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ANALYSIS OF THE EFECTS OF AN AC ELECTROMAGNETIC FIELD EXPOSURE IN MICROCIRCULATION OF HUMANS BY USING A 2D LASER SPECKLE FLOWMETRY

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ABSTRACT: To date, there are only a few reports evaluating non-thermal alternating current electromagnetic exposure for medical therapeutic applications. Here, we analyzed the acute effects of hand and forearm exposure to a 50 Hz electromagnetic field (EMF; peak magnetic flux density B_{max} 180 mT, B_{rms} 127 mT, 15-min duration of exposure) on cutaneous microcirculation in 11 healthy human subjects (10 males and 1 female, age betwen 22-57 years). The blood flow volume values in the back of the hand were monitored and analyzed using a 2D laser speckle flowmetry. Regional blood flow volume values in sham control exposure were significantly reduced from baseline values during resting conditions. In contrast, the EMF exposure did not significantly decreased the blood flow volume from the baseline values during and after the EMF exposure period. There were significant differences between the EMF and sham exposure groups. Therefore, the EMF exposure significantly prevented the reduction of blood flow volume. Thus, the EMF could improve blood flow volume in cutaneous tissue under ischemic conditions. These findings imply that the physiological role of an EMF-enhanced blood circulation might help eliminate the metabolic waste products including endogenous pain producing substances inducing muscle hardness and pain.

KEYWORDS: *AC Electromagnetic Field; 2D Laser Speckle Flowmetry; Ischemic Conditions; Cutaneous Microcirculation; Humans*

1.0 INTRODUCTION

A number of studies have been conducted to investigate the biological and health effects on extremely low frequency electromagnetic fields (ELF-EMF) in the range of 1 to 300 Hz, and the exposure systems for medical treatment applications have been evaluated and reviewed [1-2]. ELF-EMF therapy with low frequency of pulsed EMF has been proposed by clinicians as alternative medicine for various applications including reducing pain, improving blood circulation, bone repair, wound healing, insomnia improvement, and reduction of arthritis [3]. Nevertheless, the mechanisms of action of EMF therapy have not been well understood.

Regarding improving blood circulation, we showed evidence that acute and local exposure to an alternating current (AC) EMF (50 Hz, B_{max} 180 mT, B_{rms} 127 mT, 15-min duration of exposure) significantly increased the blood flow velocity in an artery relative to the sham control (CTL) exposure [4]. These EMF effects seem to be dose dependent manner and moreover may depend on the parts of the body. However, the effects of EMF on blood flow volume itself have not examined. To extend the previous study, we attempted to investigate the acute effects of EMF exposure on cutaneous microcirculation in healthy human adults.

2.0 METHODOLOGY

2.1 Subjects

Healthy volunteers (10 males, 1 female, age range 22-57 years, heights 158-175 cm and weights 52-65 kg) participated in the present study. All study procedures were reviewed and approved by the Institutional Review Board of Saitama University. All subjects signed informed consent before any study procedures were performed. During the study period, subjects did not use any form of physical therapy and did not take any vasoactive medication. Subjects' body temperature, and systolic and diastolic blood pressures were within normal ranges. All trials were carried out during daytime (11:00 a.m.–17:00 p.m.) at room temperature of 25±0.5°C and relative humidity of 50±10%.

2.2 Study Protocol

The study protocol is shown in Figure 1. Monitoring of cutaneous microcirculation in the back of the right hand was conducted under hand and forearm exposures to 50 Hz EMF (B_{max} 180 mT, B_{rms} 127 mT). The blood flow volume values analyzed from the microcirculation images were compared with two different exposures namely, EMF exposure and sham control (CTL) exposure. In a randomized, double blind and crossover study design, EMF and sham exposure experiments were carried out by switching on and off an AC EMF exposure device. The initiation of monitoring of blood flow volume was done after more than 10-min rest with sitting position.

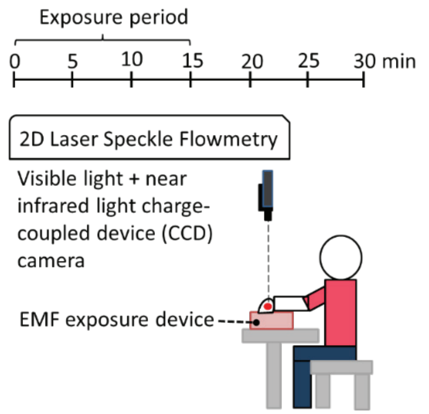

Figure 1: Study protocol for hand and forearm exposures

The microcirculation images were recorded and analyzed at 5-min intervals for 30 min using a 2D laser speckle flowmetry (Omegazone OZ-3, Omegawave, Fuchu, Tokyo, Japan). The EMF or sham exposure was performed continuously for 15 min. For hand and forearm exposures, the ventral side of the right hand and forearm were positioned on an EMF exposure device for 30 min to keep the arm motionless as long as possible during the clinical trial in each individual as shown in Figure 2.

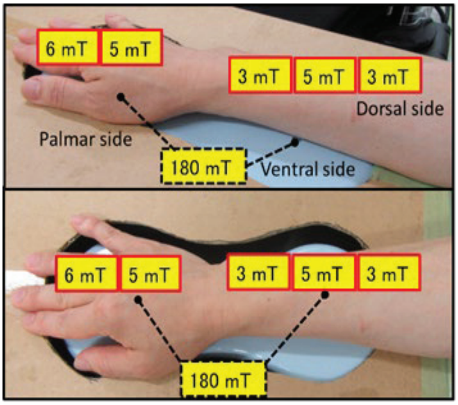

Figure 2: Photograph of hand and forearm exposures using an AC EMF exposure device

2.3 AC EMF Exposure Device

In this research, 50 Hz EMF exposure was conducted using an AC EMF exposure device (Soken MS, Toride, Ibaraki, Japan), which has two separate magnetic coils inside the device. The value of peak magnetic flux density B_{max} is 180 mT and B_{rms} is 127 mT on the surface of the EMF exposure device above the center of the coils. The spatial distribution of the Bmax from the surface of the EMF exposure device is shown in Figure 3.

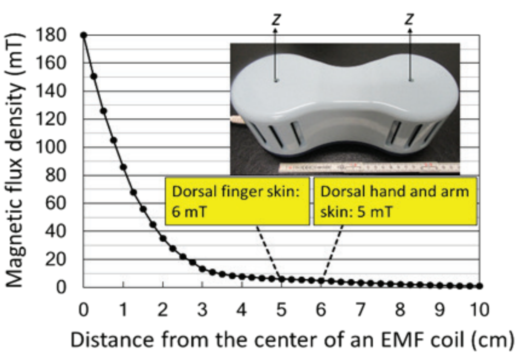

Figure 3: Spatial distribution of the peak magnetic flux density B_{max} values along the z-direction

The magnetic flux density values of AC EMF decrease exponentially with distance. The estimated B_{max} values of the measurement points in the dorsal skin surface of hand and fingers are approximately 5 mT and 6 mT, in which the distances from the surface B_{max} 180 mT of the EMF exposure device are approximately 6 cm and 5 cm, respectively, as shown in Figure 2.

The measurement of root mean square (rms) values (a) was made by means of a Hall probe magnetometer in AC mode (AC/DC Magnetometer, AlphaLab, Salt Lake City, UT, USA). Here, the B_{max} values (b) of AC EMF were calculated from the measured B_{rms} values (a) using the following equation:

$$b = \sqrt{2}a \quad (1)$$

The room temperature and the temperature in the surface of the EMF exposure device during the EMF exposure period were maintained at 25±0.5°C. The relative humidity was controlled at 50±10%. No vibration was detected during the EMF exposure period by using a horizontal checking device (PWM-25-100, KOD, Ayabe, Kyoto, Japan).

2.4 2D Laser Speckle Flowmetry

The principle of laser speckle flowmetry has been reported in detail elsewhere [5-7]. In this study, we used a charge-coupled device (CCD) camera. The fluctuation in every pixel in a certain time is important to calculate blood flow volume values in every pixel. When the number density of red blood cells (RBCs) in tissue increases, many scattered light will be detected and the deviation of the averaged electric charge of the CCD pixel become slower. Compared with the Doppler flowmetry mechanism, this 2D laser speckle blood imager shows higher blood flow volume values when the deviation of the detected light intensity is smaller. The reduced speckle image indicates the highest level of blood flow that can be measured over the entire area of tissue for a given CCD camera integration time, as a reference to quantify regional blood flow in the captured speckle image. Lower blood flow regions of the tissue have a greater speckle structure, while higher flow regions show less structure approaching a complete reduction of speckle with sufficient flow. Thus, we know that the volume of blood flowing under the skin is increased when the integrated electric charge of a CCD pixel keeps decreasing over time as shown in Figure 4.

The incident and receiving points are separated, and the distribution of light intensity in the tissue is a function of the distance of the fiber laser flowmeter. Thus, the relative measurement depth depends on the distance between the incident point and the receiving point. However, the laser light is illuminated over a wide area, and the pixels detect scattered light from the same point as the illumination point of the 2D laser speckle blood flow imager. In a fiber-optic laser blood flow meter, the incident point and the light receiving point are at the same point, which is the same as the measurement depth becoming shallow. The measured depth of human skin is assumed to be less than about 1 mm from the surface [7].

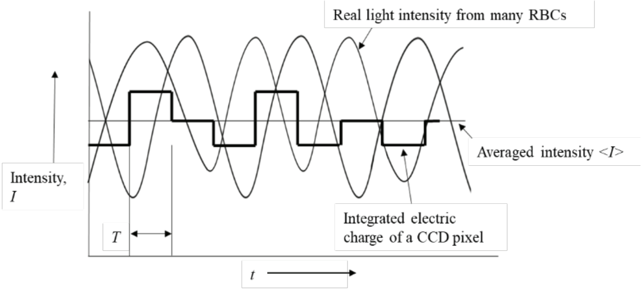

Figure 4: Intensity of a pixel when RBC number density is high

According to the instruction manual of a 2D laser speckle flowmetry, a black sponge sheet made of a chloroprene rubber foam (C4305, INOAC Nagoya, Aichi, Japan) was spread under the right hand and forearm to obtain clear blood flow images. The black sheet does not reflect the laser light, and the effect makes the blood flow images clear. The whole sequential 10 images in the back of the right hand for 10 seconds were captured by the pixel of the CCD camera simultaneously in high resolution mode (1 image/sec with image resolution 750 × 560). After recording the images, three measurement points such as f1 is a nail of index finger (diameter 1.32 cm with 50 pixels), f2 is a nail of ring finger (diameter 1.32 cm with 50 pixels) and h1 is a center of hand (diameter 5.29 cm with 200 pixels) were selected and circled using the region of the interest (ROI) as shown in Figure 5. The blood flow volume values were analyzed from every ROI using the built-in software in the blood imager.

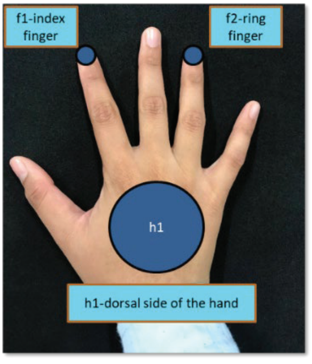

Figure 5: Measurement points in the back of the right hand

2.5 Statistical Analysis

Statistical analysis of differences in mean values of EMF and CTL groups was made by using the Wilcoxon rank-sum test (between groups) and the Wilcoxon paired signed rank test (within a group) for non-parametric data. For all comparisons, a P value less than 0.05 was considered significant.

3.0 RESULTS AND DISCUSSION

3.1 The Effects of EMF Exposure on Cutaneous Microcirculation

Blood flow volume values of 11 individuals were measured 1 to 3 times for EMF and sham exposure experiments, and mean values were calculated for each individual. Because the variability of baseline values is so great among individuals, we analyzed the change rate (%) of blood flow volume from baseline values. This can be associated with slight body movements over times. The results of blood flow volume values in the back of the right hand were shown in Figure 6. Moreover, the color zone indicates 15 minutes duration of EMF or sham exposure. Values are expressed as mean ± SEM (n = 11 in each group).

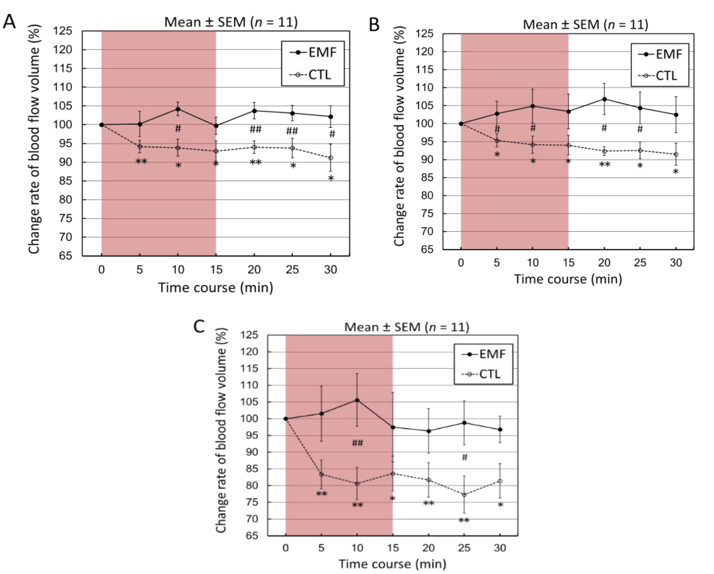

Figure 6: The time course of the change rate of blood flow volume in EMF exposure and sham control (CTL) exposure groups: A is a nail of index finger, B is a nail of ring finger and C is a central part of hand (*$P < 0.05$; **$P < 0.01$ compared with the baseline (within a group) and #$P < 0.05$; ##$P < 0.01$ compared with the CTL (between groups))

Blood flow volume values in the CTL group decreased significantly from baseline values (shown as 100%) during resting conditions. For this reason, for example, the blood flow volume was reduced by the immobility of the hand thereby inducing an ischemic condition [8].

In contrast, EMF exposure did not significantly reduce blood flow volume from baseline values during and after the EMF exposure period. There were significant differences between EMF and CTL groups. Thus, EMF exposure significantly prevented the decrease in blood flow volume. Together with the previous results of the increased blood flow velocity induced by EMF [4], we speculate on the following mechanism.

3.2 Plausible Biophysical Mechanism of AC EMF for Hemodynamics

Transcranial magnetic stimulation (TMS) has been used to evaluate the relationship between nerve stimulation and blood flow increase [9-10]. However, in contrast, the decreased blood flow induced by TMS has been reported [9-10]. Thus, the effects of TMS on blood flow modulation are variable depending on the stimulation area and stimulation conditions such as stimulation frequency, intensity, and duration. The optimal stimulation conditions have not been established.

The eddy current density (*J*) is based on the Lenz's law, and in this study the estimated values of eddy current for an AC EMF of B_{max} 180 mT were calculated using the following equation [11]:

$$J = \pi \times f \times \sigma \times Br \tag{2}$$

where f is the frequency (Hz), σ is the conductivity of living tissue (S/m), the B is the magnetic flux density (T), and *r* is the electromagnetic coil radius (m). Measurement results of each parameter were that $f = 50$ Hz, $\sigma = 0.7$ S/m in blood [11-13], $B = 0.005$ T (6 cm depth from the surface of the EMF exposure device) to 0.18 T (on the surface), and $r = 5 \times 10^{-2}$ m. The current density in blood has not been estimated and discussed in the context of TMS and EMF. The calculated values of J were ranged from 27.5 to 989.6 mA/m² in blood. Here the maximum value of ≈1 A/m² was 1/3 or less of the maximum current density of the standard TMS method used for brain stimulation to gray and white matters, i.e., the peak values for coil positions are 2.82 A/m² in the dorsal lateral prefrontal cortex and 3.57 A/m² in the motor strip [14]. As the main biophysical mechanism of EMF, EMF-induced eddy currents may be sufficient to induce changes in blood flow volume, presumably through neural stimulation, but the values of current density are under those of the standard TMS method.

According to the report from World Health Organization (WHO), the biological effects of ELF-EMF-induced eddy current density ranging 10 to 100 mA/m² have been well established, which can produce faint flickering visual sensations (magnetophosphenes), possible nervous system effects, and facilitation of bone fracture reunion [15]. In the case of the eddy current density ranging 100 to 1000 mA/m², the eddy current density in this range can influence neuron excitability [15]. It is speculated that the thresholds for stimulation of sensory receptors and of nerve and muscle cells may also lie in this range [15]. However, this raises the concern that unexpected stimulation of muscle tissue can result in a dangerous response, and that changes in excitability or direct stimulation of central nervous tissue can result in adverse changes in mental function [15].

3.3 Plausible Biochemical Mechanism of AC EMF for Hemodynamics

The plausible biochemical mechanisms of AC EMF for the promotion of hemodynamic responses have been reported in experimental studies [16-19]. Most importantly, the inhibitory effect of AC EMF on acetylcholinesterase (the lytic enzyme of acetylcholine) was observed in the magnetic flux density of 0.74 mT or more [17]. For additional pathways, the exposure of HaCaT cells to AC EMF (50 Hz, B_{rms} 1 mT, for 3 h) increased inducible and endothelial nitric oxide synthase (NOS) expression levels [18]. These AC EMF-dependent increased expression levels were paralleled by increased NOS activities and increased nitric oxide (NO) production [18]. Moreover, a recent clinical study reported that 40 Hz EMF at 7 mT for 15 min/day significantly increased 3-nitrotyrosine and nitrate/nitrite levels in post-stroke patients, and improved functional and mental status [19]. Regarding the physiological mechanism of NO, it has been reported that NO formed via endothelial and neuronal NOS causes vasodilation, hypotension and increased blood flow [20]. Therefore, in this context, AC EMF-induced NO production could promote blood circulation.

3.4 Plausible Integration Mechanism of AC EMF Effects for Pain Relief and Recovery of Muscle Fatigue

When given both plausible biophysical and biochemical mechanisms of the effects of AC EMF on pain relief and recovery of muscle fatigue, we speculate the following integration mechanism as shown in Figure 7. Here, we put forward a hypothesis that the eddy current induced by AC EMF could play a crucial role in the initiation of a series of the physiological response processes involved in activation of parasympathetic nerve and hemodynamic responses via cholinergic pathways together with NO-mediated vasodilation. In general, blood circulation and microcirculation play a pivotal role on transporting the nutrients and growth substances as well as eliminating the metabolic waste products including endogenous pain producing substances that induce muscle hardness and pain [21].

Thus, these results imply that the physiological impact of EMF-facilitated blood circulation may be helpful in the elimination of the metabolic waste products. In addition, EMF can promote wound healing by transporting the nutrients and growth substances. Further studies are needed to investigate EMF-based therapeutic applications and to elucidate the underlying mechanisms of EMF effects on pain relief and recovery of muscle fatigue.

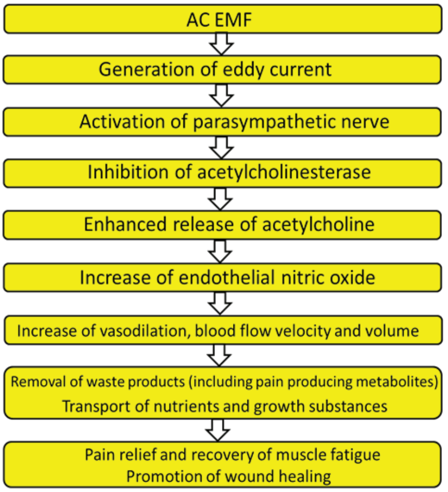

Figure 7: Plausible integrated mechanisms of AC EMF effects on pain relief and recovery of muscle fatigue

4.0 CONCLUSION

The AC EMF can improve blood flow volume in cutaneous tissue under ischemic conditions. The physiological role of EMF-promoting blood circulation may help to eliminate the metabolic waste products that induce muscle hardness and pain. As the main biophysical mechanism of EMF, EMF-induced eddy currents may be sufficient to induce changes in blood flow, presumably through neural stimulation.

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