Biochemical and Behavioral Alterations Induced by Experimental Hyperthyroidism in Male Rats

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Abstract

Neurological and psychological disorders are the main complications specifically correlated with an overactive thyroid gland. Our study aimed to assess neurological diseases and behavioral abnormalities in relation to hyperthyroidism. Hyperthyroidism was induced by administering L-thyroxine sodium at a dosage of 240 µg/kg B.W via gastric gavage once daily for a duration of 20 days. A comparative analysis was conducted using a dosage of 10 mg/kg B.W of the commonly used anti-thyroid drug "propylthiouracil" to assess its effects concerning the hyperthyroid rats. A total of twenty-four adult male albino rats were selected and assigned to three groups using a random allocation method as follows: negative control, positive control and propylthiouracil groups. The findings indicated that the animal model of hyperthyroidism showed a notable rise in the levels of serum Free T3 and T4, alongside a decline in serum TSH level. There were significant alterations in the dopaminergic and cholinergic systems; dopamine level was greatly boosted, accompanied by a substantial decrease in acetylcholine levels. Hyperthyroid rats displayed significantly poorer performance in the Novel recognition memory task, demonstrating the occurrence of memory impairment in the hyperthyroidism state.

Keywords: Hyperthyroidism; Propylthiouracil; Acetylcholinesterase; Dopamine; Behavioral assessment

Introduction

Thyroid dysfunction is a commonly observed endocrine condition, with a prevalence rate of approximately 1-2% among the adult population ***(Taylor et al., 2018)***. The thyroid gland functions as a crucial regulator of the body's metabolism by synthesizing, storing, and releasing the hormones thyroxine (T4), triiodothyronine (T3), and calcitonin ***(Summers and Macnab, 2017)***. There exists a clear association between the functioning of the thyroid gland and many metabolic processes ***(Wang et al., 2023)***. When there is suboptimal functioning of the thyroid gland, it can result in a confluence of endocrine disorders, including diabetes, hypertension, cardiovascular issues and neurological complications ***(Cruz-Flores, 2021; Al-Suhaimi and Khan, 2022)***. With a female-to-male ratio of approximately 5 to 10:1, it was shown to be more common in females than in males ***(Yadav et al., 2013)***.

Additionally, proper thyroid metabolism is crucial for human development, encompassing the formation and operation of both the central and peripheral neural systems ***(Kurian and Jungbluth, 2014; Kumar et al., 2022)***. Several studies have unequivocally shown that the brain is a specific recipient of thyroid hormones. Undoubtedly, the brain relies significantly on thyroid hormones for its growth, morphological, and biochemical development ***(Braun et al., 2011; Rovet, 2014; Moog et al., 2017)***, which impact neuronal processing and integration, glial cell proliferation, myelination, migration, maturation, and the production of essential enzymes necessary for neurotransmitter synthesis ***(Shahat et al., 2022; Alcaide Martin and Mayerl, 2023)***.

In addition to the pivotal function of thyroid hormones in neural development and metabolic processes, current studies have emphasized the involvement of thyroid hormones in neurotransmission in the developed mammalian brain ***(Losi et al., 2008; Gilbert and Zoeller, 2010)***. Specifically, very close interactions presented between the thyroid hormones and the functioning of cholinergic and dopaminergic neurons in the brain ***(Smith et al., 2002; Duval et al., 2006)***. The aforementioned effects are mostly detected within distinct cholinergic nuclei and their corresponding pathways, namely the base of the forebrain and the hippocampus ***(Bavarsad et al., 2019)***.

Acetylcholine (ACh) performs an essential function as a neurotransmitter in the central nervous system (CNS) ***(Sam and Bordoni, 2022)***. The efficacy of this compound is dependent on its processing enzyme, acetylcholinesterase, which has been demonstrated to have a role in the formation of ACh ***(Day and Greenfield, 2002)***. It has been discovered that acetylcholinesterase

(AchE) is released simultaneously with dopamine from the dopaminergic neurons, implying a noteworthy interplay between these two compounds that play a crucial role in dopaminergic function ***(Emmett and Greenfield, 2005)***. Research has shown that thyroid dysfunction has an impact on the cholinergic system, synaptic proteins, and activity of AChE in both growing and mature rats ***(Wang et al., 2015)***.

The interplay between thyroid hormones and dopamine (DA) neurons is firmly established. Triiodothyronine (T3) and thyroxine (T4) have been identified as crucial elements in the stimulation of dopamine neurons ***(Lee et al., 2019)***. Hyperthyroidism significantly affects the levels of dopamine in several regions of the brain ***(Shahat et al., 2022)***.

Psychological and cognitive dysfunctions including, memory impairment, have long been observed in adults with impaired thyroid function ***(Zhu et al., 2022; Sahin et al., 2023)***. The correlation between thyrotoxic conditions, and mental disorders was initially documented in the late nineteenth century ***(Graves, 1835)***. Thyroid hormones play a crucial role in regulating cognitive functioning. They govern the processes of cell division, cell movement, and specialization in the nervous system. ***(Lillevang-Johansen et al., 2014; Cho et al., 2015)***.

Considerable investigation has been undertaken to examine the association between reduced or elevated levels of thyroid hormones during periods of development and the following adverse effects on neurobehavioral development in experimental animals ***(Singh et al., 2020)***.

Propylthiouracil (PTU) is frequently utilized as a pharmacological agent for the treatment of thyroid disorders, owing to its well-established and well-elucidated mode of action. PTU is a pharmacological substance that acts as an inhibitor of thyroid hormone production in the thyroid gland, as well as transformation of tetraiodothyronine into triiodothyronine in peripheral tissues ***(Tan et al., 2021)***.

This research aimed to acquire a deeper understanding of the neurochemical and behavioral alterations associated with hyperthyroidism. This was accomplished by evaluating the impact of induced hyperthyroidism on the concentrations of dopamine (DA) and acetylcholinesterase (AchE) in the blood of adult male albino rats. In addition to clarifying the influence of hyperthyroidism on memory and other behavioral activities.

Material and methods

Drugs and Chemicals

Tablets of euthyrox (levothyroxine sodium) were purchased from Merck KGaA Co., Germany. Thiouracil

(Propylthiouracil, PTU) was obtained from Amoun Pharmaceutical Co., Egypt.

Experimental animals

A total of 24 male albino rats, weighing 140-180 gram, were housed in cages containing four to five mice each, ensuring a pathogen-free environment. The animals were acquired from the animal facility of the Medical Research Center, Faculty of Medicine, Ain Shams University. The animals were provided unrestricted access to a regular meal and water ad libitum. Every possible measure was taken to reduce the animals' distress and minimize the quantity of animals utilized. The experimental procedure received acceptance and approval from the Research Ethical Committee of the Faculty of Veterinary Medicine, Suez Canal University, Egypt (Approval number is 2022040).

Experimental design

After acclimatization for two weeks, rats were haphazardly divided into three groups, each containing 8 rats, housed in individual cages, and categorized as follows: **Negative Control Group**; rats were serving as a non-treated euthyroid group and were given distilled water daily by gastric gavage for 50 days. **Positive Control Group:** rats served as a hyperthyroid group. Hyperthyroidism was induced by orally delivering euthyrox (levothyroxine sodium tablets, 240 µg/kg B.W, mixed with distilled water) once daily for 20 days as described by ***Chen et al. (2021)***. They were then administered distilled water by gastric gavage once daily for 30 days. **Propylthiouracil group**: rats were induced to develop hyperthyroidism for 20 days. Subsequently, they were treated with a reference medication, propylthiouracil, at a dosage of 10 mg/kg B.W administered orally for a period of 30 consecutive days ***(Panda and Kar, 2007; Kasim et al., 2020)***.

Collection of samples

Rats were euthanized using ketamine and xylazine anaesthesia. Micro-hematocrit tubes were used to collect blood samples from the medial canthus of the eye at the end of the experiment and after an overnight fast. Blood samples were delivered into dried and thoroughly cleaned screw-capped centrifuge tubes and permitted to coagulate at ambient temperature before being centrifuged for 15 minutes at 3000 rpm in order to separate clear serum samples for further biochemical analysis.

Biochemical parameters

Thyroid serum hormonal profile (free T3, freeT4, and TSH level) was determined using rats' reagent ELISA-kits (CSB-E05079r, CSB-E05076r, CSB-E05115r, respectively) purchased from Cusabio Biotech Company. Estimation was conducted using the methodology outlined ***Wada et al. (1982)***. AchE levels were determined using Rat Acetylcholinesterase (AchE) ELISA

Kit (Kamiya Biomedical Company, Catalog No: KT-5344), according to the method described by ***Magnotti Jr et al. (1987)***. The dopamine (DA) level was determined using Rat dopamine ELISA Kit (Cusabio Biotech Company, Catalog No: CSB-E08660r), according to the method defined by ***Arnt (1982)***.

Neurobehavioral assessments

The open field test (OFT)

The open field test (OFT) was employed to evaluate the behavioral activities of rats that were raised under various treatment conditions. The open field apparatus consists of a transparent cubic box made of plexiglass, with dimensions of 40 cm in width, 60 cm in length, and 30 cm in height. The floor was partitioned into six small, uniform squares delineated by a black line, facilitating the observation of mobility. To limit visual communication between the tested subjects, a sheet of cardboard was placed between each instrument. The experimental setup was equipped with a high-definition video camera. The rats were relocated from their enclosures to the experimental setup under the supervision of a familiar individual. Subsequently, each rat was introduced into the central square of the apparatus, marking the commencement of a 10-minute session. Each group consisted of 8 rats that were tested. The length of behavioral activities was recorded according to the specifications outlined in **Table 1** as described by according to ***(Mohamed et al., 2016)***.

Novel object recognition test (NOR)

The researchers employed the new object recognition test (NOR) to evaluate potential changes in long-term recognition memory across various treatment circumstances. The NOR apparatus consists of a transparent cubic box made of plexiglass with dimensions of 40 cm in width, 60 cm in length, and 30 cm in height. The floor was partitioned into six equally sized squares, each delineated by a black line, in order to facilitate the observation of movement. To limit visual communication between the tested subjects, a sheet of cardboard was placed between each instrument. The rats were relocated from their enclosures to the experimental setup under the supervision of a familiar individual. Subsequently, each rat was introduced into the central square and allowed to remain there for 10 minutes. Each experimental group consisted of 8 rats. The NOR apparatus exhibited comparable light hue and intensity to that of the home cages utilized for rats.

The examination was structured into three distinct phases, including the adaptation stage, training period, and examining stage. During the adaptation stage, the animals are provided with the opportunity to freely explore an arena that is devoid of any objects or stimuli. Following 24 hours of habituation, the animals are subsequently subjected to a

familiar arena containing two identical objects, denoted as A and B, which are positioned equidistantly. During the subsequent day, which corresponds to the testing phase, the rat is granted the opportunity to navigate the arena while being exposed to both a familiar object (B) and a novel object (C), with the intention of evaluating its long-term recognition memory.

The study involved the observation of various behavioral activities, specifically focusing on the preference index. The preference index was determined by dividing the frequency at which the subject selected object A or B by the sum of the choices for both objects (A and B) and then multiplying the result by 100%. This calculation was performed during the training session. In the test phase, the preference index was generated by dividing the frequency with which the subject selected object B or C by the sum of the choices for both objects (B and C) and then multiplying the result by 100%. The Recognition Index (RI) is determined by dividing the amount of time dedicated to investigating the new item (TN) by the total duration of object examination %%TN + familiar item (TF)%%; All the previous behavioral elements were according to ***(Antunes and Biala, 2012)***.

Statistical analysis

The statistical analysis was performed utilizing the Statistical Package for Social Science (SPSS) version 22.0 for Windows, developed by IBM Corp. SPSS, Inc. in Chicago, IL, USA. The Shapiro-Wilk test was employed to assess the normality of the data. The treatment groups were compared using a one-way analysis of variance (ANOVA) in terms of biochemical parameters and behavioral measures. Subsequently, Duncan's post hoc multiple comparisons (DMR) test was performed when necessary. The data were presented as the mean ± standard error (SE). The null hypothesis was dismissed with a significance threshold of $\alpha = 0.05$.

Table 1. *Description of the different behavioral activities measured in the Open field test in rats reared under different treatment groups.*

Behavior activities	Definition
Latency till the first step	The time spent at the central square from the start of the session until the first move to another square.
Walking duration	The time spent in movement between different squares.
Exploratory activities	Pecks are directed to the floor or the walls of the arena.

Results

Thyroid hormones levels are displayed in **Table 2** showed that there were indicated statistically significant (*p < 0.05)* elevations in the serum concentrations of thyroid hormones. (FT3, FT4 and TSH) in the hyperthyroid rats with mean values of 11.04 ± 0.42 pmol/L, 13.39 ± 0.57 pmol/L and 0.52 ± 0.03 µIU/ml, respectively), as compared to the control (3.67 ± 0.16 pmol/L, 4.78 ± 0.36 pmol/L and 1.14 ± 0.04 µIU/ml respectively). Nevertheless, the levels of these hormones were dramatically reduced ($p < 0.05$) in the animal groups that received the chemical medicine PTU to levels that were very similar to the control rats.

Results are presented as Mean ± SE. standard error. Superscripts indicating different values are considered substantially different at a threshold of significance of $P < 0.05$, as determined by the Duncan multiple test.

Moreover, rats with experimentally induced hyperthyroidism exhibited significant abnormalities in the serum levels of brain markers (acetylcholinesterase and dopamine). **Figure 1.** Brain markers levels, showed substantially lower levels of acetylcholinesterase in the hyperthyroid rats compared to the healthy animals, while revealing markedly elevated levels of dopamine. notably, administering PTU therapy to the group with hyperthyroidism substantially raised the blood levels of AchE, while simultaneously reducing the levels of DA **(Figure 1)**.

Behavioral observation at open field test (OFT)

The outcomes pertaining to the behavioral reactions of rats in various treatment groups during the open field test are presented in **Table 3**.The latency until the first step exhibited no statistically significant changes in either the control negative group or the other treatment groups. The rats that were raised in the positive control group demonstrated a statistically significant increase in walking duration activity when compared to the other treatment groups ($P < 0.05$). Nevertheless, the rats in the positive control group, as well as the Propylthiouracil group, exhibited a substantially lower length of exploratory activities ($P < 0.05$) when compared to the negative control group.

Novel object recognition test (NOR)

Results of the behavioral responses of rats to the NOR in different treatment groups are shown in **Figure 2.** Across the testing session, results showed that the overall preference of positive control and propylthiouracil-treated rats to the familiar object was significantly higher than negative control group ($P = 0.01$). However, on the opposite side, the presence of a novel object in the familiar environment led to significantly higher explorative and interactive activity toward it ($P = 0.02$) in the negative control group than the positive control and propylthiouracil groups.

Table 2. *Serum levels of thyroid hormones (FT3 , FT4 and TSH) in L-thyroxine induced rats and PTU- treated group compared to control group.*

Animal groups	FT3 (pmol/L)	FT4 (pmol/L)	TSH (µIU/ml)
Negative control	$3.67^{c} \pm 0.16$	$4.78^{c} \pm 0.36$	$1.14^{a} \pm 0.04$
Positive control	$11.04^{a} \pm 0.42$	$13.39^{a} \pm 0.57$	$0.52^{c} \pm 0.03$
Propylthiouracil	$6.52^{b} \pm 0.36$	$7.28^{b} \pm 0.46$	$0.78^{b} \pm 0.06$

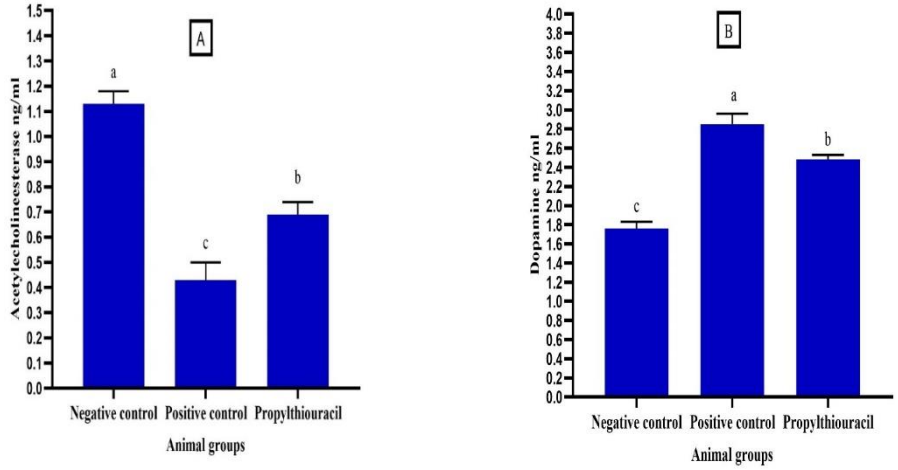

Figure 1. (A, B) Serum AchE and DA levels of hyperthyroidism-treated animal group as compared to control groups. Results are presented as Mean ± standard error. Superscripts indicating different values are considered substantially different at a threshold of significance of $P < 0.05$, as determined by the Duncan multiple test.

Table 3. *Behavioral observations (sec.) of rats reared at different treatments at the open field test compared to the negative control group.*

OFT	Latency till first step	Walking duration	Exploratory activities
Negative Control	**$0.99^{a} \pm 0.11$**	**$42.47^{c} \pm 12.39$**	**$49.16^{a} \pm 6.78$**
Positive Control	**$1.13^{a} \pm 0.32$**	**$75.59^{a} \pm 13.62$**	**$34.36^{b} \pm 4.33$**
Propylthiouracil	**$1.22^{a} \pm 0.18$**	**$29.58^{bc} \pm 3.36$**	**$28.30^{c} \pm 4.63$**

Results are presented as Mean ± standard error. Superscripts indicating different values are considered substantially different at a threshold of significance of $P < 0.05$, as determined by the Duncan multiple test.

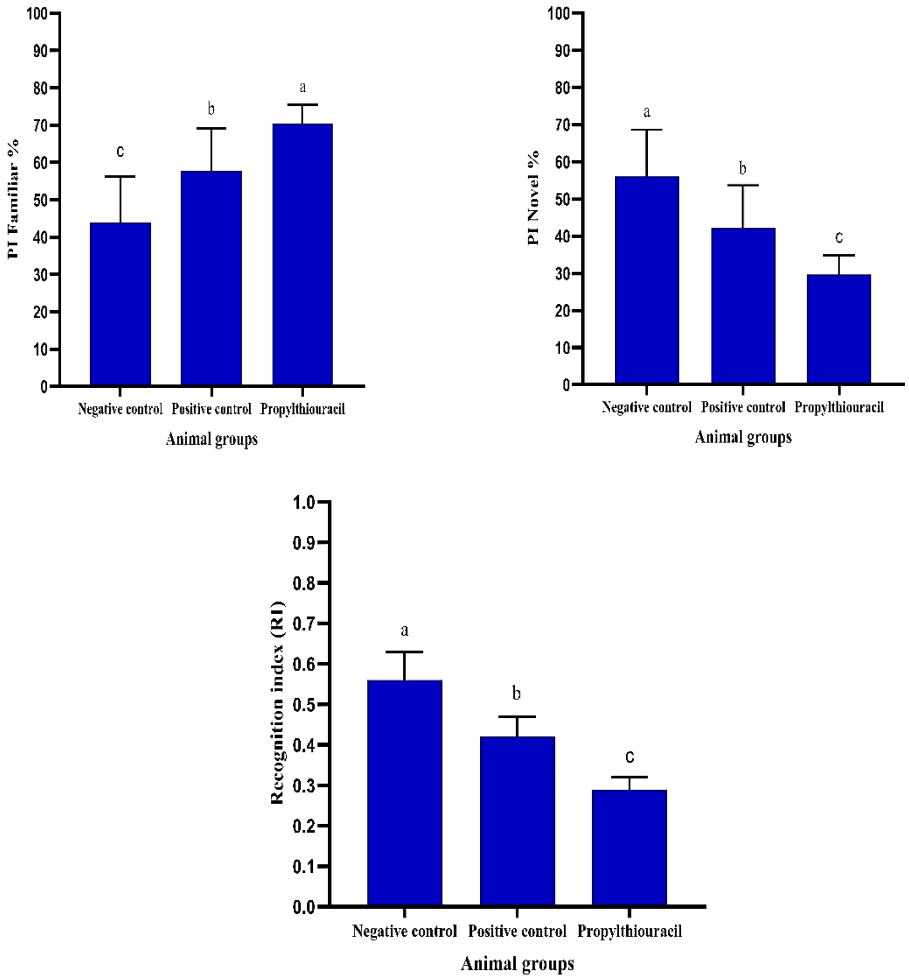

Figure 2. PI Familiar (%), PI novel (%), and RI of rats reared at different treatments at the NOR test. Results are presented as Mean ± standard error. Superscripts indicating different values are considered substantially different at a threshold of significance of $P < 0.05$, as determined by the Duncan multiple test.

Discussion

Excessive synthesis and release of free thyroid hormones (T3 and T4) as well as downregulation of thyroid stimulating hormone collectively are responsible for the occurrence of

hyperthyroidism, commonly referred to as a hyperactive thyroid gland ***(Hwang et al., 2017)***. Hyperthyroidism animal model exhibited a significant elevation in levels of serum total T3, FT3, total T4, and FT3, accompanied by decrease in serum TSH level; these findings align with the studies conducted by ***Rajab et al. (2017); Aiouaz and Bitam (2022); Sanwal et al. (2022).*** L-thyroxine (LT4) has been reported to enhance thyroid function by largely suppressing oxidative iodination in the thyroid gland, hence influencing the production of thyroid hormones. In addition, LT4 disrupts the process of extrathyroidal converting T4 to T3, leading to the production of TSH outside of the thyroid gland ***(McAninch and Bianco, 2014)***.

The most common anti-thyroid drug (ATDs) used to treat hyperthyroidism is PTU ***(John et al., 2015)***. Thyroid iodide peroxidase is able to catalyze the first step of thyroid hormone production; PTU is a potent inhibitor of this enzyme ***(Duan et al., 2016)***. By blocking thyroid peroxidase activity, PTU limits T4 production. On the other hand, PTU can impede the conversion of T4 to T3, leading to a drop in serum-free T3 levels ***(Prescott, 2006)***. Therefore, PTU expectedly modulated thyroid hormones levels.

Elevated levels of thyroid hormones, known as hyperthyroidism, are anticipated to result in significant brain damage ***(Yuan et al., 2015)***. The influence of hyperactive thyroid gland on the developing neurological system and has been extensively researched ***(Ahmed et al., 2010; Gilbert and Zoeller, 2010; Andersen and Andersen, 2021)***. Elevated levels of thyroid hormones throughout the developmental phase can lead to lifelong impairments, including structural and cellular abnormalities, disorganization, maldevelopment, and physical retardation. These impacts could potentially cause the deterioration of essential brain functioning and subsequently result in metabolic dysfunctions ***(Hassan et al., 2013)***.

There is insufficient and inconsistent information on the impact of thyroid hormones on the activity of the enzymes AchE and DA, which play a crucial role in neurotransmission in the adult rat brain. The inconsistency appears to be caused by several factors, including the utilization of various animal strains and the implementation of different experimental protocols (either in vivo or in vitro), the examination of diverse brain regions, variations in dosage, method of administration, and type of TH dysfunctions ***(Sarkar and Ray, 2001; Chakrabarti and Ray, 2003)***.

In this study, we observed a decline in AchE activity. ***Carageorgiou et al. (2005)*** also noted a reduction in acetylcholinesterase (AchE) activity throughout the entire brain during hyperthyroidism produced by T4. Overall, ***Phillips et al. (2021)*** found that a decrease in AchE activity was

slightly linked to greater fT4 levels, but not related to TSH levels.

By applying a different treatment protocol of L-T4 administration (2.5 mg/kg B.W for 4 days followed by either 5 or 10 mg/kg B.W every third day for 28 days), there was a notable increase in AchE activity observed in both the frontal cortex and hippocampus during the initial dosing regimen. The enzyme activity was specifically enhanced solely in the hippocampus when the second dosing regimen (28 days) was administered ***(Smith et al., 2002)***.

However, ***Almeida and Santos (1993)*** did not observe any alterations in the activity of acetylcholinesterase (AchE) in rats treated with T3. ***Carageorgiou et al. (2007)*** found that hyperthyroidism did not have an impact on the activities of AchE, Na^+, K^+-ATPase, and Mg^{2+}-ATPase in the frontal cortex of adult rats. However, hypothyroidism led to a significant increase in AchE activity (approximately 22%, P <0.01) and a significant decrease in Na^+, K^+-ATPase activity in the hippocampus. Nonetheless, it is essential to consider the potential for increased synaptic ACh release and modulation of AchE activity (particularly in the hippocampus) due to the diminished TH-dependent Na^+, K^+-ATPase activity. The aforementioned modifications caused by thyroid hormones are anticipated to have varying effects on the relevant monoamine neurotransmitter systems and other enzymatic parameters of the brain ***(Carageorgiou et al., 2007)***

The findings derived from our investigation indicated that hyperthyroidism elicited significant elevations in blood dopamine levels. It is in concurrence with an earlier report that been shown that administrating young and adult rats a daily dose of 500 g/kg B.W of L-T4 via s.c. injection for 21 consecutive days resulted in the manifestation of hyperthyroidism symptoms, and a notable rise in dopamine (DA) levels was found in the majority of brain regions investigated in both juvenile and mature animals, with statistical significance at $P < 0.05$ or $P < 0.01$ ***(Hassan et al., 2013)***.

Furthermore, numerous additional publications concurred with our findings***. Jacoby et al. (1975)*** reported that inducing hyperthyroidism in rats with the administration of 15 mg T4/100 g BW for 25 days resulted in an increased rate of buildup of catecholamine and serotonin. Additionally, ***Ito et al. (1977)*** highlighted that the rate of accumulation of DA and 5-HT in hyperthyroidism enhanced in the meso-diencephalon and pons-medulla. Moreover, the findings of ***Rastogi and Singhal (1976)*** demonstrated that the treatment of thyroxine to neonatal rats for a duration of 30 days resulted in an elevation of dopamine levels in the brain. ***Puymirat (1985)*** determined that hyperthyroidism escalated the

rate of catecholamine production and triggered heightened sensitivity of noradrenergic receptors. Multiple studies have provided evidence supporting this idea, showing an increase in the activity of tyrosine hydroxylase, the initial and controlling enzyme in the production of catecholamine, after experiencing hyperthyroidism.

Dopamine elevation can be elucidated through many mechanisms. For instance, the increased concentrations of dopamine in multiple brain regions may be associated with the modification of dopamine receptor site sensitivity caused by hyperthyroidism ***(Yudiarto et al., 2006)***. These factors encompass the presence of chorea during hyperthyroidism, the effectiveness of dopamine antagonists in treating hyperthyroid chorea, and the impact of thyroid function on brain dopamine metabolism, as indicated by levels of cerebrospinal fluid homovanillic acid ***(Weiner and Klawans, 2012)***. In addition, hyperthyroidism heightened the amount of the chemical catecholamine production and triggered increased sensitivity of noradrenergic receptors, while also inhibiting the uptake of 5-HT in the hippocampus and cerebral cortex of adult male rats. Thus, the augmented production of this amine's synthetic routes may be a result ***(Shahat et al., 2022)***.

Propylthiouracil treated rats have shown slightly adjusted levels of AchE and DA. We speculated that alleviated hyperthyroidism status by PTU administration has altered levels AchE and DA.

Ultimately, the rats underwent the open field test to evaluate various behavioral activities. The study revealed that the time of walking was much longer in the hyperthyroid group in comparison to the propylthiouracil and negative control groups, indicating a heightened sense of anxiety and physical activity in rats with hyperthyroidism. This result is consistent with the findings reported in earlier literature ***(Redei et al., 2001; Levine et al., 2003; Zhu et al., 2022)***. Exploratory activities were observed to be lower in both the positive control group and the hyperthyroidism treatment group compared to the control rats. This suggests a defect in exploring a novel environment in these groups, which aligns with findings from earlier studies ***(Sala-Roca et al., 2002; Bruno et al., 2006)***.

Subsequently, rats were exposed to learning and memory activities, including the Novel Object Recognition (NOR) test. Throughout the training phase, every rat successfully differentiated between the two indistinguishable objects. During the testing phase, the control rats successfully differentiated between the novel object and the familiar object, while the hyperthyroid and propylthiouracil groups were unsuccessful in doing so. Learning and memory

difficulties resulting from hyperthyroidism have been extensively documented, with over 50% of hyperthyroid patients typically experiencing memory loss ***(Göbel et al., 2016; Bavarsad et al., 2019; Nicola et al., 2021; Sahin et al., 2023)***. As far as we know, this is the initial instance where a NOR test has been employed to identify learning and memory in hyperthyroid rat. Our findings are consistent with the research performed by ***Zhu et al. (2022)***, who were the pioneers in utilizing the NOR test on hyperthyroid mice.

Conclusion

The current study indicates that hyperthyroidism significantly impacts the levels of acetylcholine and dopamine. Nevertheless, further research is required to clarify the fundamental mechanisms of the association between thyroid dysfunctions and neurochemical alterations as all the existing literature on this subject is outdated.

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الملخص العربي

المضـاعفات العصـبية هي واحدة من المضـاعفات الرئيسـية المرتبطة على وجه التحديد بحالات فرط نشاط الغدة الدرقية. حاولت الدراسة الحالية تقييم الاضطرابات العصبية الناجمة عن فرط نشاط الغدة الدرقية والمظاهر السـلوكية ذات الصـلة في ذكور الجرذان التجريبية. تم إحداث فرط نشـاط الغدة الدرقية عن طريق إعطاء ل-ثيروكسين الصوديوم بجرعة 240 ميكروجرام / كجم عن طريق أنبوب المعدة لمدة 20 يومًا، مرة واحدة يوميًا. تم إجراء مقارنة تحليلية باسـتخدام جرعة 10 ملجم/كجم من الدواء الشـائع الاسـتخدام "بروبيل ثيوراسـيل" لتقييم آثاره بالنسـبة للفئران المصـابة بفرط نشـاط الغدة الدرقية. تم اختيار أربعة وعشـرين ذكراً من الجرذان البيضـاء البالغة وقسـمتهم إلى ثلاث مجموعات عشـوائياً على النحو التالي: المجموعة الضـابطة السـلبية، المجموعة الضـابطة الإيجابية ومجموعة البروبيل ثيويوراسـيل. أشـارت النتائج إلى أن نموذج فرط نشـاط الغدة الدرقية أظهر ارتفاعًا ملحوظًا في مسـتويات هرومانات الغدة الدرقية(الثيروكسـين يودوثيرونين) الحرة في المصـل، إلى جانب انخفاض في مستوى TSH في المصـل. كانت هناك تغييرات كبيرة في أنظمة الدوبامين والكولين. تم تعزيز مستوى الدوبامين بشكل كبير، مصحوبًا بانخفاض كبير في مستويات الأسيتيل كولين. أظهرت الفئران المصـابة بفرط نشـاط الغدة الدرقية أداءً أقل بكثير في مهمة ذاكرة التعرف على الأشـياء الجديدة، مما يدل على حدوث ضعف في الذاكرة في حالة فرط نشاط الغدة الدرقية.