Effect of EMF Radiation from Mobile Handsets on hypothalamic glucosensing mechanisms in Developing Rats

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Abstract

Globally the lifestyle of children-adolescents and young adults has recorded a paradigm shift to include ubiquitous use of mobile phones and intake of fructose-rich diet such as beverages, soda, cakes and pastries. Simultaneously, there has been an increase in the incidence of insulin resistance and obesity amongst children-adolescents and young adults. Till now, these morbidities were restricted to adult and geriatric age-groups and hitherto unknown in growing population. Considering the debilitating effect of this epidemic on active work force and economy, it has become critical to investigate the combined effects of exposure to electromagnetic field radiation (EMF) from the mobile phone and fructose intake on insulin resistance/obesity in growing age-group. The results of the study lead to the hypothesis that the exposure to EMF radiations from mobile phone during pre, peri and post pubertal stages of development initiates a change in the food preference of the growing animals from normal pellet food to palatable fructose drink. The two together skew the talk between orexigenic and anorexigenic signals between hypothalamus and liver, in favor of former that may lead to early onset of fatty liver, insulin resistance and overweight-obesity.

1 Introduction

Globally the use of mobile phones has become ubiquitous with an estimated 6.9 billion subscriptions by W.H.O report. According to a survey by e-Marketer, India is estimated to have over 800 million mobile phone users in 2019. Mobile phones are low-powered radiofrequency transmitters, operating at frequencies between 450 and 2700 MHz with peak powers in the range of 0.1 to 2 watts. Although there is paucity of data that concretely establishes the biological effects of EMF radiations from mobile handsets, there is growing body of evidence that correlates the exposure with detrimental effects on the central nervous system, cardiovascular and hematopoietic systems, reproductive functions [1] as well as the development of insulin resistance, hyperglycemia and central obesity.

Alarmingly, the use of the mobile phones is not restricted to the adult population, but finds extensive favor amongst children/adolescents and young adults. The lifestyle of modern-day adolescents also includes fructose-rich diet in the form of beverages, soda, pastries and confectionaries, which has been attributed to induce early-onset of obesity.

The combined effects of EMF radiation from mobile handsets and fructose-rich diet on the cross-talk between brain and liver that regulates eating and satiety behavior and metabolic functions of growing population remains uninvestigated, and is crucial for delineating the pathogenesis of the global epidemic of early-onset of obesity.

In the hypothalamic region of the brain, distinct set of specialized neurons have been identified that primarily function as ‘Glucose-sensors’ as they respond to changes in extracellular glucose concentration with changes in their firing rate [2-4]. The glucose-sensing neurons are critical for establishing the body energy status and coordinate changes in hormone release, metabolic rate, food intake and locomotor activity, to ensure homeostasis [5]. The proopiomelanocortin (POMC) and neuropeptide Y (NPY) neurons in the hypothalamus, sense central and peripheral glucose levels and regulate glucose metabolism through the vagal nerve as well as neuroendocrine signals. In pathological states such as obesity, several brain energy mechanisms are reportedly altered [6] to influence food intake as well as glucose and energy homeostasis [7, 8]. Normally, the absence of glucose, stimulates the expression of the orexigenic mediator neuropeptide Y (NPY) while the presence of the glucose induces the anorexigenic mediator proopiomelanocortin (POMC) [8]. Failure of these glucose-induced responses could have a role in the pathogenesis of obesity [9]. The hypothalamic glucose transporter (GLUT2) is also critically involved in the glucose sensing and feeding regulation mechanisms that operate at the hypothalamus [10-12].

The combined effects of EMF radiation from mobile handsets and fructose-rich diet on the cross-talk between the orexigenic and anorexigenic signals of brain and liver in rats that were exposed during their pre, peri and post-pubertal stages of development is investigated and reported here.
2 Material and Methodology

Animals: Weaned male Albino Wistar rats (44.5 ± 10 g; 28 days old) were housed under standard conditions of light, temperature and humidity and used in accordance with the guidelines of the Committee for the Purpose of Control and Supervision on Experiments on Animals. All experimental protocols were approved by Institutional Animal Ethics Committee (IAEC/2014/II-04; DIPSAR/IAEC/2015-II/07).

Animal radiation exposure model: The rats were randomly divided into four groups (n=6) - Normal, Exposure Only (ExpO), Fructose Only (FruO) and Exposure+Fructose (EF). The study spanned over 8 weeks, i.e., from post weaning (28 day old) to early adulthood (84 day old) to mark the pre, peri and post-pubertal stages of the rats, respectively. The EF group received EMF radiation from mobile phone in “switched-on mode” (2h/d×8weeks, Samsung j5 Prime, 2100 MHz, GSM, specific absorption rate 1.3 W/Kg) and normal chow+fructose (15%) as drinking solution, ad libitum. The ExpO and FruO received EMF exposure (2h/d)+normal chow+drinking water, ad libitum and no exposure+normal chow+fructose (15%) as drinking solution, ad libitum, respectively, over 8 weeks.

For exposure, the rats were randomly placed in a plexiglas cages, fixed with anechoic material (radio absorbing material) and ventilated with holes of 1 cm diameter. The mobile phone was kept on the top of the exposure chamber housing with one rat at a time. The placing of the mobile phone antenna on the top of the animal cage was such that it ensured preferential emission towards the rat and there was no scattering of radiations. The platform carrying the mobile phone was firmly tied with a string to a pulley which is controlled by the stepper motor. The motor was programed to have angular momentum from 2-45 degrees.

The rats from all the groups were assessed daily (food, water/fructose solution (15%) intake, body weight), weekly (fasting blood glucose) or at the end of the study (total caloric intake, oral glucose tolerance test, insulin tolerance test, lipid profile, uric acid, Alanine transaminase (ALT), Aspartate transaminase (AST), hepatic glycogen, leptin, ghrelin and Phosphoenolpyruvate carboxylase (PEPCK), and hepatic and hypothalamic levels of glucose-6 phosphatase, fructose-1,6-bisphosphatase, hexokinase, phosphofructokinase, lactate dehydrogenase and GLUT 2, Glucokinase, Neuropeptide Y (NPY), pro-opiomelanocortin (POMC) protein) as per standard protocols.

Data are represented as Mean ± SD (n=6). Statistical comparison of groups was done using the one way ANOVA with post one tailed analyses on Graph Pad Prism 5.0 Software.

3 Result and Discussion

The present study reports the combined effects of EMF radiation from mobile handset and fructose as drinking solution on orexigenic and anorexigenic signals from brain and liver of rats exposed during their pre, peri and post-pubertal stages of development.

At the start of the study, there was no significant difference in the daily food intake of the rats of the different groups. As the study progressed, there was decreased in the daily food intake of the EF and FruO that became significantly lower (p<0.05) than Normal and ExpO by the eighth week of the study (Fig1a). Concomitantly, a rise in the daily fructose intake by EF and FruO was recorded, that was significantly higher (P<0.05) than water intake of Normal and ExpO between 5th-8th week of the study (Fig1b). Together, the total caloric intake over the study duration was significantly higher (p<0.05) in EF and FruO than Normal and ExpO (Fig1c). This translated into steady rise in the body weight of EF that attained significance (p<0.05) as compared to Normal at the eighth week of the study (Fig1d). It may be hypothesized the exposure to EMF radiations from mobile phone during pre, peri and post pubertal stages initiated a change in the food preference of the growing animals from normal pellet food to palatable fructose drink. However, the two together lead to early onset of overweight-obesity.

There was no statistical difference between the fasting blood glucose (FBG) levels of the different groups (Fig1e). However, from fourth up till the eighth week of the study, an increase in the FBG was recorded in FruO and EF that gained significance (p<0.05) against ExpO and Normal groups which is in accordance with the literature report [13]. At the end of the study, the Area Under the Curve in OGTT and ITT was significantly (p<0.05) higher in EF and FruO as compared to Normal (Figs1f&g). The expression of the protein GLUT 2 in liver was significantly reduced in EF, ExpO and FruO than Normal (Fig1h). Taken together, the data indicates that the chronic exposure to EMF radiations from mobile phone during pre, peri and post pubertal stages lead to the early development of hepatic insulin resistance in the developing rats.

Further, the hepatic enzymes involved in glycolysis (hexokinase, glucose-6-phosphatase, fructose1,6-bisphosphatase, lactate dehydrogenase) and gluconeogenesis (PEPCK, Phosphofructokinase) were measured. There was a significant (p<0.05) rise in the levels of all the enzymes sans hexokinase in EF and FruO vs Normal (Figs2a-f). Additionally, there was a significant increase in the glycogen, triglyceride uric acid and total cholesterol levels in EF and FruO, as compared to Normal (Figs2g-j). As compared to ExpO, the ALT and AST levels in EF were significantly (p<0.05) lower and higher, respectively (Figs2k-l). Taken together, it appears that the chronic exposure to EMF radiations from mobile phone radiations and fructose intake during pre, peri and post pubertal stages, skews the hepatic metabolic milieu...
in favor of lipogenesis and development of fatty liver. The enzyme hexokinase catalyzes the first step of glycolytic pathway, i.e., conversion of glucose to glucose-6-phosphate. It is also a site of control of glycolysis, as the end-product inhibits its activity. Thus, the low concentrations of hexokinase indicate high flux. On the other hand, the activity of phosphofructokinase increases when the ATP/AMP ratio is lowered. Thus metabolic milieu of EF represents an insulin resistant state.

Similarly, in the hypothalamus, activities of hexokinase was significantly (p<0.05) reduced but those of PEPCK and LDH were significantly (p<0.05) raised in EF and FruO as compared to Normal (Figs3a-c). Interestingly, a significant (p<0.05) rise in the orexigenic molecule-grelin, but not of anorexigenic molecule-leptin was recorded in EF as compared to Normal (Figs3d-e). The expression of important signals of orexigenic and anorexigenic pathway, i.e., Neuropeptide Y (NPY), pro-opiomelanocortin (POMC), GLUT2 and hexokinase were significantly reduced (p<0.05) in EF as compared to Normal (Figs3f-i). The Neuropeptide Y (NPY) is one of the most potent orexigenic peptides found in the brain. It stimulates food intake with a preferential effect on carbohydrate intake. It decreases latency to eat, increases motivation to eat and delays satiety by augmenting meal size. Long-term exposure to high-fat or high-energy palatable diets leads to the development of adiposity and is associated with a decrease in hypothalamic NPY content or expression, consistent with the existence of a counter-regulatory mechanism to diminish energy intake and limit obesity development, and similar hypothesis may be extended to the present study [14]. The chronic fructose consumption has been associated with leptin resistance that is also the case here [15]. Further, leptin is identified as the signal linking peripheral energy stores with POMC signalling activity in the hypothalamus which subsequently may promote the development of obesity [15]. Thus, for the first time we report here that the chronic exposure to EMF from mobile phone and fructose drinking affect central and peripheral signals that regulate feeding/satiety behaviour to initiate the pathogenesis of fatty liver, insulin resistance and obesity at developing stage.

**Figure 1.** Chronic exposure to EMF radiation from mobile handset and fructose drinking during pre, peri and post pubertal stages skews (a) food intake (b) fructose weight, (c) fasting blood glucose levels (FBG), (f) AUC-Oral glucose tolerance test (OGTT), (g) AUC-Insulin tolerance test (ITT), (h) Hepatic GLUT 2 protein expression, leading to the development of insulin resistance and overweight at early adulthood. All values are mean ± SD; (n=6), *p<0.05 vs Normal

**Figure 2.** Chronic exposure to EMF radiation from mobile handset and fructose drinking during pre, peri and post pubertal stages skews the hepatic paradigms of (a) Hexokinase, (b) Glucose-6-Phosphatase, (c) Fructose-6-Phosphatase, (d) Lactate Dehydrogenase (LDH), (e) PEPCK (f) Phosphofructokinase (PFK), (g) Glycogen, (h)Triglyceride (i) Uric acid, (j) Total Cholesterol, (k) ALT, (l) AST, leading to the development of fatty-liver at early adulthood. All values are mean ± SD; (n=6), *p<0.05 vs Normal.
Figure 3. Chronic exposure to EMF radiation from mobile handset and fructose drinking during pre, peri and post pubertal stages skews activities of hypothalamic proteins and enzymes that regulate carbohydrate metabolism (a) Hexokinase, (b) PEPCK, (c) Lactate Dehydrogenase (LDH), (d) Glutamate, (e) Leptin, Protein expression:(f) peptide Neuropeptide Y (NPY), (g) Proopiomelanocortin (POMC), (h) GLUT 2, (i) Glucokinase to tilt in favor of oregenic behavior at early adulthood. All values are mean ± SD; (n=6), *p<0.05 vs Normal.

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5 References


