of the 3th week of experiment, behavioral memory tests were performed as follow:

1- Passive avoidance task:

The passive-avoidance paradigm was used to evaluate the hippocampus-dependent associative memory [25,26], in which animals learned to associate the aversive unconditioned stimulus (mild electric foot-shock) with the conditioned stimulus (the dark chamber). It was assessed using the passive avoidance apparatus which consists of two compartments, one was illuminated and the other was dark which were separated by a sliding door and the task was performed as described previously [1,27].

On day 22 of the experiment, each rat was placed in the apparatus for 300 seconds for habituation. On the following day (day 23), a single learning trial was performed in which rats were introduced individually into the light compartment and allowed 1min to explore the area before the trap door was opened. Immediately after the mouse entered the dark compartment, the trap door was closed, and 3-5 electric shocks (0.5mA) were applied to the stainless steel floor of the compartment. The initial latency of entrance into the dark room was recorded before inducing the electrical shock.

A retention trial was performed 24-h after the learning trial. Evaluation of recall of this inhibitory stimulus was done by placing the animals in the light compartment and recording their latency to enter the dark compartment. If the animal did not enter the dark compartment within 300sec, it was returned to its cage, and retention latency of 300sec was recorded, which is an indicator for retention performance of the PA response. Increased retention

latency time to enter the dark compartment is a good index of long-term memory.

2- The T-maze task:

The spatial working memory was tested by spontaneous alternation behavior in T-maze tasks [28]. This test depends on the strong exploratory drive of rats, thus rats tend to choose the arm not visited before, reflecting memory of the first choice, this is called spontaneous alternation, which is very sensitive for hippocampal dysfunction [29].

The T maze apparatus was specially designated, which is a black painted wooden T shaped apparatus, measuring 30cm length, 10cm width, and 20cm height, for start and the two goal arms. Manual guillotine doors were located at the entrances to each arm. In brief, rats were placed into the start arm of T-maze and allowed to choose freely between the two goal arms. Once the rat enters one goal arm, the other arm was closed, where it is confined for a 30 seconds, after which it is placed again in the start arm to start another trial. A total of 6 trials were performed. Alternation was recorded when the mice accessed one arm in the first trial and chose the other arm in the second trial. The percentage of alternation for each animal was calculated (actual alternations/total possible alternations) X 100 [30].

3- Object recognition task:

Recognition memory was assessed using the object recognition task which needs integrity of hippocampus and depends on the preference of rodents to explore novel objects rather than familiar objects [31].

This task was conducted as described by Bevins and Besheer [32]. Briefly, habituation was done by placing each rat in a dimly illuminated open field box measured (20 X 20 X 17 X 4) for 15min. The following day, two plastic sample objects about 12 inches apart were placed in one of the boxes and the rats were allowed to explore for 10min. After 3h, the retention test was conducted by placing the rats once again in the box, but with a novel object replacing one of the objects placed during the training session. The rats were allowed to explore for 5min, total time spent exploring each of the two objects was recorded. Recognition Index (RI) was indicator for recognition memory performance, calculated as:

$$RI = \frac{\text{Time exploring novel object}}{\text{Time exploring novel object} + \text{Time exploring familiar object}} \times 100$$

Tissue homogenization and biochemical assessment:

After completing the experimental regimen, the animals were sacrificed by cervical decapitation and brains were collected. The hippocampi of each brain were dissected, weighted then homogenized by PBS PH 7.2-7.4, and centrifuged at 4°C, at a speed of 2000-3000rpm, for 20min. The resultant supernatant was taken and kept frozen till the time of biochemical analysis. Total protein content was estimated based on the method of Bradford [33].

Lipid peroxidation in hippocampal homogenates was determined by measuring Thiobarbituric Acid Reactive Substances (TBARS) as described by Ohkawa et al., [34], while brain activity of GPx and TrxR were assessed based on the method of Chiu et al., [35] and Holmgren and Bjornstedt, [36], respectively. Moreover, hippocampal BDNF and glutamate were evaluated using their respective MyBioSource ELISA kits, while the level of brain Aβ and p-TAU proteins were detected using Elabscience Biotechnology Co., Ltd. (Wuhan, China) ELISA kits. All Assay procedures were performed according to the manufacturer's guidelines. Finally, AchE activity level was determined by a modified method of Ellman et al., [37]. As described by Gorun et al., [38].

Statistical analysis:

The data were expressed as the mean ± standard deviation. Data were analyzed using one-way ANOVA. All the analyses were performed using SPSS for windows (Version 21.0) with Tukey post hoc test analysis. *p*-values <0.05 were considered statistically significant.

Results

Effect of Se on behavioral memory tasks in experimental rats:

As regard the PA task, data of (Table 1) depicted insignificant differences in initial latency values between all studied groups. However, retention latency was significantly reduced in CRS-group as compared to the normal control one, indicating the reduced passive avoidance memory as a result of the restraint stress. Meanwhile, Se co-treatment for 3 weeks significantly enhanced the retention latency in treated CRS group as compared to the untreated CRS one. Noteworthy, the retention latency returned back to near control values by Se co-treatment.

We further explored the beneficial effect of Se on memory function of CRS-exposed rats using the T maze task. Our data demonstrated a signif-

icant reduction in the percentage of continuous alternations of T maze task in CRS rats compared to normal control ones, whereas se co-treatment significantly improved the alternation performance in treated CRS rats versus the untreated CRS ones (Table 1).

The current object recognition paradigm revealed a significant decrease in RI in CRS exposed rats compared to normal control ones, indicating a recognition memory deficits which was significantly improved upon Se co-treatment (Table 1).

Table (1): Effect of Se treatment on behavioral memory tasks in experimental rats.

Parameters	Group I	Group II	Group III	Group IV
• Initial latency of PA (sec)	40±3.98	39±3.59	42±5.71	45±3.10
• Retention latency of PA (sec)	178±16	192±21b	51±4.7a	167±19b
• Percentage of spontaneous alteration (%)	65±4.81	67±5.44b	41±3.96a	61±4.79b
• Recognition index %	63±5.7	66±5.5b	47±4.6a	68±6.4b

Group I : Normal control. Data are expressed as mean ± SD.
 Group II : Drug control. a: $p < 0.05$ Vs. Group I.
 Group III: CRS. b: $p < 0.05$ Vs. Group III.
 Group IV : Se-treated CRS groups.

Effect of Se on hippocampal oxidative stress markers in experimental rats:

Results of (Table 2) showed that, compared to the normal control rats, exposure to CRS significantly increased level of TBARS while significantly decreased GPx and TrxR levels in hippocampus. Notably, co-administration of Se, significantly decreased hippocampal levels of TBARS and increased GPx and TrxR in treated CRS rats as compared to untreated CRS-ones, which were restored to near control values.

Table (2): Effect of Se treatment on CRS-induced oxidative stress markers in rats hippocampi.

Parameters	Group I	Group II	Group III	Group IV
• TBARS (nmol/g of tissue)	59±3.07060	55±2.12b	99±4.31a	63±3.81b
• GPx (IU/g of tissue)	26±2.12	29±2.31b	17±1.78a	25±2b
• TrxR (nmol/min/mg protein)	10.6±0.76	10.9±0.96b	7.50±0.83a	10.3±1.39b

Group I : Normal control. Data are expressed as mean ± SD.
 Group II : Drug control. a: $p < 0.05$ Vs. Group I.
 Group III: CRS. b: $p < 0.05$ Vs. Group III.
 Group IV : Se-treated CRS groups.

Effect of Se on hippocampal levels of BDNF, Aβ and TAU in experimental rats:

These data were shown in (Table 3), the levels of BDNF were significantly decreased, while Aβ and TAU were significantly increased upon exposure to CRS as compared to the normal control

group. Mean while, Se co-treatment significantly reversed these values, but, their levels were still significant versus to those observed in the normal control group.

Table (3): Effect of Se treatment on hippocampal levels of BDNF, Aβ and p-TAU in experimental rats.

Parameters	Group I	Group II	Group III	Group IV
BDNF (ng/g tissue)	132±6.2	126±4.7b	99±4.9a	122±5.2ab
Aβ (pg/ml)	48.9±3.48	45.3±2.38b	93.8±3.69a	61.8±3.37ab
P-TAU (pg/ml)	83±5.1	79±3.8b	130±5.7a	93±4.6ab

Group I : Normal control. Data are expressed as mean ± SD.
 Group II : Drug control. a: $p < 0.05$ Vs. Group I.
 Group III: CRS. b: $p < 0.05$ Vs. Group III.
 Group IV : Se-treated CRS groups.

Effect of Se on hippocampal levels of glutamate and AchE activity in experimental rats:

As compiled in Figs. (1,2), rats exposed to CRS showed a significant increase in hippocampal glutamate and AchE activity levels when compared to normal control ones. Interestingly, Se co-treatment showed an insignificant effect on glutamate levels, whereas it significantly reversed the excessive activity of Ach E toward the control values in treated CRS group compared to untreated CRS one.

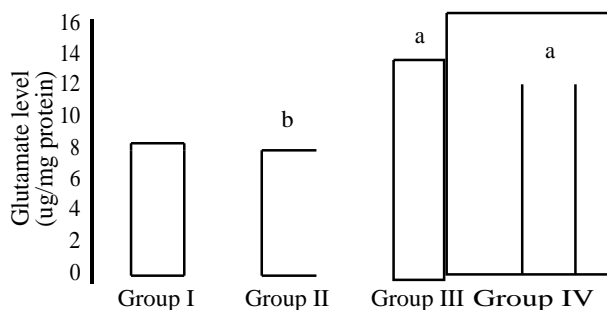


Fig. (1): Effect of Se treatment on glutamate levels in rats hippocampi.

Group I : Normal control. Data are expressed as mean ± SD.
 Group II : Drug control. a: $p < 0.05$ Vs. Group I.
 Group III: CRS. b: $p < 0.05$ Vs. Group III.
 Group IV : Se-treated CRS groups.

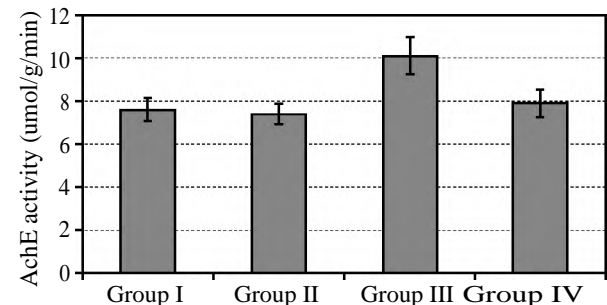


Fig. (2): Effect of Se treatment on AchE activity levels in rats hippocampi.

Group I : Normal control. Data are expressed as mean ± SD.
 Group II : Drug control. a: $p < 0.05$ Vs. Group I.
 Group III: CRS. b: $p < 0.05$ Vs. Group III.
 Group IV : Se-treated CRS groups.

Discussion

This current study was designated to explore the possible protective potential of Se on CRS induced memory deficits in rats. The main finding of this work was that, 21 days of Se treatment reversed the CRS induced memory deficits which correlated with attenuation of biochemical parameters in the hippocampus.

Our investigations supported the hypothesis of that CRS impairs memory performance as indicated by a significant decrease in the time of latency to enter the dark compartment in PA task together with the decreased spontaneous alteration performance in T maze and decreased RI index in object recognition tasks upon CRS exposure, these results were in conformity with previous studies [39,40]. In contrast to the present findings, one study recorded the habituation of animals to chronic stress [41]. This discrepancy may be attributed to difference in the types and durations of stress evoked or the task paradigm used in both studies [42].

The mechanism of CRS induced memory deficits is multifactorial. Noteworthy, results herein demonstrated a significantly increased TBARS with decreased TrxR and GPx antioxidants levels in hippocampi of CRS exposed rats compared to control ones, indicating a triggered oxidative stress response, which came in line with previous studies [9]. Oxidative stress induced lipid peroxidation results in alteration of synaptic membrane depolarization, dysfunction of neurotransmission systems [43], and may lead to atrophy and even death of hippocampal neurons [44]. In addition, the maintenance of normal levels of GSH and TrxR antioxidants was shown to be critical in acquisition of spatial memory, since their deficiency triggers hippocampal apoptosis and failure of synaptic plasticity mechanisms which related to spatial memory impairment [45,46]. Taken together, these data suggested an emerging role of antioxidants in modulating such memory deficits.

Appealingly, our investigations showed that Se cotreatment dampened the CRS evoked oxidative stress response and thereby, alleviated the subsequent pathological events underlying the CRS induced memory impairment as supported previously [20,22]. Selenium antioxidant capacity may be attributed to its promotion to transcription and enzymatic activity of many antioxidant enzymes including TrxR and GPx [22], or due to its scavenging to reactive oxygen species from brain tissue preventing lipid peroxidation [24,47]. Moreover, seleno-derivatives, acting as antioxidants was

shown to directly affect synaptic transmission and/or plasticity improving memory performance [16,48,49].

BDNF, a neurotrophic growth factor, widely expressed in the hippocampus [50] and has a pivotal role in regulation of neuronal transmission and plasticity with potentiation of memory consolidation [51]. In contrast, A β protein is well documented for its neurotoxicity and its deleterious effect on synaptic function with its involvement in memory loss in various neurological disorders [52].

The results obtained herein showed a significantly decreased BDNF while increased A β levels in hippocampi of CRS exposed rats compared to control ones, suggesting their integration in the pathology of CRS induced cognitive deficits, which was inconsistency with previous studies [52-55].

An interrelation between amyloid β and BDNF was documented, since A β may trigger its neurotoxicity partly via down regulation of proteins integrated in the transcription of BDNF [56,57]. Moreover, the decreased level of BDNF under chronic stress conditions may interfere with the repair process and consequently exacerbating the effect of A β protein [58]. Meanwhile, stress itself may induce A β accumulation via its alteration to the processing and production of Amyloid Precursor Protein (APP) and driving its processing toward the amyloidogenic pathway with subsequent increased A β levels [52,59].

Interestingly, Se co-treatment significantly counteracted the notable changes in BDNF and A β levels, giving an evidence of their involvement in its neuroprotective effect in this rat model, which agree previous studies [60,61]. The attenuating effect of Se on BDNF and A β levels may be attributed to its antioxidant capacity, as the relation between oxidative stress, the reduction in BDNF level and A β overproduction was previously documented [49,62]. In addition, the suppressing effect of Se on A β pathology may be mediated by its inhibition to APP with subsequent increasing the turnover of A β , decreasing its accumulation [63,64]. Consequently, this inhibition to A β molecules also may release the BDNF from its inhibition by A β overproduction, restoring its normal level, as mentioned above.

Tau protein is a member of microtubule-associated proteins family, stabilizing axonal microtubules, facilitating diverse processes as axonal transport and synaptogenesis, with tau phosphorylation being critical for normal function and is

the main mediator of the pathological properties of tau [65,66].

The results obtained herein showed that behavioral impairment was associated with a significant elevated levels of p-TAU in CRS group compared to normal control one, which could be attributed to decreased protein phosphatases 2A (MAP2) or activation of glycogen synthase kinase 3 β (GSK3 β), the main regulators of TAU phosphorylation [67,68].

Accumulation of p-Tau was suggested to be essential for chronic stress to induce dendritic atrophy and interrupt neuronal connectivity in the hippocampus [66,69]. Moreover, a sequestration of p-TAU into an insoluble pre pathogenic form may also occur under stress condition, which may constitute a link between stress and an AD-related pathogenic mechanism [70].

On the other hand, Se co-treatment significantly attenuated the increased levels of p-TAU in hippocampi of treated CRS group compared to untreated one. In consistence, selenium improved TAU pathology in AD rat models [16,71], further the improvement in learning and memory in selenium-treated tau transgenic mice was suggested to be mediated by its diminution to hippocampal p-tau levels [72].

The suppressing effect of Se on p-TAU overproduction could be attributed to its modulating effect on Akt/GSK3 β and/or PP2A activities [72-74] or may be mediated by indirectly reducing the oxidative stress induced tau toxic species with subsequent improving memory performance [16,49]. In addition, suppression to A β pathology under Se treatment may have a role, since A β was shown to trigger tau phosphorylation, most probably via A β -induced protease activation [75], and upregulation of GSK-3 β [76].

Among the large number of stress induced neurochemical changes, excessive release of glutamate, the predominant excitatory neurotransmitter in brain, was suggested to play an important role in chronic stress induced hippocampal neurotoxicity [77]. In consistence, the results of the present work demonstrated a significant elevated level of hippocampal glutamate in CRS group compared to normal control one, which could be attributed to decreased hippocampal glutamate clearance and increased glutamate release from synaptosomes under chronic stress conditions [78]. Moreover, it was recorded that restraint stress induced spatial memory impairment was blocked by inhibiting glutamate release or interrupting its excitatory inputs to the hippocampus, suggesting a role of

glutamate neurotoxicity in stress induced memory deficits [79].

The results obtained herein also demonstrated an insignificant effect of Se treatment on hippocampal level of glutamate of treated CRS group, nevertheless, studies recorded that Se may indirectly counteracted glutamate induced neurotoxic insult in hippocampal neurons by different mechanism [80], and that Se deficiency may increase the susceptibility to neurotoxic insults of glutamate [81], these data may give the assumption that the effect of se on glutamate toxicity may be mediated indirectly through antagonizing its toxic effects rather than affecting its basal level.

Acetylcholine-esterase is a key enzyme for correct cholinergic transmission, with its excessive activity had been associated with cognitive and memory impairment in different experimental models [82,83].

In this current study and in accordance with previous studies [77,84], CRS exposure led to excessive activation of hippocampal AChE enzyme. Meanwhile this activity was inhibited under Se co-treatment which may be another explaining mechanism of its alleviating effect on memory. Consistently anticholinesterases were shown to be effective in modulating memory deficits [85]. Moreover, Pinton et al., [86] reported that organoselenium reversed the increased activity of Ach E improving learning and cognitive deficits induced by intracerebro-ventricular injection of streptozotocin, which may be mediated at least in part by its antioxidant activity, especially that oxidative stress induced activation to AchE had been assumed previously [87].

Conclusion:

As proved in this current work, Se could alleviate the CRS-evoked memory deficits in rats. Its neuroprotective mechanism might be explained by its antioxidant potential, its augmentation to BDNF, its modulating effect on abnormal A β and TAU pathologies, as well as its attenuation to AchE activity in the hippocampi of CRS exposed rats. These data suggested the potential therapeutic value of Se for memory dysfunction associated with stress and its related disorders, thus further studies are needed to replicate this work on human beings.

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Conflict of interest:

We have no conflict of interest to declare.

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التأثير الواقي المحتمل للسيلينيوم ضد اضطرابات الذاكرة الناتجة عن التوتر المزمن المستحث بالتقييد في ذكور الجرذان البيضاء

الهدف من الدراسة: تم تصميم هذه الدراسة الحالية لفحص تأثير العلاج بالسيلينيوم ضد اضطرابات الذاكرة الناتجة عن التوتر المزمن المستحث بالتقييد في فئران التجارب.

المواد والطرق: تم تقسيم الجرذان إلى أربع مجموعات، كل منها 8 جرذان. المجموعة الأولى وتمثل المجموعة الضابطة، وأعطيت المجموعة الثانية السيلينيوم عن طريق الفم لمدة ثلاثة أسابيع، بينما تم تعريض المجموعة الثالثة للتوتر عن طريق التقييد لمدة 6 ساعات يوميا لمدة 3 أسابيع متواصلة، بينما تم إعطاء المجموعة الرابعة السيلينيوم بالتزامن مع التعرض للتوتر يوميا لمدة ثلاثة أسابيع. وفي نهاية التجارب تم إجراء الإختبارات السلوكية الخاصة بالذاكرة ثم تم ذبح الفئران وتشریح المخ لتجميع عينات الحصين لقياس الدلالات الكيميائية.

النتائج: كشفت هذه الدراسة أن العلاج بالسيلينيوم لمدة ثلاثة أسابيع في الفئران التي تعرضت للتوتر المستحث بالتقييد المزمن قد أدى إلى تحسين في أداء الذاكرة بشكل ملحوظ والذي كان مصحوبا بتحسين ذي دلالة إحصائية في مستوى الإجهاد التأكسدي في أنسجة الحصين مع تعزيزه لمستوى BDNF والذي كان موازيا لإنخفاض ذي دلالة إحصائية في مستويات P-TAU, $\alpha\beta$ ونشاط إنزيم AchE.

الخلاصة: هذه النتائج تشير إلى الآثار الواقية المفيدة للسيلينيوم على اضطرابات الذاكرة الناتجة عن التوتر المزمن المستحث بالتقييد في الفئران.