ORIGINAL ARTICLE

Effects of mobile phone electromagnetic radiation on thyroid glands and hormones in *Rattus norvegicus* brain: An analysis of thyroid function, reactive oxygen species, and monocarboxylate transporter 8

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J. Adv. Pharm. Technol. Res.

ABSTRACT

The aim of this study was to investigate the effects of mobile phone electromagnetic radiation (MP-EMR) on the thyroid glands and hormones in *Rattus norvegicus* brain in term of thyroid function, reactive oxygen species (ROS), and monocarboxylate transporter 8 (MCT8) concentration. Forty rats were divided into different groups: control (without EMR exposure), EMR1 (120-min/day exposure), EMR2 (150-min), and EMR3 (180-min). The levels of serum thyroid stimulating hormone (TSH), thyroxine (T_4), and malondialdehyde (MDA) and brain and MCT8 were measured using enzyme-linked immunosorbent assay. One-way analysis of variance followed by the Duncan test was used to analyze the data. Our data indicated that the levels of serum TSH and T_4 in all the EMR groups were lower significant postexposure compared to the control with $P < 0.01$ (EMR1 and EMR2) and $P < 0.001$ (EMR3), suggesting hypothyroidism due to MP-EMR exposure. Increased MDA and decreased MCT8 levels were also observed following the intervention; however, the changes in both concentrations were notably significant after being subjected to 150-min and 180-min of exposure. In conclusion, a significant reduction in TSH, T_4, and MCT8 levels indicated thyroid dysfunction due to MP-EMR exposure.

Key words: Electromagnetic radiation, monocarboxylate transporter 8, mobile phone electromagnetic radiation, mobile phone, reactive oxygen species, thyroid

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Submitted: 06-Dec-2022 **Revised:** 27-Jan-2023
Accepted: 06-Feb-2023 **Published:** 13-Apr-2023

Access this article online	
Quick Response Code:	Website: www.japtr.org
	DOI: 10.4103/japtr.japtr_680_22

INTRODUCTION

The number of mobile phones (MPs) users has increased significantly due to increased demand for electronic

How to cite this article: Zufry H, Rudijanto A, Soeatmadji DW, Sakti SP, Munadi K, Sujuti H, *et al*. Effects of mobile phone electromagnetic radiation on thyroid glands and hormones in *Rattus norvegicus* brain: An analysis of thyroid function, reactive oxygen species, and monocarboxylate transporter 8. J Adv Pharm Technol Res 2023;14:63-8.

communication and rapid advances in technology.[1] MPs receive and send out radiofrequency-electromagnetic radiation (RF-EMR) to transfer information, producing nonionizing electromagnetic waves with frequencies ranging from 450 to 3800 MHz.[2,3] Frequent use of MPs has led to unprecedented human exposure to this form of EMR, which has been suggested to affect human body functions and induce cellular alterations, including the increment of free radical concentrations.[4-7] Studies have evidenced the increase in malondialdehyde (MDA) level, elevated nitric oxide, decreased glutathione and several antioxidant enzyme activities, and increased several pro-oxidant enzymes following nonionizing EMR.[5,8] These cellular alterations may then lead to other phenomena in the body in the absence of the adaptive immune response, including elevated reactive oxygen species (ROS) formation, which makes EMRs as a considerably possible carcinogen for humans.[3]

The thyroid gland has been considered the most frequently affected organ in the endocrinology system by MP-EMR due to its superficial location, while MPs are often used in proximity to the thyroid gland.[9,10] However, data related to the effects of nonionizing EMR on the thyroid gland and its hormones are conflicting.[11,12] A review exploring the effect of MP-EMR on thyroid hormone and thyroid histopathology summarized that nonionizing EMR had impacts on morphological, histological, and physiological characteristics of the thyroid gland and hormones.[11] However, another review exhibited that of the total 2,653 *in vivo* and *in vitro* studies analyzed, more than half (1.168) suggested no effects on body function, including the thyroid gland, owing to MPs use.[12] Therefore, more investigations regarding the effect of MP-EMR on thyroid function is required to obtain a more definitive conclusion. The aim of this study was to investigate the effect of MP-EMR on thyroid glands and hormones in brain through the analysis of thyroid function, ROS, and monocarboxylate transporter 8 (MCT8) concentrations.

METHODS

Study design, setting, and procedure

The study was conducted at the Thermal, Vibration, and Acoustic Laboratory, Universitas Syiah Kuala for 12 weeks. A true experimental design was employed to evaluate the effect of MP-EMR on the levels of serum thyroid stimulating hormone (TSH), thyroxine (T_4) MDA, and pituitary MCT8 concentration. Wistar rats (*Rattus norvegicus*), 3–4 months old with 160–250 g, were divided into four groups randomly containing 10 rats each group: one control (without EMR exposure) and three EMR-exposed groups (EMR1: Exposed to 120-min/day; EMR2: 150-min/day; and EMR3: 180-min/day EMR). Before and after the EMR exposure, the level of serum TSH and T_4 were measured. On the last day of the intervention, the animals were euthanized by a cervical dislocation procedure for the analysis of MCT8 concentration in the brain. The protocol of this study was approved by the Veterinary Ethics Committee, Universitas Syiah Kuala, Indonesia (Ref No. 69/KEPH/XII/2020).

Experimental setup and mobile phone electromagnetic radiation exposure

During the experiment, the animals were placed in an anechoic chamber to prevent unwanted signals from outside the chamber. In the chamber, the animals were housed in a pentagon ventilated glass cage divided into 5 partitions, where each partition consisted of one rat. There was also a hole in center of the cage to spot a MP as the source of EMR. All the EMR rats were exposed to MPs emitting a 4G LTE multiband global system for mobile communications (GSM) signal at 1800 MHz with their respective daily exposure duration for 12 weeks. The control group was also placed under identical condition, but received no exposure to EMR.

To generate cellular signals, two GSM modules were used. These modules were connected to a microcontroller programmed to consecutively make and receive calls at their specified time. A real time clock module was used to control an automatic bidirectional communication between the two GSM modules. GSM1 module was placed inside the chamber while GSM2 module was spotted outside the chamber. During the 120-min/day irradiation, GSM1 was set to make calls in the first 60 min and then received calls during another 60 min. The same procedure was also applied for the 150-min and 180-min EMR exposure process.

Serum thyroid stimulating hormone and thyroxine levels

Blood sample was collected and the serum was separated and preserved at −80°C until used. TSH and T_4 quantification was carried out using a commercial Enzyme-linked immunosorbent assay (ELISA) kit for *R. norvegicus* (Bioenzy, Jakarta, Indonesia).

Serum malondialdehyde concentration

The levels of MDA were assessed using Rat Malondialchehyche ELISA kit following the manufacturer protocol (Bioenzy, Jakarta, Indonesia). The concentration of MDA was measured by spectrophotometer at a wavelength of 450 nm and the kit has sensitivity 0.01 nmol/mL.

Brain monocarboxylate transporter 8 concentration

The rats were euthanized by cervical dislocation technique and the pituitary gland was removed and frozen in isopentane solution. The sample was then thawed on a slide super frost (Thermo Scientific) before being kept in a −80°C until used. The concentration of MCT8 was measured using Rat MCT8 (SLC16A2) ELISA kit (My BiosSource Inc, San Diego, USA).

Statistical analysis

All analyses were conducted by comparing MP-EMR-exposed groups with the control group. We used one-way analysis of variance followed by a Duncan test to compared the effects of MP-EMR between exposure groups and control group.

RESULTS

The levels of serum thyroid stimulating hormone and thyroxine before electromagnetic radiation exposure

To ensure that all the rats were under similar condition in terms of thyroid function before being exposed to MP-EMR, early serum TSH and T_4 levels of each rat was assessed. The average TSH and T_4 levels of the rats in each experimental group before the intervention [Table 1]. The mean levels of serum TSH and T_4 had no differences in among all the experimental groups before the 1800 MHz MP-EMR exposure ($P > 0.05$).

Effect of mobile phone-electromagnetic radiation on the levels of thyroid stimulating hormone, thyroxine, malondialdehyde, and monocarboxylate transporter 8

Following 12 weeks of MP-EMR exposure, laboratory changes were observed in all the variables tested. The average serum TSH, T_4, and MDA concentrations, as well as the levels of MCT8 concentration in the animals' brains are presented in Table 2. There were statistically significant differences in the levels of TSH, T_4, MDA, and MCT8 among all the experimental groups after the intervention ($P < 0.05$).

Our data revealed that TSH levels were significantly lower in the EMR1, EMR2, and EMR3 groups compared to the control with $P = 0.008$, $P = 0.003$, and $P < 0.001$, respectively. The highest THS drop was recorded in the group with the longest exposure duration. However, despite reduced TSH levels were perceived along with the increased period of exposure, no different of the level of this hormone between the 120-min- and 150-min-irradiated groups ($P = 0.662$) [Figure 1a].

A very significant decrease in mean T_4 levels was also noticed in all the exposed groups in comparison with the control ($P < 0.001$ each). However, when compared within the EMR groups themselves, the average T_4 values did not differ significantly, suggesting that exposure to 1800-MHz MP-EMR for 120–180 min/day resulted in similar serum T_4 levels reduction [Figure 1b].

While TSH and T4 levels declined following EMR exposure, MDA levels were found to be increasing in all the treated groups; however, this elevation did not reach statistical significance in the EMR1 group in comparison with the control. Significant rises in the levels of serum MDA were noted in the EMR2 and EMR3 groups as compared to the control ($P < 0.001$ and $P < 0.01$, respectively) [Figure 1c], suggesting that rat exposure to MP-EMR for more than 150 min/day might lead to ROS formation.

A similar significance pattern of reduction was also seen in MCT8 concentration. The levels of MCT8 in the pituitary tissue of the control also did not significantly differ from those of the EMR1 (the shortest duration of exposure); however, significant declines were observed in the EMR2 ($P < 0.001$) and EMR3 ($P < 0.001$). MP-EMR was found to significantly suppressed MCT8 concentrations in a time-dependent manner, where the longer the duration of exposure, the lower the amount of MCT8 in the rats' pituitary. Our data revealed approximately 48.3% and 60% MCT8 levels reduction in the brains of Wistar rats when subjected to 150-min and 180-min MP-EMR, respectively [Figure 1d].

DISCUSSION

Our data suggested reduction of circulating TSH and T_4 levels after 1800 MHz MP-EMR exposure for 12 weeks and the reduction was proportional to the duration of exposure. This finding confirmed the results of several previous investigations, suggesting that TSH and T_4 levels decreased in humans and animals upon exposure to RF EMRs, such as those emitted by MP devices in particular, with frequencies ranging from 500 to 1800 MHz for certain periods of time.[13,14] This suggests that MP exposure might have detrimental effects on thyroid gland function and hormone production and this could be direct effect or indirect effect by disrupting the hypothalamic-pituitary-thyroid (HPT) axis.[11] Thyroid dysfunction, owing to MPs exposure, has also been suggestively associated with its thermal effects on the thyroid gland of which it increases thyroid gland temperature and promotes cellular stress leading disruption of the iodine uptake by thyroid follicles.[2,14]

MPs use RF -based technology that produces a nonionizing form of radiation, causing thermal and nonthermal effects on body tissues.[5,7,10,15] The heat is produced when the body

Table 1: Levels of thyroid stimulating hormone and thyroxine in each treatment group before the intervention

Parameters	Treatment groups (mean±SE)				*P*
	EMR1	EMR2	EMR3	Control	
TSH (μIU/mL)	2.13±0.11	2.06±0.08	2.01±0.11	2.11±0.13	0.865
T4 (μg/dL)	15.08±0.39	15.14±0.67	15.30±0.46	15.96±0.54	0.629

EMR1: 120-min, EMR2: 150-min, EMR3: 180-min exposure/day, Control: No exposure to MP-EMR. TSH: Thyroid stimulating hormone, T4: Thyroxine, SE: Standard error, EMR: Electromagnetic radiation, MP: Mobile phone

Table 2: The levels of thyroid stimulating hormone, thyroxine, malondialdehyde and monocarboxylate transporter 8 after the intervention

Variables	Treatment groups (mean±SE)				*P*
	EMR1 (120-min/day)	EMR2 (150-min/day)	EMR3 (158-min/day)	Control	
TSH (μIU/mL)	1.91±0.81	1.88±0.26	1.67±0.50	2.13±0.50	<0.001**
T4 (μg/dL)	10.61±0.40	10.92±0.30	10.95±0.30	15.86±0.40	<0.001**
MDA (μmol/L)	0.58±0.27	0.67±0.28	0.64±0.28	0.53±0.15	0.002*
MCT8 (μmol/L)	0.90±0.03	0.46±0.28	0.35±0.024	0.89±0.042	<0.001**

TSH: Thyroid stimulating hormone, T4: Thyroxine, SE: Standard error, EMR: Electromagnetic radiation, MP: Mobile phone, MDA: Malondialdehyde, MCT8: Monocarboxylate transporter 8. *Statistically significant at 0.05, **Statistically significant at 0.01

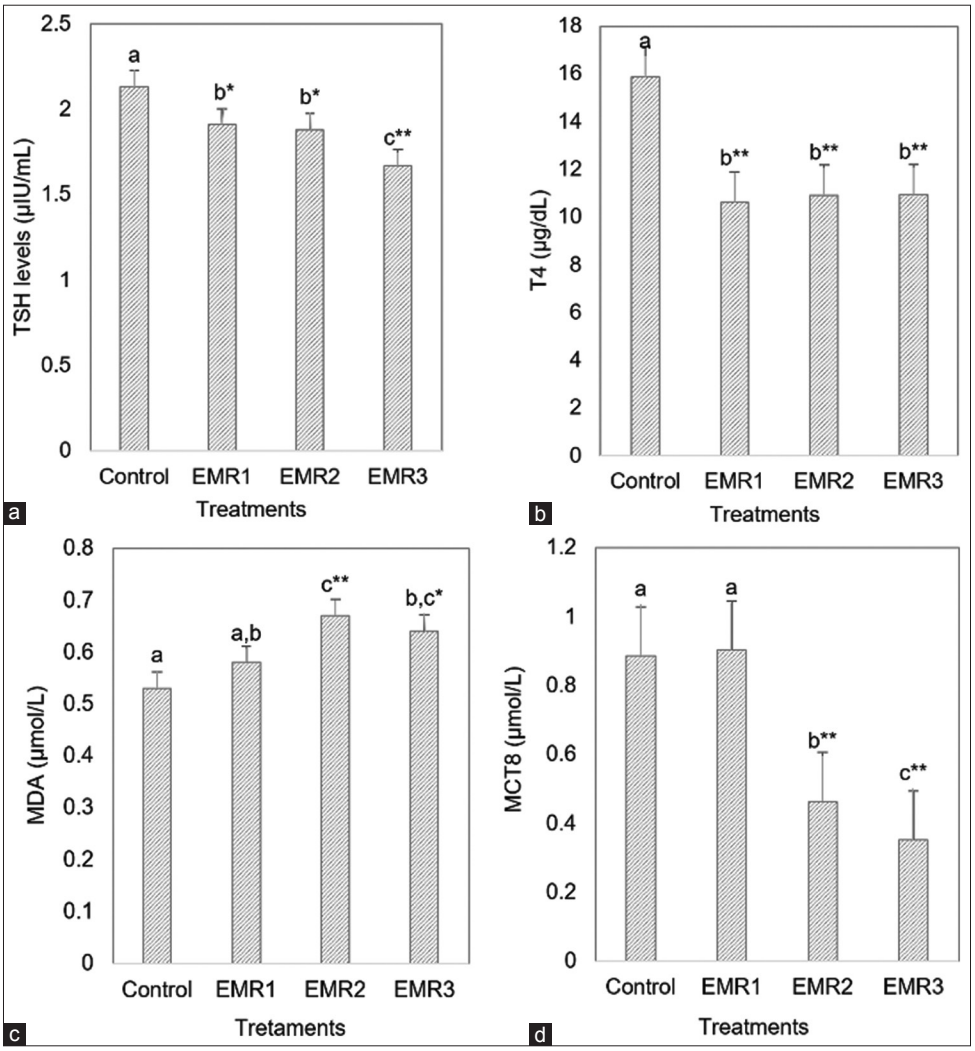

Figure 1: The mean levels of TSH (a), T_4 (b), MDA (c), and MCT8 (d) after being subjected to 120-min (EMR1), 150-min (EMR2), and 150-min (EMR3) MP-EMR exposure. Error bars represent standard error (n = 10). The treatments followed by the same letter above each column indicate no significant different between groups using a Duncan test ($P \leq 0.05$). *Significant at $P < 0.05$ as compared to control, **Significant at $P < 0.001$ as compared to control. TSH: Thyroid stimulating hormone, T4: Thyroxine, EMR: Electromagnetic radiation, MP: Mobile phone, MDA: Malondialdehyde, MCT8: Monocarboxylate transporter 8

absorbs some of the radiation during the exposure and converts it into kinetic energy. Once the temperature is above an acceptable limit, the harmful effects could occur to the cells. In terms of nonthermal effects, EMRs works by inducing an electrical current that stimulates nerves in the body and changes cell membrane permeability, resulting in cell metabolism alterations without affecting its temperature.[10,15] A study suggested that EMR with lower intensity can lead to cellular stress, ROS formation, and genetic damage.[16]

MCT8 is a crucial marker for the determination of thyroid function. It is recognized as the transporter that shows the highest specificity for thyroid hormone and plays a role in the regulation of the intracellular thyroid concentrations.[17] Higher concentrations were mainly detected in the hypophysis, although it can also be found in other organs such as the pituitary gland, cerebral cortex, heart, lung, thyroid, heart, kidney, liver, pancreas, testis, and skeletal muscle.[18,19] A deficiency of MCT8 impairs the hypothalamus-pituitary-thyroid axis.[18] We found that MCT8 levels in the pituitary tissue of the control group did not differ significantly from those of EMR1 (120-min exposure). It exemplifies the presence of pituitary tissue's adaptive reaction after 120-min exposure to EMR. However, the levels of MCT8 dropped very significantly when the rats were subjected to longer periods of exposure (150 and 180 min) with $P < 0.001$ and $P < 0.001$, respectively [Figure 1d]. Since the decrease in MCT8 levels was in conjunction with the decrease in TSH, and subsequently the decrease in T_4 levels, MP-EMR exposure has been confirmed to cause HPT axis impairment. Furthermore, elevated MDA levels upon exposure to 150-min and 180-min MP-EMR suggested the contribution of oxidative stress to the lowering effect of MCT8 levels as a manifestation of the nonthermal effects of MP-EMR exposure. As reported previously, reductions in MCT8 levels can also be influenced by the thermal and nonthermal effects of MPs.[10,11]

During oxidative stress, the level of ROS is increased that leads to cellular damage. MPs have been reported to biochemically cause oxidative damage by elevating the levels of MDA activities in rat brain upon exposure to EMR.[20] Increased serum MDA levels has been reported in animal models under hypothyroid condition and reduced MDA levels have been reported in those with hyperthyroid condition,[21] suggesting a strong association between lipid peroxidation and pathogenesis of thyroid dysfunction.

CONCLUSIONS

MP-EMR exposure at the frequency of 1800 MHz has caused significant changes in the levels of serum TSH, T_4, MDA, and MCT8 concentration in the Wistar rats. The levels of TSH, T_4, and MCT8 decreased in a direct proportion to the EMR exposure duration, whereas MDA levels increased along with the increase of exposure period (after 150-min and 180-min exposure). These suggest that MP exposure could affect thyroid either directly or indirectly via HPT axis.

Acknowledgments

We would like to thank all the staff at the Faculty of Veterinary Medicine and all the staff at the Thermal, Vibration, and Acoustic Laboratory, Universitas Syiah Kuala, for their assistance during the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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