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Effects of electromagnetic radiation from 3G mobile phone on heart rate, blood pressure and ECG parameters in rats

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Abstract

Effects of electromagnetic energy radiated from mobile phones (MPs) on heart is one of the research interests. The current study was designed to investigate the effects of electromagnetic radiation (EMR) from third-generation (3G) MP on the heart rate (HR), blood pressure (BP) and ECG parameters and also to investigate whether exogenous melatonin can exert any protective effect on these parameters. In this study 36 rats were randomized and evenly categorized into 4 groups: group 1 (3G-EMR exposed); group 2 (3G-EMR exposed + melatonin); group 3 (control) and group 4 (control + melatonin). The rats in groups 1 and 2 were exposed to 3G-specific MP's EMR for 20 days (40 min/day; 20 min active (speech position) and 20 min passive (listening position)). Group 2 was also administered with melatonin for 20 days (5 mg/kg daily during the experimental period). ECG signals were recorded from cannulated carotid artery both before and after the experiment, and BP and HR were calculated on 1st, 3rd and 5th min of recordings. ECG signals were processed and statistically evaluated. In our experience, the obtained results did not show significant differences in the BP, HR and ECG parameters among the groups both before and after the experiment. Melatonin, also, did not exhibit any additional effects, neither beneficial nor hazardous, on the heart hemodynamics of rats. Therefore, the strategy (noncontact) of using a 3G MP could be the reason for ineffectiveness; and use of 3G MP, in this perspective, seems to be safer compared to the ones used in close contact with the head. However, further study is needed for standardization of such an assumption.

Keywords

3G mobile phone, blood pressure, ECG signals, heart rate, melatonin, rat

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Introduction

Mobile phones (MPs) are now substituting the land-line phones and becoming ubiquitous in our lives. The increase in the use of MPs raises the concern about health-related risks that influence the quality of life (Patrick et al., 2008). Today, the third-generation (3G)-specific MPs are taking place in the world's largest mobile telecommunication systems. No doubt, 3G MP applications, such as video-based calling, messaging, conferencing and so on, emit more continuous electromagnetic radiation (EMR) to the environment (Smith and Collins, 2000).

Survey studies show that EMR emitted by MPs may cause a series of diseases such as headache, extreme irritation, increase in carelessness and forgetfulness, decrease in reflexes, sound in the ears, inner ear damage, blurring of vision, inflammation in the eyes, endometrial apoptosis (Oral et al., 2006), retinal oxidative stress, brain tumor and cancer. Also, it has been shown that occupational exposition to EMR could somewhat cause fluctuations in heart rate (HR) (Ahamed et al., 2008; Koyu et al., 2005; Myung et al., 2009; Ozguner et al., 2006; Panda et al., 2010). The emitted EMR by MP may influence the autonomic nerve tone and thus modify the function of circulatory system (Andrzejak et al., 2008). So far, a few studies assessed the influence of EMR on cardiovascular functions including HR, blood pressure (BP) and ECG analyses, however, the obtained results are controversial both in human (Atlasz et al., 2006; Barker et al., 2007; Szmigielski et al., 1998; Tahvanainen et al., 2004; Tamer et al., 2009; Vangelova et al., 2006) and in animals (Ciejka and Goraca, 2009; Dasenbrock, 2005).

Within the last decade, *in vivo* animal studies have shown that oxidative stress develops in response to MP-induced EMR, which might disturb antioxidant protection system by increasing the production of reactive oxygen species (ROS) or by decreasing the antioxidant enzyme activities (Balci et al., 2007; Meral et al., 2007). Studies have also demonstrated that antioxidants such as melatonin (Oktem et al., 2005), caffeic acid phenyl ester (Ozguner et al., 2005a), vitamin C and vitamin E (Guney et al., 2007) can prevent oxidative stress or apoptosis caused by MP-induced EMR in animal tissues. Also, it has been hypothesized that extremely low-frequency (40–50 Hz) EMR could suppress melatonin production from pineal gland (Hata et al., 2005). Based on this relationship, Ozguner et al. (2006) showed that melatonin can protect retinal oxidative stress and skin changes relative to the use of MP.

The pineal secretory product, melatonin, was shown to have free radical scavenging ability. Also, melatonin activates several antioxidative enzymes and reduces lipid peroxidation (Reiter et al., 1995, 2009).

As we have searched the literature, we did not come across a study establishing a correlation between the cardiovascular effects and the EMR emitted by 3G-specific MPs. From this standpoint, the current study was designed to investigate (a) whether the EMR from 3G-specific MP can cause acute changes in the HR, BP and ECG parameters; (b) whether exogenous melatonin can exert any effect on these parameters.

Materials and methods

Animals and groups

A total of 36 male Wistar rats weighing 200–300 g produced at Experimental Animal Research Center of Inonu University were placed in a quiet controlled room where the temperature (21 $\pm$ 2°C), humidity (60 $\pm$ 5%) and light–dark cycle (12–12 h) were maintained. All the rats were housed into polypropylene cages on wood chip bedding and allowed free access to pelleted diet and drinking water. The animals were maintained and used in accordance with the Animal Welfare Act and the Guide for the Care and Use of Laboratory animals founded by the Inonu University, Animal Ethical Committee, Malatya, Turkey.

The rats were randomly set into 4 groups, each with 9 rats: group 1 (3G-EMR exposed); group 2 (3G-EMR exposed + melatonin); group 3 (control) and group 4 (control + melatonin). Randomization procedure used in this study was the simple randomization. Vehicle or melatonin (5 mg/kg) was administered intraperitoneally (i.p.) daily and continued for 20 days (during the experimentation period). Melatonin (Sigma, St Louis, MO, USA) was dissolved in ethanol and further diluted in saline to give a final concentration of 1%. All pharmacologic agents were given in equal volumes (0.5 ml). Also, in all groups, melatonin and saline (vehicle) including 1% ethanol were administered between 17:00 and 18:00 h. According to our previous studies, i.p. route was chosen for vehicle and melatonin administration, because of the ease of application and the reproducibility of dosing (Parlakpinar et al., 2002).

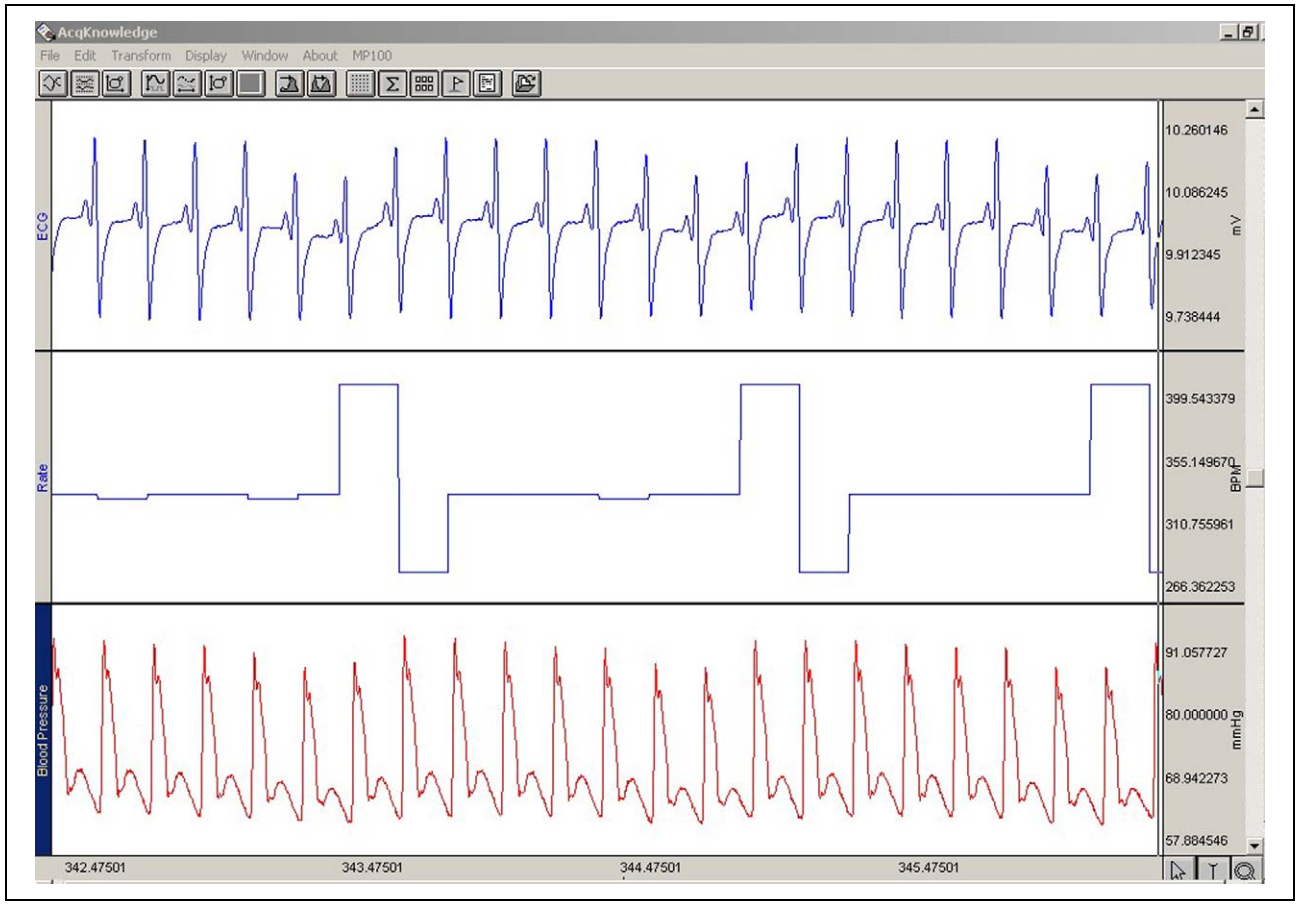

Figure 1. Example of measured ECG, heart rate and blood pressure signals through BIOPAC MP-100 A-CE data acquisition system.

Blood pressure, heart rate and electrocardiographic analyses

The rats were weighted and then anesthetized with ketamine hydrochloride (75 mg/kg) and xylazine (8 mg/kg), which were administered i.p. All rats were marked with permanent pen for their identification in pre- and postexperimental studies. Systemic BP and HR from the cannulated carotid artery were monitored and recorded by a BIOPAC MP-100 A-CE data acquisition system (Goleta, CA, USA). Also, the ECG signal activity was recorded for at least 5 min, with a sampling frequency of 500 Hz under anesthesia using disposable electrodes attached to the thorax of the rat (Figure 1). These parameters were recorded on the first (preexperimental data) and on the final (22nd day) day of the experiment (postexperimental data) while the 3G MP is turned off (Figure 2). After the parameters were successfully recorded in all the 36 rats, they were weighed and then killed under an overdose of anesthesia, for further studies. Next, the ECG traces were visually analyzed by two clinician experts for assessing HR, ventricular ectopic beats (VEBs), ventricular tachycardia (VT), ventricular fibrillation (VF), ST depression, QRS enlargement and major ECG anomalies such as atrioventricular (AV) blocks or branch blocks. The hemodynamic parameters were calculated during the 1st, 3rd and 5th min of recording. Afterward, changes in the ECG signal, P and QRS durations and R–R periods, for assessing HR variability, were analyzed through a specific program that was developed by our group using Matlab (R6; The MathWorks, Natick, MA, USA).

3G-EMR exposure experiment

Before the start of the experiment, two fluent graduate students (a girl and a boy) separately read the same chapter from a textbook (Katzung et al., 2009) and their speech was recorded into digital recorders (Premier, PDR-6015) for 20 min in a silent room. To demonstrate an interactive conversation, these records (male and female voices) were alternately used as the speech of orator group that linked to the microphone

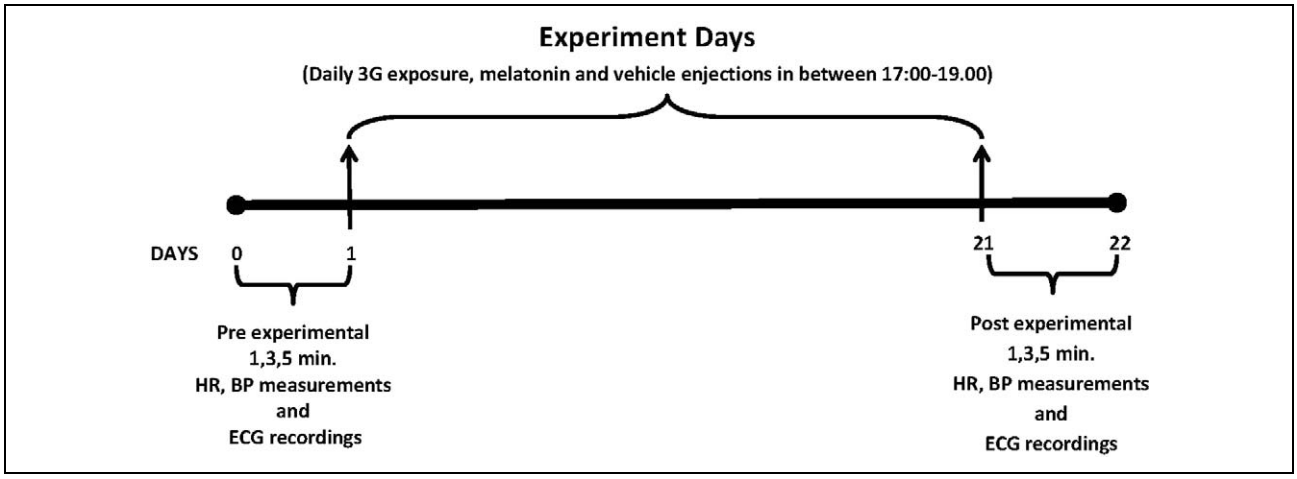

Figure 2. Flow chart of the experimental days.

on 3G MP, while MP in the video streaming mode, transmitting rat's profile to another 3G-EMR exposed group, as listener. Afterward, the roles of the groups (listener and speaker) were reversed and the same procedure was conducted for another 20 min. This procedure was repeated everyday from the 2nd to the 21st day (between 17:00 and 19:00 h daily) of experiment. The employed 3G MP was a Nokia N-70 MP (900, 1800 and 1900 MHz with general packet radio service (GPRS) and enhanced GPRS (EGPRS) (EDGE) data rate capabilities, Nokia Corporation, Helsinki, Finland), and the commercial mobile communication operating system was operating approximately at 2 MB/sec data rate in 1.9–2.2 GHz frequency band. During the course of the experiment, the 3G-EMR exposure groups (groups 1 and 2) were kept in specifically designed plastic cages (length: 40 cm, width: 30 cm, height: 15 cm and without wood chip bedding) and the MPs for both orator and listener were placed in contact with the transparent underside of the cages. The rats were placed in close contact above the cell phone and the cage ventilated to decrease the stress of the rats while in the cage box. The orator's and listener's cages were placed at 10 m distant from each other. MPs were manually turned on for activating (40 min) incessant conservation and turned off (standby mode) for the rest of the day (23 h and 20 min) while their batteries were charged continuously. The digital recorders were kept away from the MPs to eliminate the possible effects of the recorder on the experiment. In the nonexposure groups (group 3 and group 4), the MP was kept in a standby mode and the batteries of MPs were charged continuously. The experiment was performed on the 3G-EMR exposure and nonexposure group pairs at the same time in separate similarly conditioned rooms as shown in Figure 3.

In order to reduce the possible environmental effects on the rat's emotional state, the ambient temperature was controlled to provide comfort to all rats during the experimental sessions. Also, to reduce the effects of other electromagnetic sources, MPs and electronic instruments were turned off and computers were removed from the exposure zone of the experimental room. MP was set in silent mode (not vibrate or illuminate) during the experiment. For achieving the same experimental protocol conditions in all groups, it was made sure that the equipments and tools used in the experiment did not include metal or iron which could affect the electromagnetic conduction, and the fluorescent lights were turned off during the experiment.

Unfortunately due to the shortage of microwave-measuring instrument, it was not possible to measure the intensity of microwave emitted by the MP. Since we did not come across any reported experimental study in the literature concerning the duration of EMR exposure from 3G MP, the available data concerning the classical MP exposure duration schemes, 15 min–1.5 h for 4 days–4 weeks, were taken as reference (Gul et al., 2009; Irmak et al., 2002; Koyu et al., 2005; Mailankot et al., 2009; Meral et al., 2007; Ozguner et al., 2005b; Tahvanainen et al., 2004). Therefore in the current study, the EMR exposure time was chosen as 40 min a day (20 min oral and 20 min aural).

Statistical analysis

For detecting even minor effects, the required sample sizes used in this experiment were identified using the statistical power analysis. The sample sizes of nine

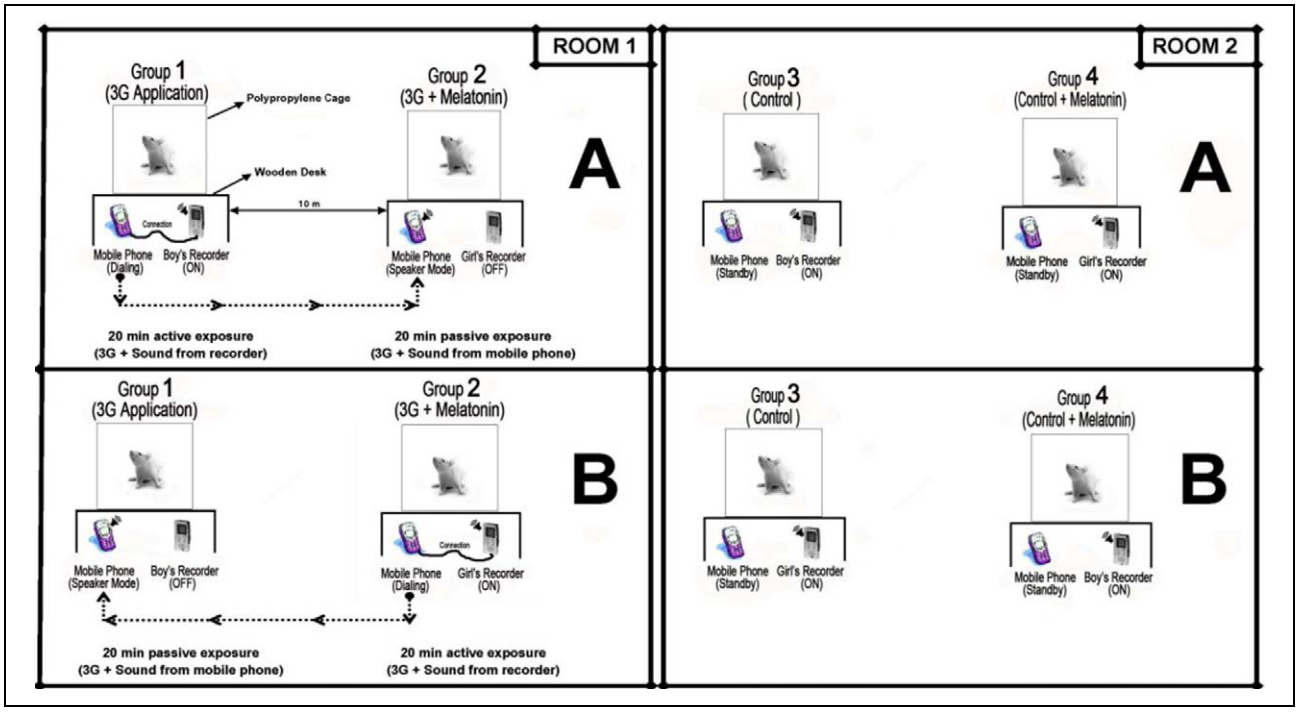

Figure 3. Experimental design is defined for both exposure group (groups 1 and 2) and control group (groups 3 and 4). The exposure group is in room 1, and A indicates the first 20-min period of daily 3G exposure procedure. B indicates the second 20-min period just after A. To further proceed B, the call direction was shifted. Control group is in room 2 and A indicates the first 20-min period of daily sound exposure procedure. B indicates the second 20-min period just after A. To further proceed B, the recorders were shifted.

rats in each group necessary for a power of 0.80 were estimated using the Number Cruncher Statistical System (NCSS) software. The normality of the distribution was confirmed through the Kolmogorov-Smirnov Z test. According to the results obtained from the normality test, one-way analysis of variance (ANOVA), Kruskal-Wallis H test and repeated measures ANOVA were used for the statistical analysis as appropriate. Multiple comparisons or pair wise comparisons were carried out by the tests of Tukey, Bonferroni, paired samples t or Wilcoxon signed rank. Data were analyzed using SPSS software program, version 16.0, for Windows (SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant. The obtained data were expressed in terms of mean $\pm$ SD or median (interquartile range) as appropriate.

Results

A simple randomization method was used for allocating nine rats to four groups equally at the beginning of the experiment. Unfortunately, during the surgical procedure 2 rats from group 3 (control) and 1 rat from group 4 (control + melatonin) died due to bleeding. Therefore, the current study was completed with 33 rats.

Body weights

There was no significant difference detected in the mean body weights (g) of the groups before (251 ± 21, 233 ± 14, 235 ± 23 and 243 ± 27) and after (252 ± 28, 236 ± 17, 246 ± 34 and 243 ± 35) the experiment.

Hemodynamics

Table 1 indicates the mean arterial BP (mm Hg) and HR (beats/min) values which were measured at 1st, 3rd and 5th min of recording time for both before (baseline or preexperiment) and end of the experiment. Based on these three temporal points, significant differences among the groups in the BP and HR values were not detected for baseline records. At the end of the experiment, BP values were not different among the groups. However, HR values in group 1 (278.8 ± 30) and group 2 (281.7 ± 18) were significantly lower than in group 4 (333.9 ± 55.1) at the 5th min. As the BP and HR values measured before and after experiment were compared, no significant differences were observed for BP values except in group 4. In this group, the postexperiment

Table 1. Blood pressure (BP) and heart rate (HR) variables with respect to groups[a]

	Variable	Time (min)	Groups				p
			3G	3G + Mel	Control	Control + Mel	
Before	*n*		9	9	7	8	
	BP	1	131 (28.50)	141 (39)	123.50 (17.75)	140.50 (12.50)[b]	0.18[c]
		3	118.0 ± 23.8	122.9 ± 21.8	115.9 ± 15.9	131.6 ± 5.8[d]	0.36[e]
		5	112.4 ± 23	115.3 ± 15.8	110.1 ± 16.6	123.3 ± 5.3[f]	0.44[e]
	HR	1	289.2 ± 65	282.3 ± 41.3	299.0 ± 45.3	273.3 ± 86.3	0.87[e]
		3	275 (62.50)	309 (48.50)	291 (138)	300 (97.25)	0.62[c]
		5	289.9 ± 42.3	302.7 ± 34.1	317.9 ± 48.6	339.1 ± 58.2	0.17[e]
After	*n*		9	9	7	8	
	BP	1	117.6 ± 15.1	118.1 ± 15.2	113.2 ± 15.1	124.0 ± 16.1	0.11[e]
		3	109.4 ± 18.2	109.2 ± 15.8	98.0 ± 9.9	116.1 ± 14.8	0.20[e]
		5	108.1 ± 13.5	100.0 ± 15.7	96.2 ± 9.0	109.5 ± 16.2	0.23[e]
	HR	1	275 (53)	278 (29)	269 (45.50)	283.50 (56.25)	0.89[c]
		3	272.9 ± 28.0	289.3 ± 38.2	284.8 ± 19.2	278.6 ± 82.4	0.90[c]
		5	278.8 ± 30.0[g]	281.7 ± 18.0[g]	289.3 ± 16.0	333.9 ± 55.1	0.009[e]

Mel: melatonin, 3G: third generation.
[a]Data are expressed as mean ± SD or median (interquartile range).
[b]Versus time 1 (paired samples *t* test or Wilcoxon signed rank test, $p < 0.05$).
[c]Kruskal-Wallis *H* test.
[d]Versus time 2 (paired samples *t* test or Wilcoxon signed rank test, $p < 0.05$).
[e]One-way ANOVA.
[f]Versus time 3 (paired samples *t* test or Wilcoxon signed rank test, $p < 0.05$).
[g]Versus control + Mel (Tukey test, $p < 0.05$).

BP values at all the three measuring points (124, 116.1, 109.5; time 1, 3, 5, respectively) were decreased (140.50, 131.6, 123.3; time 1, 3, 5, respectively) when compared to the preexperiment BP values.

ECG analysis

The ECG analysis was performed in two cooperating ways: (a) visual evaluation and (b) computerized assessment.

Both pre- and postexperiment ECG data were visually evaluated by two specialist clinicians who were blind to the status of animals. Although they have observed minor ECG changes such as ST depression, QRS enlargement, branch block, AV complete block, VEB, VT, VF, sinus bradycardia and sick sinus syndrome at some periods of ECG traces of some subjects, they did not consider these arrhythmias as significant and specific for any group to speculate any heart disorder caused by the 3G MPs' EMR.

Both pre- and postexperiment ECG data were analyzed through the developed software. In this case, the analysis takes into account the high precision measurement of the duration and fluctuations in the P and QS waves and the HR variability across the groups. Therefore, first the mean and standard deviation (SD) of the P and QS waves for each individual ECG signal were determined, and second from this data the gross mean and SD of P and QS waves over the subjects in each group were calculated. Similarly the gross mean and SD of the HR were calculated. Also to measure the variability of P, QS waves as well as HR across the animals within each group, SD of the gross mean values of P, QS and HR for each group were calculated as SD_P, SD_{QS} and SD_{HR}, respectively. The obtained results, that is, the gross mean and SD values were given in Table 2, which are expressed as mean ± SD and SD of the gross mean values.

Discussion

Although the emerging 3G cellular technology offers diverse services to users and contributing to social and economic benefits, there are still some issues with the 3G MPs not ascertained, as it is not clear whether this technology has any hazardous effect on the body. There is no satisfactory report concerning experimental exploration regarding the 3G MP effects either on heart or on other tissues. The common belief is that the technologies emitting electromagnetic field

Table 2. The hemodynamic parameters derived from before (preexperiment) and after (postexperiment) ECG traces of rat groups

Groups	P	SD_P	QS	SD_{QS}	HR	SD_{HR}
Before						
1	9.08 ± 2.28	2.03	18.60 ± 1.53	3.89	269.15 ± 5.31	37.20
2	10.98 ± 0.96	1.44	19.52 ± 1.58	2.62	279.29 ± 6.30	41.49
3	11.06 ± 1.43	1.35	18.68 ± 2.06	2.41	305.35 ± 5.26	49.55
4	10.92 ± 1.5	1.34	19.37 ± 1.20	2.60	314.07 ± 4.23	46.77
After						
1	9.57 ± 0.92	0.50	19.92 ± 1.11	1.05	258.38 ± 3.22	21.22
2	9.09 ± 1.06	2.75	18.75 ± 1.36	2.47	274.04 ± 2.77	20.23
3	9.83 ± 0.73	1.61	19.35 ± 1.43	1.73	283.77 ± 3.22	19.17
4	11.08 ± 0.43	1.64	19.30 ± 0.48	4.97	297.72 ± 4.01	24.04

P: gross mean ± SD of P wave, SD_P: SD of gross P values, QS: gross mean ± SD of QS wave, SD_{QS}: SD of gross QS values, HR: gross mean ± SD of HR wave, SD_{HR}: SD of gross HR values.

(EMF), particularly the communication systems, are associated with the rate of exposure of people to EMFs. It has been reported that EMF increases free radical activity in cells (Grundler et al., 1992) and the EMF radiating from MP gives rise to the development of ROS (Desai et al., 2009). Various studies concerning the effect of EMR on heart showed that EMR exposure can increase BP, and the levels of BP and HR changed in subjects working with EMFs (Barker et al., 2007). Tamer et al. (2009) reported that the EMR from MP enhanced the oxidative stress in the heart tissue and also, in normal volunteers, it affected the HR and BP by increasing the BP to about 5–10 mm Hg. However, they did not consider this effect to be related with MP according to previous studies that evaluated the acute effects of MP on HR and BP. All of these results are based on conventional MPs. Here, as a first trial, we investigate the effect of EM radiated from a 3G MP on the rat's heart tissue.

Our results showed no significant differences in the BP values as evaluated among the groups both before and at the end of the experiment. However, in the evaluation of postexperiment records, HR values in groups 1 2 were significantly lower than in group 4 at the 5th min. Within each group the BP values both pre and post experiment were compared, and no significant differences were observed in BP values except in the melatonin-treated group (group 4). In this group, BP values at all the three measuring points were found decreased when compared to the baseline values. This result is not surprising; because it has been well documented that melatonin treatment can cause reduction in BP by vasodilatation via nitric oxide-dependent pathway. Owing to this reason, HR values were found increased in groups 1 and 2 for continuing the homeostatic status of body by autonomic nerves reflex system. Therefore, the investigation toward therapeutic usage of melatonin in patients with hypertension still continues (Simko and Pechanova, 2009). This foresight is also in accordance with the previous studies reporting no significant changes in arterial BP and HR during or after RF exposures to 900 MHz or 1800 MHz MPs (Tahvanainen et al., 2004). Also, according to our gross mean HR values (Table 2), there were no significant differences both in the preexperiment and in the postexperiment hemodynamic parameters values, among all the groups.

As mentioned before, the minor arrhythmia that was observed through visual analysis was not considered significant as well as not common to any group to, therefore, put forward any words regarding the effect of 3G MP on the heart. Even in the case of normal MPs, the effect of EMR on heart remained either uncertain; for example, Koivisto et al. (2001) did not find an association between exposure to 900 MHz cellular phones and the subjective symptoms complained by users or speculative otherwise.

It has been demonstrated that ROS are directly involved in oxidative damage induced by EMR exposure of cellular phones on macromolecules (e.g. lipids, proteins and nucleic acids in tissues). ROS can spur myocyte hypertrophy, re-expression of fetal gene programs and apoptosis in cardiac myocytes in culture. Also some investigators declared that ROS production increases in biological system particularly in the myocardium of patients with ischemic–reperfused heart and heart failure caused by induced oxidative stress (Ozguner et al., 2005). As Reiter et al. (1998) had mentioned, the EMF exposure gives rise to augmentation in the levels of free radicals and therefore

reduction in serum melatonin due to the increase in uptake of melatonin by tissues. Also, Irmak et al. (2002) declared that treatments of rats before and after EMR exposure with melatonin and vitamin E were found to block the adverse effect of EMR, possibly by affecting the lifetime of the radicals. In this respect, Jauchem (2008) mentioned two contrary studies investigating the relation of melatonin metabolite excretion with MP usage. In one of them (77 subjects), a linearly decreasing trend of melatonin metabolite excretion across categories of increasing MP use had been observed. In another study (149 subjects), however, no significant changes had been observed. Sahna et al. (2002) investigated melatonin's protective effect on heart tissue and reported that melatonin substitution or supplement might suspend the incidence of sudden cardiac death induced by VF.

In this study, in order to investigate the possible protective effects of melatonin against 3G EMR exposure on the heart which may manifest through the ECG records, melatonin-treated groups were employed in the design of the study. The parameters derived from ECG records given in Table 2 showed a significant effect of 3G-EMR exposures which could not be perceived. However, the values given in Table 2 could be coevaluated by the experts researching on this subject. The minor variations in P, QS and HR values of the groups were considered as natural not due to the 3G-EMR exposures. Accordingly, it was considered that this study did not demonstrate a significant effect of 3G EMR on BP, HR and ECG parameters in the rats. Although melatonin is a potent free radical scavenger and antioxidant hormone, it did not exhibit any additional effects (neither beneficial nor hazardous) on the hemodynamics of rat hearts. The fact that the hemodynamics of rat hearts were not affected by 3G-exposed EMR could be because in the experiment the 3G MPs were not placed in contact with the head or chest, which is not the actual format of 3G MP usage. Therefore, the strategy of usage of a 3G MP seems to be much safer compared to the ones used in close contact with the head.

According to the results obtained here, when 3G MP is placed distant to the chest or head, it seems that significant effects of EMR from 3G MP on the rats' cardiovascular functions or hemodynamic parameters could not be demonstrated. Nonetheless, this issue needs to be further investigated in a variety of perspectives to be able to elucidate the effects of 3G-exposed EMR on cardiovascular functions. For example, investigating the intensity of EMR from 3G MP as a function of distance from the MP's antenna might provide some more specific information about the hazardous rate of MP. Also, to understand the effect of melatonin, further study perhaps in the light of biochemical and histopathological analysis might be beneficial.

Authors' note

Dr Cengiz Colak and Dr Ahmet Acet are the coordinators of this study. Dr Cengiz Colak and Dr Hakan Parlakpinar were involved with the planning of the study protocol design. Dr Cengiz Colak and Dr Hakan Parlakpinar made the mandatory requirements for the study. Dr Cengiz Colak, Dr Hakan Parlakpinar, Dr Necip Ermis and Dr Mehmet Emin Tagluk were in charge of injections, cannulation of carotid artery and data collection. Omer Faruk Dilek (undergraduated student-class 6) and Sevtap Bakir (undergraduated student-class-4) were involved with reading the chapter from a textbook. Omer Faruk Dilek (under-graduated student-class 6), Bahadır Turan (under-graduated student-class-4) and Sevtap Bakir (under-graduated student-class-4) were involved with the application of 3G-EMR exposure experiment by mobile phones. Dr Cengiz Colak, Dr Hakan Parlakpinar, Dr Necip Ermis, Dr Mehmet Emin Tagluk, Dr Ediz Sarihan were responsible for data analysis and interpretation of the results. Dr Cemil Colak was involved with statistical analysis. Dr Hakan Parlakpinar, Dr Mehmet Emin Tagluk, Dr Cemil Colak and Omer Faruk Dilek (under-graduated student-class 6) were responsible for the design of figures and tables. This manuscript was written by Dr Cengiz Colak, Dr Hakan Parlakpinar, Dr Necip Ermis, Dr Mehmet Emin Tagluk, Dr Ediz Sarihan and Dr Ahmet Acet. The final manuscript is revised collaboratively by Dr Cengiz Colak, Dr Hakan Parlakpinar, Dr Mehmet Emin Tagluk and Dr Ediz Sarihan.

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References

Ahamed VI, Karthick NG, and Joseph PK (2008) Effect of mobile phone radiation on heart rate variability. *Computers in Biology and Medicine* 38(6): 709–712.

Andrzejak R, Poreba R, Poreba M, Derkacz A, Skalik R, Gac P, et al. (2008) The influence of the call with a mobile phone on heart rate variability parameters in healthy volunteers. *Industrial Health* 46(4): 409–417.

Atlasz T, Kellényi L, Kovács P, Babai N, Thuróczy G, and Hejjel L (2006) The application of surface plethysmography for heart rate variability analysis after GSM radiofrequency exposure. *Journal of Biochemical and Biophysical Methods* 69(1-2): 233–236.

Balci M, Devrim E, and Durak I (2007) Effects of mobile phones on oxidant/antioxidant balance in cornea and lens of rats. *Current Eye Research* 32(1): 21–25.

Barker AT, Jackson PR, Parry H, Coulton LA, Cook GG, and Wood SM (2007) The effect of GSM and TETRA mobile handset signals on blood pressure, catechol levels and heart rate variability. *Bioelectromagnetics* 28(6): 433–438.

Ciejka EB, Goraca A (2009) The influence of low-frequency magnetic field on plasma antioxidant capacity and heart rate. *Wiadomości Lekarskie* (Warsaw, Poland: 1960) 62(2): 81–86.

Dasenbrock C (2005) Animal carcinogenicity studies on radiofrequency fields related to mobile phones and base stations. *Toxicology and Applied Pharmacology* 207(2 suppl): 342–346.

Desai NR, Kesari KK, and Agarwal A (2009) Pathophysiology of cell phone radiation: oxidative stress and carcinogenesis with focus on male reproductive system. *Reproductive Biology and Endocrinology* 7: 114.

Grundler W, Kaiser F, Keilmann F, and Walleczek J (1992) Mechanisms of electromagnetic interaction with cellular systems. *Naturwissenschaften* 79(12): 551–559.

Gul A, Celebi H, and Ufra S (2009) The effects of microwave emitted by cellular phones on ovarian follicles in rats. *Archives of Gynecology and Obstetrics* 280(5): 729–733.

Guney M, Ozguner F, Oral B, Karahan N, and Mungan T (2007) 900 MHz radiofrequency-induced histopathologic changes and oxidative stress in rat endometrium: protection by vitamins E and C. *Toxicology and Industrial Health* 23(7): 411–420.

Hata K, Yamaguchi H, Tsurita G, Watanabe S, Wake K, Taki M, et al. (2005) Short term exposure to 1439 MHz pulsed TDMA field does not alter melatonin synthesis in rats. *Bioelectromagnetics* 26(1): 49–53.

Irmak MK, Fadilloglu E, Gulec M, Erdoğan H, Yağmurca M, and Akyol O (2002) Effects of electromagnetic radiation from a cellular telephone on the oxidant and antioxidant levels in rabbits. *Cell Biochemistry and Function* 20(4): 279–283.

Jauchem JR (2008) Effects of low-level radio-frequency (3 kHz to 300 GHz) energy on human cardiovascular, reproductive, immune, and other systems: a review of the recent literatures. *International Journal of Hygiene and Environmental Health* 211(1-2): 1–29.

Katzung BG, Masters SB, and Trevor AJ (2009) Agents used in cardiac arrhythmias. In: Hume JR (ed.). *Basic and Clinical Pharmacology*. 11th ed. Columbus, OH: Mc Graw Hill, 225–249.

Koivisto M, Haarala C, Krause CM, Revonsuo A, Laine M, and Hämäläinen H (2001) GSM phone signal does not produce subjective symptoms. *Bioelectromagnetics* 22(3): 212–215.

Koyu A, Ozguner F, Cesur G, Gokalp O, Mollaoglu H, Caliskan S, et al. (2005) No effects of 900 MHz and 1800 MHz electromagnetic field emitted from cellular phone on nocturnal serum melatonin levels in rats. *Toxicology and Industrial Health* 21(1-2): 27–31.

Mailankot M, Kunnath AP, Jayalekshmi H, Koduru B, and Valsalan R (2009) Radio frequency electromagnetic radiation (RF-EMR) from GSM (0.9/1.8GHz) mobile phones induces oxidative stress and reduces sperm motility in rats. Clinics 64(6): 561–565.

Meral I, Mert H, Mert N, Deger Y, Yoruk I, Yetkin A, et al. (2007) Effects of 900-MHz electromagnetic field emitted from cellular phone on brain oxidative stress and some vitamin levels of guinea pigs. *Brain Research* 1169: 120–124.

Myung SK, Ju W, McDonnell DD, Lee YJ, Kazinets G, and Cheng CT, et al. (2009) Mobile phone use and risk of tumors: a meta-analysis. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology* 27(33): 5565–5572.

Oktem F, Ozguner F, Mollaoglu H, Koyu A, and Uz E (2005) Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone: protection by melatonin. *Archives of Medical Research* 36(4): 350–355.

Oral B, Guney M, Ozguner F, Karahan N, Mungan T, Comlekci S, et al. (2006) Endometrial apoptosis induced by a 900-MHz mobile phone: preventive effects of vitamins E and C. *Advances in Therapy* 23(6): 957–973.

Ozguner F, Altinbas A, Ozaydin M, Dogan A, Vural H, Kisioglu AN, et al. (2005a) Mobile phone-induced myocardial oxidative stress: protection by a novel antioxidant agent caffeic acid phenethyl ester. *Toxicology and Industrial Health* 21(9): 223–230.

Ozguner F, Bardak Y, and Comlekci S (2006) Protective effects of melatonin and caffeic acid phenethyl ester against retinal oxidative stress in long-term use of mobile phone: a comparative study. *Molecular and Cellular Biochemistry* 282(1-2): 83–88.

Ozguner F, Oktem F, and Armagan A (2005b) Comparative analysis of the protective effects of melatonin and caffeic acid phenethyl ester (CAPE) on mobile phone-induced renal impairment in rat. *Molecular and Cellular Biochemistry* 276(1-2): 31–37.

Panda NK, Jain R, Bakshi J, and Munjal S (2010) Audiologic disturbances in long-term mobile phone users. *Journal of Otolaryngology-Head & Neck Surgery* 39(1): 5–11.

Parlakpinar H, Sahna E, Ozer MK, Ozugurlu F, Vardi N, and Acet A (2002) Physiological and pharmacological concentrations of melatonin protect against cisplatin-induced acute renal injury. *Journal of Pineal Research* 33(3): 161–166.

Patrick K, Griswold WG, Raab F, and Intille SS (2008) Health and the mobile phone. *American Journal of Preventive Medicine* 35(2): 177–181.

Reiter RJ, Melchiorri D, Sewerynek E, Poeggeler B, Barlow-Walden L, Chuang J, et al. (1995) A review of the evidence supporting melatonin's role as an antioxidant. *Journal of Pineal Research* 18(1): 1–11.

Reiter RJ, Paredes SD, Manchester LC, and Tan DX (2009) Reducing oxidative/nitrosative stress: a newly-discovered genre for melatonin. *Critical Reviews in Biochemistry and Molecular Biology* 44(4): 175–200.

Reiter RJ, Tan DX, Poeggeler B, and Kavet R (1998) Inconsistent suppression of nocturnal pineal melatonin synthesis and serum melatonin levels in rats exposed to pulsed DC magnetic fields. *Bioelectromagnetics* 19(5): 318–329.

Sahna E, Olmez E, and Acet A (2002) Effects of physiological and pharmacological concentrations of melatonin on ischemia-reperfusion arrhythmias in rats: can the incidence of sudden cardiac death be reduced? *Journal of Pineal Research* 32(3): 194–198.

Simko F, and Pechanova O (2009) Potential roles of melatonin and chronotherapy among the new trends in hypertension treatment. *Journal of Pineal Research* 47(2): 127–133.

Smith C, and Collins D (2000) *3G wireless networks*. 2nd ed. Columbus, OH: Mc Graw Hill, 136.

Szmigielski S, Bortkiewicz A, Gadzicka E, Zmyslony M, and Kubacki R (1998) Alteration of diurnal rhythms of blood pressure and heart rate to workers exposed to radiofrequency electromagnetic fields. *Blood Pressure Monitoring* 3(6): 323–330.

Tahvanainen K, Niño J, Halonen P, Kuusela T, Laitinen T, Länsimies E, et al. (2004) Cellular phone use does not acutely affect blood pressure or heart rate of humans. *Bioelectromagnetics* 25(2): 73–83.

Tamer A, Gunduz H, and Ozyildirim S (2009) The cardiac effects of a mobile phone positioned closest to the heart. *Anadolu Kardiyoloji Dergisi* 9(5): 380–384.

Vangelova K, Deyanov C, and Israel M (2006) Cardiovascular risk in operators under radiofrequency electromagnetic radiation. *International Journal of Hygiene and Environmental Health* 209(2): 133–138.