Progress in Biophysics and Molecular Biology xxx (2017) 1–8

Contents lists available at ScienceDirect

Progress in Biophysics and Molecular Biology

journal homepage: www.elsevier.com/locate/pbiomolbio

miRNA expression profile is altered differentially in the rat brain compared to blood after experimental exposure to 50 Hz and 1 mT electromagnetic field

Mehmet Emin Erdal [a], Senay Görücü Yılmaz [b, *], Serkan Gürgül [c], Coşar Uzun [d], Didem Derici [e], Nurten Erdal [d]

[a] Faculty of Medicine, Department of Medical Biology and Genetics, Mersin University, Mersin 33343, Turkey
[b] Faculty of Health Science, Department of Nutrition and Dietetics, Gaziantep University, Gaziantep, Turkey
[c] Faculty of Medicine, Department of Biophysics, Gaziosmanpaşa University, Tokat TR-60100, Turkey
[d] Faculty of Medicine, Department of Biophysics, Mersin University, Mersin TR-33343, Turkey
[e] Faculty of Medicine, Department of Biostatistics and Medical Informatics, Mersin University, Mersin TR-33343, Turkey

ARTICLE INFO

Article history:
Received 23 June 2017
Received in revised form
25 July 2017
Accepted 2 August 2017
Available online xxx

Keywords:
Alzheimer's disease
MicroRNA
Electromagnetic field exposure
Rat
Blood
Brain
Host-environment interaction

ABSTRACT

Common complex diseases are a result of host and environment interactions. One such putative environmental factor is the electromagnetic field exposure, especially the occupational extremely low frequency (ELF) magnetic field, 50 Hz, 1 mT, whose neurobiological relevance remains elusive. We evaluated the effects of long-term (60 days) ELF-MF exposure on miRNAs previously related to brain and human diseases (miR-26b-5p, miR-9-5p, miR-29a-3p, miR-106b-5p, miR-107, miR-125a-3p). A total of 64 young (3 weeks-old) and mature (10 weeks-old) male/female Wistar-Albino rats were divided into sham and ELF-MF exposed groups. After sacrifice of the animals, blood samples from rat's tail vein and brain tissues were collected. The expression levels of miRNAs were investigated with Real-Time PCR technique and TaqMan probe Technology. All miRNA expression levels of the young female rats show a significant decrease in blood according to brain samples ($p < 0.05$), but fewer miRNAs displayed a similar significant decrease in the blood. In conclusion, these new observations might inform future clinical biological psychiatry studies of long-term electromagnetic field exposure, and the ways in which host −environment interactions contribute to brain diseases.

Contents

* Corresponding author. Department of Nutrition and Dietetics, Gaziantep University, Gaziantep 27310, Turkey.
E-mail addresses: merdal@mersin.edu.tr (M.E. Erdal), gorucu@gantep.edu.tr (S.G. Yılmaz), sgurgul@gmail.com (S. Gürgül), cosaruzun@gmail.com (C. Uzun), didemderici@hotmail.com (D. Derici), nerdal@mersin.edu.tr (N. Erdal).

http://dx.doi.org/10.1016/j.pbiomolbio.2017.08.001
0079-6107/

1. Introduction

Common complex diseases such as cancer, dementia and major depression are often caused by an interplay of host − environment interactions (Singh et al., 2015; Yılmaz et al., 2016a, 2016b). Brain disorders are complex and progressive in that some are aged-related and subject to marked host-environment interactions as well. One of the important mediators of such host − environment interactions is MicroRNAs (miRNAs). These molecules are a large group of 18–25 nucleotide long, non-coding RNAs that regulate posttranscriptional modifications of protein-coding genes leading to translational inhibition, mRNA destabilization or degradation, depending on the degree of sequence complementarity (Delay et al., 2012; Satoh, 2012; Van den Hove et al., 2014; Tan et al., 2014). A single miRNA has ability to affect numerous target mRNAs. This causes a decrease in the production of hundreds of proteins that provide miRNA-regulated gene expression (Friedman et al., 2009). MiRNAs regulate more than the half of the protein-coding genes in human brain and play critical roles in neuronal and glial development, differentiation, proliferation, apoptosis and metabolism (Fineberg et al., 2009; Jeffries et al., 2011; OldeLoohuis et al., 2012).

Accumulating evidence indicates that the aberrant expression and dysfunction of miRNAs several neurodegenerative disorders such as AD and Parkinson's disease (PD) (Lau and De Strooper, 2010; Van den Hove et al., 2014). In this context, a number of miRNAs, including miR-9, miR-29a/b, miR-106, miR-107, and miR-125a/b has found dysregulated in AD brain and are known to play a vital role in the AD pathogenesis (Yılmaz et al., 2016a, b; Cogswell et al., 2008; Delay et al., 2012; Satoh, 2012 Hebert et al., 2012; Lukiw and Alexandrov, 2012; Van den Hove et al., 2014).

Our study presented here has focused on miRNAs associated with brain disorders as Alzheimer's Disease (AD), Schizophrenia, Huntington's Disease (HD) (mir2Disease database, Accession date: Tuesday, Apr 4, 2017). For example, AD is characterized by amyloid plaques (accumulation of amyloid-β (Aβ) peptide generated by amyloid precursor protein (APP) and presenilin (PSEN) genes), neuronal tangles (aggregation of hyper phosphorylated tau protein), and neurofibrillary degeneration in some brain regions such as entorhinal cortex, hippocampus, basal forebrain and amygdala, resulting in gradual loss of memory and irreversible impairment of higher cognitive functions (Mattso, 2004; Schifilliti et al., 2010; Lau et al., 2013; Van den Hove et al., 2014). Some genetic mutations or polymorphisms in APP, PSEN, and β-site APP cleaving enzyme 1 (BACE1) genes have been found to be strongly associated with AD pathogenesis (Rovelet-Lecrux et al., 2006; Theuns et al., 2006; Steiner, 2008; Hass et al., 2009; De Strooper and Annaert, 2010; Delay et al., 2012; McNaughton et al., 2012).

In terms of the environmental exposures that impact the human host, electromagnetic variation is increasingly important. The use of electricity has been the reason of the environmental exposure to extremely low frequency (ELF) magnetic fields (MF) generated by power-lines and by household and industrial appliances used in the present world. Consequently, the effects of ELF-MF on human health have become a subject of considerable interest by health professionals, government administrators and regulators, scientists, and the general public (Erdal et al., 2005, 2007). Several epidemiological studies have shown that the association between cancer (brain cancer, lymphatic leukemia, lymphomas, breast tumors, and childhood leukemia) and ELF-MF exposure (Valberg, 1996; Ahlbom, 1997; Gurney and VanWijngaarden, 1999; Greenland et al., 2000). Besides studies investigating the biological effects of ELF-MF in *ex vivo* and *in vivo* conditions, particular attention is given to decipher cellular interactions and biological mechanisms of ELF-MF. Although some authors have indicated that the ELF-MF may have a direct effect on DNA (Blank and Goodman, 1999; Rao et al., 2002), it is generally accepted that the ELF-MF may not transfer enough directly energy to cells to damage DNA (Ruiz-Gómez and Martínez-Morillo, 2009). ELF-MF are capable of regulating gene expressions by increasing levels of some transcription factors such as activator protein 1 (AP-1), early growth response protein 1 (Erg-1) and B-cell lymphoma 2 (Bcl-2) (Goodman et al., 1983, Goodman and Henderson, 1986a, 1986b, 1987; Phillips and McChesney, 1991; Lin et al., 1998; Jin et al., 2000; Ruiz-Gómez and Martínez-Morillo, 2009; Shin et al., 2011; Seong et al., 2014). Moreover, increased mRNA levels of histone H3 and tumor suppressor protein 53 (p53; Cantini et al., 1986), insulin-like growth factor 2 (IGF-II; Fitzsimmons et al., 1992), histone H2B, cellular myelocytomatosis oncogene (c-myc; Lin et al., 1996), viral myelocytomatosis oncogene (v-myc; Goodman et al., 1989), and cellular fos (Finkel–Biskis–Jinkins osteosarcoma) oncogene (c-fos; Rao and Henderson, 1996 have been determined in response to the ELF-MF exposure (Erdal et al., 2007).

Recently, several epidemiological studies have indicated that the occupational exposure (typical of electric power installers and repairers, power plant operators, electricians, telephone line technicians, welders, carpenters, and machinists) (D'Angelo et al., 2015) to ELF-MF have been a risk factor for neurological disease as AD (Sobel et al., 1995, 1996; Feychting et al., 2003; Harmanci et al., 2003; Håkansson et al., 2003; Qiu et al., 2004; Park et al., 2005; Davanipour and Sobel, 2009, Vergara et al., 2013). Dysregulation of calcium homeostasis, alterations in oxidative stress (Yokus et al., 2008), rises in Aβ secretion, nitric oxide level (Akdag et al., 2010) and reductions in melatonin production were represented as possible mechanisms which are responsible for the effects of ELF-MF on AD pathogenesis (Feychting et al., 1998; Del Giudice et al., 2007; Davanipour and Sobel, 2009 Artacho-Cordón et al., 2013). However, the mechanisms through that ELF-MF might influence AD are still unknown. To our knowledge, it has not been investigated to date whether ELF-MF can affect the expression levels of the miRNAs that are related with differs tissue. Therefore, the aim of this study was to investigate the effects of long-term (60 days) ELF-MF exposure (50 Hz, 1 mT) on the expression levels of miR-9, miR-29a, miR-106b, miR-107, and miR-125a in brain tissues and blood samples of rats. Secondly, we also aimed to determine whether or not long-term ELF-MF exposure may pose as a risk factor for some neurological disease due to the alterations in the miRNA regulatory system.

2. Materials and methods

2.1. Animal preparation and experimental protocol

A total of sixty-four Wistar-Albino male [mature (N = 16; 10

Please cite this article in press as: Erdal, M.E., et al., miRNA expression profile is altered differentially in the rat brain compared to blood after experimental exposure to 50 Hz and 1 mT electromagnetic field, Progress in Biophysics and Molecular Biology (2017), http://dx.doi.org/10.1016/j.pbiomolbio.2017.08.001