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RESEARCH ARTICLE

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Effects of 3.5-GHz radiofrequency radiation on energy-regulatory hormone levels in the blood and adipose tissue

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Abstract

In recent years exposure of living beings to radiofrequency radiation (RFR) emitted from wireless equipment has increased. In this study, we investigated the effects of 3.5-GHz RFR on hormones that regulate energy metabolism in the body. Twenty-eight rats were divided into four groups: healthy sham ($n = 7$), healthy RFR ($n = 7$), diabetic sham ($n = 7$), and diabetic RFR ($n = 7$). Over a month, each group spent 2 h/day in a Plexiglas carousel. The rats in the experimental group were exposed to RFR, but the sham groups were not. At the end of the experiment, blood and adipose tissues were collected from euthanized rats. Total antioxidant, total oxidant, hydrogen peroxide, ghrelin, nesfatin-1, and irisin were determined. Insulin expression in pancreatic tissues was examined by immunohistochemical analysis. Whole body specific absorption rate was 37 mW/kg. For the parameters analyzed in blood and fat, the estimated effect size varied within the ranges of 0.215–0.929 and 0.503–0.839, respectively. The blood and adipose nesfatin-1 ($p = 0.002$), blood and pancreatic insulin are decreased, ($p = 0.001$), gherelin ($p = 0.020$), irisin ($p = 0.020$), and blood glucose ($p = 0.040$) are increased in healthy and diabetic rats exposed to RFR. While nesfatin-1 are negatively correlated with oxidative stress, hyperglycemia and insulin, ghrelin and irisin are positively correlated with oxidative stress and hyperglycemia. Thus, RFR may have deleterious effects on energy metabolism, particularly in the presence of diabetes.

KEYWORDS

3.5 GHz radiofrequency radiation, diabetes, energy metabolism, insulin, oxidative stress

1 | INTRODUCTION

The increasing use of wireless communication tools such as mobile phones and Wi-Fi have led to a growing concern about the effects of radiofrequency (RF) radiation on living organisms. The effects of RF radiation on living beings are divided into thermal and nonthermal effects, and researchers have generally focused on the latter due to the low-energy nature of the RF radiation used in wireless communication technologies. There are numerous studies on the effects of RF radiation on different tissues and organs, including the central nervous system, cardiovascular system, hematopoietic system, and reproductive functions. Additionally, it has been suggested that RF radiation exposure may contribute to the development of insulin resistance, hyperglycemia, and obesity (Bektas et al., 2022).

In recent years, the incidence of diabetes has increased, and oxidative stress has been found to play an important role in its development, as well as in the development of related complications such as cardiovascular diseases, neuropathies, blindness, and kidney failure (Balgetir & Kocaman, 2016; Vincent et al., 2004). It has been postulated that the disruption of the redox balance caused by exposure to RF radiation contributes to the development of these conditions by inducing oxidative stress (Dasdag & Akdag, 2016; Lai & Singh, 1996). Furthermore, some studies reported that RF radiation exposure affects metabolism, including insulin and blood glucose levels (Dasdag et al., 2008; Fahmy et al., 2015; Kleiber, 2017; Masoumi et al., 2018;

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Mortazavi, 2017; Pelletier et al., 2013; Salah et al., 2013; Sommer et al., 2004).

Despite the growing body of research on the effects of RF radiation on living organisms, the impact of RF radiation on human health remains a controversial topic in the literature (Röösli, 2013). Possible reasons for the contradictory data include differences in the frequency and intensity of RF radiation exposure, as well as differences in the duration of exposure. Additionally, the effects of chronic exposure on energy metabolism over several weeks have not been assessed.

Nesfatin-1, ghrelin, and irisin are hormones that regulate energy metabolism and have been found to be effective in disease processes such as obesity and diabetes, inflammation, cancer, as well as psychiatric and neurological diseases (Stengel & Tache, 2011; Young et al., 2019). Previous research by our team investigated the effects of 3.5 GHz RF radiation on the brain of rats and found that it caused cell damage induced by oxidative stress in brain tissue, as well as elevated levels of ghrelin and irisin, while reducing the level of nesfatin-1 compared to control groups (Bektas et al., 2022).

In this study, we aimed to examine the impact of 3.5 GHz RF radiation on ghrelin, nesfatin-1, irisin, insulin hormones, as well as total antioxidant status (TAS), total oxidant status (TOS), and H_2O_2 levels in the blood and adipose tissue of rats. The objective of this study was to investigate whether RF radiation is linked to energy metabolism disorders and diabetes.

Highlights

- 3.5 GHz radiofrequency radiation (RFR) may induce alterations in hormones regulating energy metabolism.
- 3.5 GHz RFR may lead to alterations in total antioxidant, total oxidant, and hydrogen peroxide levels.
- Particularly in conjunction with diabetes, 3.5 GHz RFR may result in adverse effects on energy metabolism.
- Although there were changes of the hormone levels in the exposed group, the actual values remained for both sham and exposed groups within the normal range.

2 | MATERIALS AND METHODS

2.1 | Animal care

This experimental study was carried out in the Experimental Research and Application Center of Van Yuzuncu Yil University. All stages of the study were designed and performed according to the guidelines of the Animal Experiments Local Ethics Committee of Van Yuzuncu Yil University (Protocol No: 2021/05-10). To minimize the risk of bias, all assessments were done in a blinded manner. The researchers performing the assessments were unaware of the group assignments and exposure status of the rats.

A total of 28 healthy male Wistar Albino rats (8–10 weeks old), weighing 200–250 g were obtained from the Experimental Animal Research Center of Van Yuzuncu Yil University. The rats were separated and placed in four stainless steel cages, seven rats per cage, and exposed to twelve-hour dark/light cycle. The rats were allowed free access to pellet feed (Purina) containing 21% crude protein and daily drinking water ad libitum in optimal environmental conditions (22 ± 2°C and 60 ± 5% humidity).

2.2 | Animals grouping and protocol

This study consists of four different experimental groups ($n = 7$ for each group). Group 1 (healthy sham group): healthy rats ($n = 7$) were kept in a plexiglass carousel for 2 h a day for 30 days while the generator turned off. Group 2 (healthy RF group): healthy rats ($n = 7$) were irradiated with RF signals in the plexiglass carousel for 2 h a day for 30 days. Group 3 (Diabetes sham group): rats with diabetes were kept in the plexiglass carousel for 2 h a day for 30 days while the generator turned off. Group 4 (Diabetes group + RF): rats with diabetes were irradiated with RF signals 2 h a day for 30 days ($n = 7$).

2.3 | Induction of experimental diabetes

Streptozotocin (STZ) is an antibiotic that produces pancreatic islet β-cell destruction and is widely used experimentally to produce a model of type 1 diabetes mellitus (T1DM) (Furman, 2015). To induce experimental diabetes, the rats were fasted overnight (groups 3 and 4) and then 45 mg/kg of STZ was administered i.p. at a single dose. Blood samples were taken from rats 72 h after STZ application for diabetes control. Blood glucose levels were measured by a glucometre (IME-DC). Blood glucose levels above 250 mg/dL were considered as diabetic (Öntürk & Özbek, 2007).

2.4 | Exposure and field measurements

In our study, we used a signal generator (3500 PM10 type Everest Comp.) that produces a 3.5 GHz band RF waveform (1/8 duty factor, pulse repetition rate of 217 Hz). The emitted power (omnidirectional on the plane perpendicular to the antenna axis) of the generator was fixed during the exposure. During the study, rats were placed in a Plexiglas carousel and exposed to RF exposure emitted from the generator. To ensure isolation from outdoor electromagnetic fields, the carousel was surrounded by electromagnetic absorber material backed by metal. The temperature within the Plexiglas carousel was maintained at a 22 ± 2°C throughout the exposure period. The electric field and power density of the RFR

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were measured using a field probe TES 593R (TES Electric Electronic Corporation). The measured electric field and power density values were 28.1 V/m and 1.6 W/m^2, respectively. Rats in the exposure groups were exposed to RFR 2 h per day, 5 days a week, for 1 month. For the sham groups, the same procedures were applied to the rats except that the generator was turned off, meaning no RF signal was present. The antenna of the generator was placed at the center of the Plexiglas Carousel to provide ideal exposure conditions, as previously described by Bektas et al. (2022).

2.5 | Specific absorption rate (SAR) analysis

Simulation setup was created to match the experimental setup as much as possible. The applicator antenna, the Faraday cage, and the rats were all modeled in 3D electromagnetic field solver using CST (CST AG). SAR value was determined as described by Bektas et al. (2022).

2.6 | Sample collection

At the end of experiment, after the cardiac blood samples were obtained under ketamine (Ketasol, Ricterphar Up) and bacillazine (Rompin) anaesthesia, all rats were sacrificed. We collected blood and fat tissues immediately after the last exposure. Blood samples were centrifuged at 4500 rpm for a period of 10 min (Heraeus Biofuge Stratos; Kendo Laboratory Products). Samples were stored at −80°C until analysis.

2.7 | Preparation of adipose tissues homogenates

At the end of treatment, the rats were sacrificed by cervical dislocation, and the adipose tissues were removed immediately for the preparation of a homogenate. Pieces of tissue were weighed, minced into small pieces and homogenized in phosphate-buffered saline (PBS; pH: 7.4; 9 mL of PBS per 1 g of tissue) with a glass homogenizer on ice. A protease inhibitor (aprotinin) was added to the PBS solution. To further disintegrate the cells, the suspension was sonicated with an ultrasonic cell disrupter (MP FastPrep-24 Tissue and Cell Homogenizer). The homogenates were then centrifuged for 15 min at 15.000*g* to obtain supernatants. Supernatants from adipose homogenates were not frozen and analyzed immediately after the study.

2.8 | Measurements of adipose and blood Nesfatin-1, Ghrelin, Irisin, TAS, TOS, H_2O_2, and insulin

Nesfatin-1 (SunRed, Catalog No: 201-11-1426; Biological Technology Co., Ltd.) (sensitivity: 28.951 ng/L assay range: 30–9000 ng/L), Ghrelin (Cat Number: 201-11-1650; Sun Red Bio Biotech Co., Ltd.) (sensitivity: 38.572 pg/mL, assay range: 40–10,000 pg/ml), Irisin (Cat Number: 201-11-1713; Sun Red Bio Biotech Co., Ltd.) (sensitivity: 0.247 ng/mL, assay range: 0.3–90 ng/mL), TAS (Cat Number: 201-11-2672; Sun Red Bio Biotech Co., Ltd.) (sensitivity: 0.175 U/mL, assay range: 0.2–60 U/mL), TOS (Cat Number: 201-11-1669; Sun Red Bio Biotech Co., Ltd.) (sensitivity: 0.073 nmol/mL, assay range: 0.1–20 nmol/mL), and H_2O_2 (Cat Number: 201-11-3366; Sun Red Bio Biotech Co., Ltd.) (sensitivity: 9.005 ng/mL, assay range: 10–3000 ng/mL) levels were determined in both adipose homogenate and serum by enzyme linked immunosorbent assay (ELISA) procedure according to the manufacturer's instructions. Moreover, the serum insulin level was measured by using an ELISA kit (Cat Number: 201-11-0708; Sun Red Bio Biotech Co., Ltd.) according to the manufacturer's protocol.

2.9 | Immunohistochemical staining

Parts of the pancreatic tissue were fixed in 10% buffered formaldehyde, and the samples were embedded in paraffin following routine histological processing steps. Sections of 4 μm in thickness were taken from paraffin blocks with a microtome and placed on lysine slides. Sections were deparaffinized and rehydrated, and then incubated in 3% H_2O_2 for 10 min to prevent endogenous peroxidase enzyme activity. To prevent antigen masking in the nucleus, they were heated in antigen retrieval solution (citrate buffer, pH 6.1) in a microwave oven twice. Then, to prevent nonspecific binding, the protein block was dropped and incubated for 10 min. Insulin antibody (sc−8033, dilution: 1/100; Santa Cruz Biotechnology) was used as the primary antibody. After adding the antibody, these samples were incubated in a humidity chamber at 4°C for one night. After rinsing with PBS, biotinylated goat antipolyvalent and streptavidin-peroxidase conjugate were dropped and incubated for 10 min, respectively. After the application of diaminobenzidine (DAB), used as a chromogen, samples were stained with Mayer's hematoxylin and examined under a light microscope (Olympus BX53; Olympus) (Altındağ et al., 2021). Immunohistochemical findings were assessed as negative (−), slightly positive (+), moderately positive (++), and intensely positive (+++) according to the immunostaining characteristics of the cells.

2.10 | Statistical analysis

Sample size calculation: According to previous study (Yavaş et al., 2021), it was observed that standard deviation for TOS value ranged from 1.81 to 2.59. Thus, in this study, standard deviation was considered as 0.11 for BIS value. In addition, for the 0.05 type I error rate, Z value and effect size were assumed to be 1.96 and 1.6 respectively. Based on this information and according to the equation of sample size calculation ($n = Z^2\sigma^2/d^2$), the minimum sample size was found 7. The SPSS statistical software program was used in the analyses. Whether the data of each group originated from the same distribution

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was tested by rank-based Kruskal–Wallis tests. For comparisons of groups, the Mann–Whitney test was used to determine if there was a statistically significant difference between them. The results were presented as medians and $p < 0.05$ was taken to be statistically significant. In addition, η^2 was presented as estimated effect size for the studied variables. In tables, the groups were labeled with letters to indicate differences such that if a group has a different letter than others a statistically significant difference exists.

3 | RESULTS

3.1 | Results of SAR

SAR distribution was calculated using the IEEE/IEC 62704-1 method. The whole-body SAR was determined to be 37 mW/kg. The 10 g (and 1 g) averaged SAR values have been linked to the predominant tissues within the exposed volume. Specifically, the maximum SAR at blood and blood vessels was measured at 162 mW/kg and 178 mW/kg for 1 and 10 g averaging, respectively, while the maximum SAR at fat tissue reached values of 220 mw/kg and 184 mW/kg for 1 and 10 g averaging, respectively. The SAR distribution averaged over 1 g is displayed in Figure 1.

3.2 | Results of fasting blood glucoses

Exposure to RFR increased blood glucose in healthy rats ($p = 0.04$). In diabetic rats, blood glucose tended to increase after RFR exposure, but it was not statistically significant (Table 1).

3.3 | Results of ELISA

While the estimated effect size for the parameters studied in the blood varies between 0.215 and 0.929, for those studied in fat, it ranges between 0.503 and 0.839. The estimated effect size for blood glucose values ranged between 0.625 and 0.034.

In the blood, the ghrelin of the group 4 was quite higher those of other groups ($p = 0.020$). In adipose tissue, the ghrelin of the group 2 was higher than that of the group 1, and that of the group 4 was higher those of other groups ($p = 0.002$). In the blood, nesfatin of the group 1 was considerably higher than those of other groups ($p = 0.002$). In the adipose tissue, nesfatin of the group 3 was lower than those of groups 1 and 2, that of the group 4 was lower than those of other groups ($p = 0.001$). In the blood the irisin of group 2, 3, and 4 was higher than that of group 1, and that of group 4 was higher than those of the group 2 and 3 ($p = 0.020$). In the adipose tissue, the irisin level of group 4 was higher than those of the other groups ($p = 0.010$). In the blood and adipose tissue, TAS of group 2 was lower than that of group 1, and TAS level of group 4 was lower than those of group 1 and 2 ($p = 0.006$, $p = 0.009$). In the blood and adipose tissue, TOS ($p = 0.004$, $p = 0.008$) and H_2O_2 ($p = 0.004$, $p = 0.004$) of the group 4 were considerably higher than that of group 1. In blood, insülin of group 2 was lower than that of group 1, that of group 4 was lower than those of other groups ($p = 0.001$) (Table 2).

3.4 | Immunohistochemical staining results

In pancreatic islets of langerhans of rats, intense insulin expression in the group 1, moderate insulin expression in the group 2, low insulin expression in the group 3 and the lowest insulin expression in group 4 were found (Figure 2).

TABLE 1 Fasting blood glucose of the experimental groups.

Groups	Blood glucose (mg/dL)	η^2	p
Healthy Sham (initial)	101.5 ± 12.0	0.521	0.037
Healthy Sham (final)	93.5 ± 9.7		
RFR (initial)	101.0 ± 10.7	0.625	0.040
RFR (final)	129.5 ± 9.1		
Diabetic Sham (initial)	366.0 ± 25.4	0.034	0.873
Diabetic Sham (final)	368.0 ± 26.7		
Diabetic RFR (initial)	325.0 ± 19.9	0.303	0.088
Diabetic RFR (final)	361.0 ± 5.3		

Note: Normal fasting blood glucose levels in healthy rats typically range from 70 to 150 mg/dL.

Abbreviations: ±, the deviation values after plus-minus represent sample standard deviation; RFR, radiofrequency radiation.

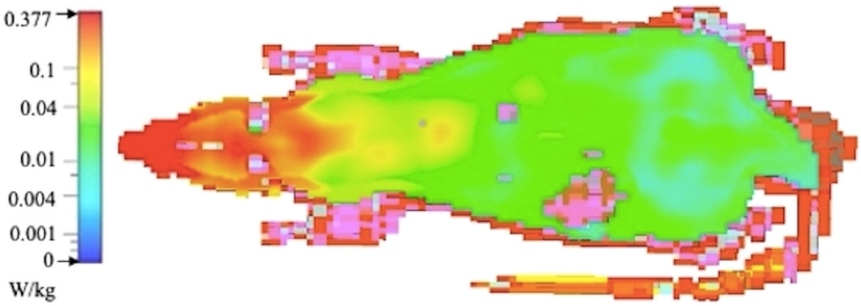


FIGURE 1 Specific absorption rate simulation results at 3500 MHz for 1 g average frontal plane.

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TABLE 2 Adipose tissue and blood levels of ghrelin, nesfatin-1, irisin, TAS, TOS, H_2O_2, and insulin.

		Healthy Sham Group 1 (*n*:7)	Healthy RFR Group 2 (*n*:7)	Diabetic Sham Group 3 (*n*:7)	Diabetic RFR Group 4 (*n*:7)	η^2	*p*
Ghrelin pg/mL	Blood	1133.5 ± 157.1^{b}	1350.8 ± 246.9^{ab}	2192.9 ± 156.1^{a}	3095.0 ± 175.1^{a}	0.215	0.020
	Adipose	2625.3 ± 23.8^{c}	3842.7 ± 219.7^{b}	3853.2 ± 196.2^{ab}	4584.3 ± 251.6^{a}	0.731	0.002
Nesfatin ng/L	Blood	1483.4 ± 138.7^{a}	482.7 ± 119.9^{b}	471.1 ± 61.77^{b}	313.4 ± 168.3^{b}	0.929	0.002
	Adipose	1525.9 ± 198.7^{a}	1330.2 ± 130.7^{a}	895.8 ± 176.9^{b}	574.2 ± 132.4^{c}	0.839	0.001
Irisin ng/mL	Blood	0.1 ± 0.001^{c}	2.5 ± 1.57^{b}	4.3 ± 3.4^{ab}	4.8 ± 2.9^{a}	0.287	0.020
	Adipose	15.3 ± 0.6^{b}	16.7 ± 1.9^{b}	16.9 ± 3.2^{b}	19.3 ± 3.1^{a}	0.503	0.010
TAS U/mL	Blood	14.3 ± 15.2^{a}	3.3 ± 0.4^{ab}	3.4 ± 0.1^{ab}	2.8 ± 0.1^{b}	0.287	0.006
	Adipose	18.1 ± 2.4^{a}	10.7 ± 2.1^{b}	10.0 ± 0.8^{bc}	7.9 ± 0.3^{c}	0.729	0.009
TOS nmol/mL	Blood	0.4 ± 0.04^{c}	0.6 ± 0.1^{bc}	0.7 ± 0.09^{b}	0.9 ± 0.2^{ab}	0.320	0.004
	Adipose	2.0 ± 1.0^{b}	3.8 ± 0.3^{a}	4.5 ± 1.2^{a}	7.0 ± 2.9^{a}	0.539	0.008
H_2O_2 ng/mL	Blood	106.7 ± 85.9^{b}	178.4 ± 34.4^{b}	198.9 ± 29.1^{b}	275.4 ± 31.6^{a}	0.581	0.004
	Adipose	728.6 ± 102.6^{b}	647.4 ± 112.4^{b}	760.3 ± 77.6^{b}	1305.0 ± 62.2^{a}	0.810	0.004
Insulin IU/L	Blood	5.9 ± 1.1^{a}	1.7 ± 0.8^{b}	1.7 ± 1.0^{b}	0.7 ± 0.3^{c}	0.921	0.001

Note: $^{a,b,c}\rightarrow$: Different superscripts small letters in the same row indicate statistically significant differences between the groups' means ($p < 0.05$).
Abbreviation: ±, The deviation values after plus-minus represent sample standard deviation; TAS, total antioxidant status; TOS, total oxidant status.

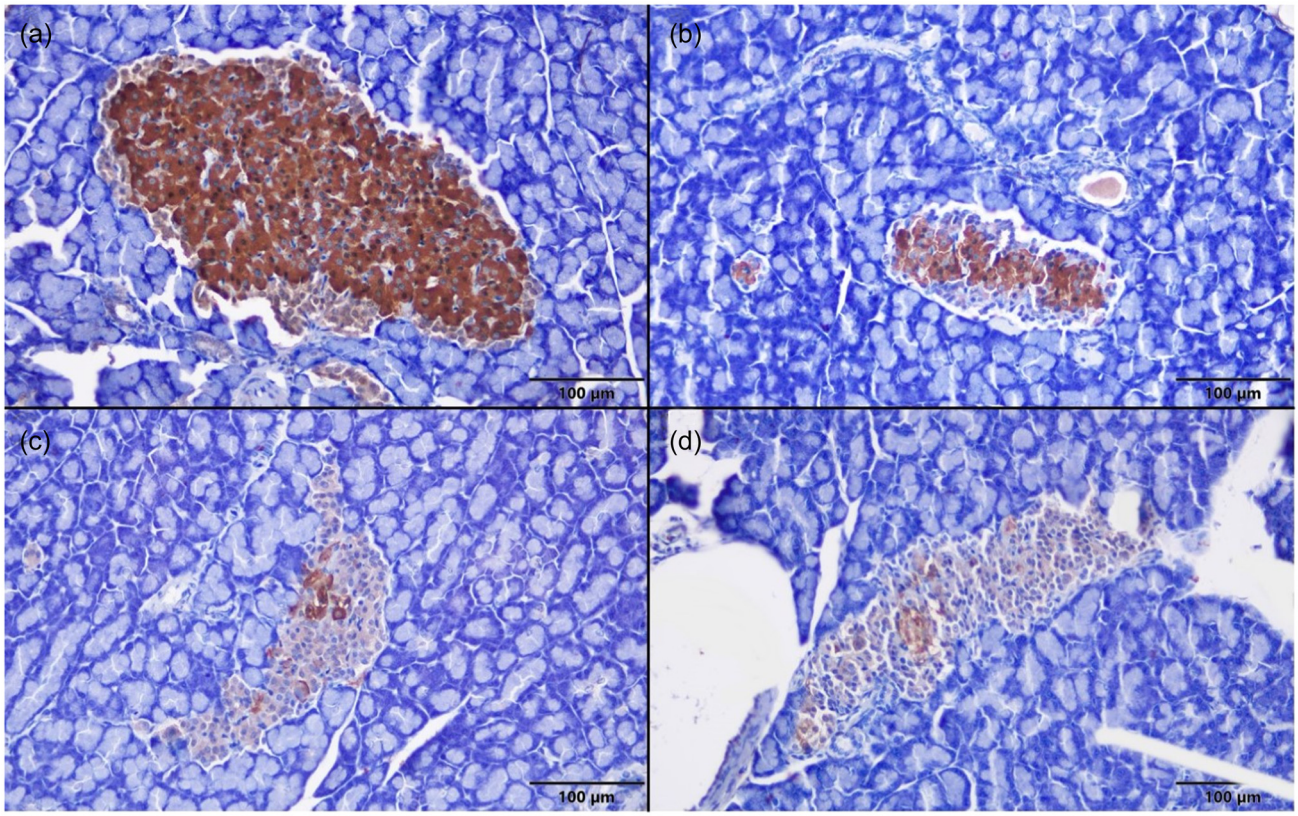


FIGURE 2 Immunohistochemical results for anti-insulin antibody in the pancreatic tissues of the experimental groups. (a) Healthy sham (Group 1), (b) Healthy RFR (Group 2), (c) Diabetic sham (Group 3), (d) Diabetic RFR (Group 4).

4 | DISCUSSION

This is a hypothesis generating study and therefore the study was planned based on the hypothesis that RFR cause oxidative stress by disrupting the redox balance, thus affecting energy metabolism of living things. In this study, the effects of 3.5 GHz RFR on blood glucose and insulin levels, ghrelin, nesfatin-1, irisin, and oxidative stress parameters (TAS, TOS, and H_2O_2) in blood and adipose tissue in healthy and diabetic rats were investigated.

In this study, it was observed that RFR increased blood glucose in healthy rats, but it did not make a difference in rats with diabetes. While the observed

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differences in glucose levels between the sham and RF-exposed groups were within the normal range, it should be noted that even small changes in glucose levels could have significant long-term effects on metabolism and increase the risk of metabolic disorders such as diabetes. Similarly, in another study, it was found that electromagnetic fields (pulsed magnetic fields, 15 Hz, burst width, 5 ms; burst wait, 60 ms; pulse width, 0.2 ms; pulse wait, 0.02 ms; pulse rise and fall time: 0.3, 2.0 μs and 0.0016 T) did not alter hyperglycemia in diabetic rats (Li et al., 2016). However, contrary to the these findings, several studies have shown that pulsed electromagnetic field are effective in antihyperglycemia in diabetic rats (Jing et al., 2011; Mert et al., 2010). Moreover, it was determined that Wistar Albino rats exposed to RFR emitted from mobile phones (1800 MHz, GSM, 15 min/day for 3 months) had higher fasting blood glucose compared to the control group (Meo & Al Rubeaan, 2013). In addition, it was stated that exposure to electromagnetic pollution cause higher blood glucose levels and may contribute to diabetes mellitus (Havas, 2008). The different effects of electromagnetic fields (EMFs) on hyperglycemia in studies may be due to the different characteristics of the applied EMF and the application of different standards in the diabetic model used.

In this study, 3.5 GHz RFR lowered blood insulin levels in both healthy and diabetic rats. Immunohistochemical analysis of pancreatic tissues also revealed reduced insulin expression in both groups. Similarly, Masoumi et al. (2018) reported that RFR exposure (2.45 GHz, 4 h/day for 45 days) led to hyperglycemia, reduced insulin secretion, and induced oxidative stress in the pancreas (Masoumi et al., 2018). In another study by Sakurai et al. (2004), insulin secretion from islet cells exposed to low-frequency magnetic fields was approximately 30% lower compared to the sham exposure group (Sakurai et al., 2004). Khaki et al. (2015) reported a decrease in plasma insulin levels in the EMF-exposed group (50 Hz, 3 mT, 4 h/day for 6 weeks) (Khaki et al., 2015). Jolley et al. (1983) observed reduced insulin release from islets of Langerhans in rabbits exposed to low-frequency pulsed magnetic fields during glucose stimulation (Jolley et al., 1983). Li et al. (2005) found that exposing hepatocytes to 50 Hz pulsed EMF in vitro led to a conformational change in the insulin molecule, resulting in decreased binding capacity to its receptors (Li et al., 2005). Mortazavi et al. (2016), however, noted that radiofrequency radiations emitted from mobile phones did not alter plasma insulin levels but caused mild damage to pancreatic islet cells (Mortazavi et al., 2016). Additionally, Kleiber (2017) suggested that RFR may induce conformational changes in insulin receptors or glucose transport receptors (Kleiber, 2017). These conflicting findings may be attributed to variations in intensity, frequency of exposure, duration, and proximity to the exposure source, which vary among individuals (Çiğ & Nazıroğlu, 2015).

In this study, 3.5 GHz RFR reduced TAS levels in both healthy and diabetic rats' blood and adipose tissues. It elevated TOS levels in healthy rats' adipose tissue and in both blood and adipose tissue of diabetic rats. H_2O_2 levels also rose in both blood and adipose tissue of diabetic rats after RFR exposure. These results indicate that 3.5 GHz RFR induces oxidative stress in blood and adipose tissue, aligning with findings in previous studies (Bektas et al., 2020; Senturk et al., 2019; Tumkaya et al., 2019; Yakymenko et al., 2016).

The results of this study showed that diabetes and RF increased ghrelin levels in both blood and adipose tissue. Recent research has highlighted ghrelin's anti-inflammatory properties, inhibiting cytokine expression and reducing oxidative stress in various organs (Akki et al., 2021). Ghrelin has also been identified as a natural antioxidant and free radical scavenger (Dong & Kaunitz, 2006). Previous research has also reported increased ghrelin levels in rats exposed to RFR (2 h/day × 8 weeks, 1760 MHz, 0.3988 mW/cm^2, GSM, SAR 0.181 W/kg) (Tripathi et al., 2021). Numerous studies since 2000 have emphasized ghrelin's pivotal role in regulating pancreatic β-cell function and glucose homeostasis (Abdalla, 2015). It is worth noting that ghrelin is believed to have a suppressive effect on insulin levels, with high ghrelin levels leading to hyperglycemia and reduced insulin levels (Abdalla, 2015). This study's findings of decreased blood insulin levels, reduced insulin expression in the pancreas, and increased ghrelin levels in blood and adipose tissue align with existing literature (Broglio et al., 2001; Saad et al., 2002; Shiiya et al., 2002).

This study revealed that 3.5 GHz RFR led to a reduction in nesfatin-1 levels in the blood and adipose tissue of healthy rats. Diabetes alone lowered nesfatin-1 levels in adipose tissue. Additionally, in diabetic rats, exposure to 3.5 GHz RFR further decreased nesfatin-1 levels in adipose tissue. The study aligns with previous research, revealing an inverse relationship between nesfatin-1 levels in both blood and adipose tissue with TOS, H_2O_2, and blood glucose, whereas a positive correlation was noted with TAS and blood insulin in rats (Hussien et al., 2020).

In this study, exposure to RFR led to a significant increase in irisin levels in the blood of both healthy and diabetic rats, as well as in the adipose tissue of diabetic rats. Elevated circulating irisin levels are known to be a compensatory response to metabolic disorders like low insulin levels and insulin resistance (Jia et al., 2019). The observed rise in irisin levels in this study may be attributed to hyperglycemia induced by diabetes and RFR, along with reduced insulin levels. In these results of this study, also, an increase in the amount of irisin was observed in accordance with the increase in the amount of free radicals in the blood and adipose tissues of healthy and diabetic rats exposed to RFR. Potential relationships between irisin concentration and oxidative stress and metabolic dysregulations were also reported (Huh & Mantzoros, 2015).

The results of this study showed that the data obtained in both control and experimental groups were within normal ranges. However, the difference observed between the control group and the experimental groups was found to be statistically significant. Although the results obtained from the control and

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experimental groups are within the normal range, it is also a fact that the difference observed between the groups is a point that should be taken into consideration in terms of health. Therefore, the results of this study reveal that new and comprehensive studies are needed to investigate the issue in more detail from the human perspective. It should not be forgotten that in studies planned to be conducted in the future, parameters at the upper and lower limits of normal values may go out of normal due to the effect of RFR, and if this situation lasts for a long time, it may pave the way for different health problems. Therefore, there is a requirement for broader-scale investigations on normal, prediabetic, and diabetic individuals to gain a deeper understanding of RFR's role in our daily lives.

5 | CONCLUSION

In light of our results we concluded that the blood and adipose nesfatin-1 and blood insulin levels are decreased, the blood and adipose gherelin, irisin levels and blood glucose levels are increased in healthy and diabetic rats exposed to 3.5 GHz RFR of cell phone radiation. Blood and adipose nesfatin-1 levels are negatively correlated with oxidative stress, hyperglycemia and insulin levels. Blood and adipose ghrelin and irisin levels are positively correlated with oxidative stress and hyperglycemia levels.

RFR causes more pancreas dysfunction associated with marked reduction of nesfatin-1, increase of ghrelin and irisin blood and adipose tissue levels and a prominent increase in oxidative stress. Also, we recommend further studies on the effect of exogenous nesfatin-1, ghrelin and irisin on the pancreas function of rats exposed to RFR.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data underlying the results are available as part of the article and no additional source data are required.

ETHICS STATEMENT

This experimental study was carried out in the Experimental Research and Application Center of Van Yuzuncu Yil University. All stages of the study were designed and performed according to the guidelines of the Animal Experiments Local Ethics Committee of Van Yuzuncu Yil University (Protocol No: 2021/05-10). Therefore, I declare that there are no ethical problems in the study titled "Effects of 3.5-GHz Radiofrequency Radiation on Energy-Regulatory Hormone Levels in the Blood and Adipose Tissue."

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