

Geomagnetic field modulates artificial static magnetic field effect on arterial baroreflex and on microcirculation

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Abstract Spreading evidence suggests that geomagnetic field (GMF) modulates artificial magnetic fields biological effect and associated with increased cardiovascular morbidity. To explore the underlying physiological mechanism we studied 350 mT static magnetic field (SMF) effect on arterial baroreflex-mediated skin microcirculatory response in conjunction with actual geomagnetic activity, reflected by K and K_p indices. Fourteen experiments were performed in rabbits sedated by pentobarbital infusion (5 mg/kg/h). Mean femoral artery blood pressure, heart rate, and the ear lobe skin microcirculatory blood flow, measured by micro-photoelectric plethysmogram (MPPG), were simultaneously recorded before and after 40 min of NdFeB magnets local exposure to sinocarotid baroreceptors. Arterial baroreflex sensitivity (BRS) was estimated from heart rate/blood pressure response to intravenous bolus injections of nitroprusside and phenylephrine. We found a significant positive correlation between SMF-induced increase in BRS and increment in microvascular blood flow (Δ BRS with Δ MPPG, $r=0.7$, $p<0.009$) indicated the participation of the arterial baroreflex in the regulation of the microcirculation and its enhancement after SMF exposure. Geomagnetic disturbance, as opposed to SMF, decreased both

microcirculation and BRS, and counteracted SMF-induced increment in microcirculatory blood flow (K -index with Δ MPPG; $r_s=-0.55$, $p<0.041$). GMF probably affected central baroreflex pathways, diminishing SMF direct stimulatory effect on sinocarotid baroreceptors and on baroreflex-mediated vasodilatory response. The results herein may thus point to arterial baroreflex as a possible physiological mechanism for magnetic-field cardiovascular effect. It seems that geomagnetic disturbance modifies artificial magnetic fields biological effect and should be taken into consideration in the assessment of the final effect.

Keywords Baroreflex sensitivity · Geomagnetic disturbance · K index · Cardiovascular risk

Introduction

Increasing evidence suggest that naturally occurring, time-varying environmental magnetic fields are associated with biological and clinical events (Presman 1970; Ronald 1994; Baeovsky et al. 1997; Ghione et al. 1998; Stoupel 1999; Stoupel et al. 2002; Stoilova and Zdravev 2000; Cornélissen et al. 2002; Gmitrov and Ohkubo 2002a,b; Gmitrov and Gmitrova 2004). The largest time-varying field component, arising intermittently from solar flares and other solar activity, generates magnetic storms, which, through modulation of the solar wind, can cause magnetic anomalies in the Earth's environment. In general, at any location a diurnal variation with an amplitude of some tens of nT occurs; additionally, magnetic storms cause field variations with amplitudes up to hundreds of nT that can last several days. The diurnal variation of the naturally occurring, time-varying geomagnetic field (GMF)—that is, the GMF

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disturbance level—is measured by each local geomagnetic observatory as the K index (Skiles 1985; Kowalski et al. 1988). The K index is a quasilogarithmic measure of the maximum disturbance horizontal component in steps of 0–9 for 3 h (UTC). Normally, its values lie between 1 and 3, 0 representing an unusually quiet period. K values of 4–9 mark magnetic storms. The conversion table from maximum fluctuation (nT) to K index varies for different geomagnetic observatories ($K=0$, 0–5 nT; $K=1$, 5–10 nT; $K=2$, 10–20 nT; $K=3$, 20–40 nT; $K=4$, 40–70 nT; $K=5$, 70–120 nT; $K=6$, 120–200 nT; $K=7$, 200–330 nT; $K=8$, 330–500 nT; $K=9$, >500 nT, for the Boulder magnetometer), depending on geomagnetic latitude. The K_p , or planetary 3-h range index, is defined to be the arithmetic mean of the K values of 13 selected worldwide geomagnetic observatories (Mayaud 1980). Several biological and clinical phenomena have been reported to be associated with geomagnetic disturbances. During “storm time”, changes in the magnetic field, in particular small pulsations of field accompanying the geomagnetic storm, have been shown in recent times to affect human health adversely, especially in persons who are prone to cardiovascular complaints. Arterial hypertension, increased incidences of myocardial infarction, cardiovascular morbidity, and mortality have been observed. Such cases show maximum frequencies of occurrence whenever the disturbance level of GMF, as indicated by the K index, peaks (Ghione et al. 1998; Stoupelet 1999; Stoupelet et al. 2002; Cornélissen et al. 2002).

To explore the mechanisms of the GMF adverse effect on the cardiovascular system, we investigated the impact of the increased geomagnetic activity, reflected by K and K_p indices, on microcirculatory blood flow in conjunction with one of the most important cardiovascular risk factors—the arterial baroreflex sensitivity (BRS) in normal conditions, and after sinocarotid baroreceptors exposure by artificial static magnetic field.

Arterial baroreceptors play a key role in blood-pressure control, located in the aortic arch and carotid sinuses, normally respond to stretch by generating impulses via afferents to vasomotor and cardiopulmonary centers in the brainstem, promoting parasympathetic and restrain sympathetic activity (Creager and Creager 1994). The arterial baroreflex results in negative feedback regulation of arterial pressure, exerting a buffering influence on blood-pressure variations. A close association was also found between BRS and microcirculation *per se* (Bernardi et al. 1997; Gmitrov 2004). Arterial baroreflex modulating the sympathetic drive to different organs significantly affects the continuously rhythmic changes in microvessel diameter and blood flow (Bernardi et al. 1997).

Previously we found in conscious rabbits and in rabbits sedated by pentobarbital infusion that artificial static

magnetic field (SMF) locally applied to sinocarotid baroreceptors, compared with sham magnet exposure, significantly increased BRS and evoked vasodilatory responses in the ear lobe cutaneous microcirculation (Gmitrov et al. 1995; Gmitrov and Ohkubo 2002a,b). On the other hand, GMF disturbance, as opposed to SMF, decreased both microcirculation and BRS (Gmitrov and Ohkubo 2002a,b; Gmitrov and Gmitrova 2004; Gmitrov 2005). The goal here was to investigate SMF- and GMF-interrelated impact on arterial baroreflex competency to regulate microcirculatory blood flow. The hypothesis was that GMF probably modify SMF effect on arterial baroreflex-mediated microcirculatory response.

Materials and methods

Animals

Fourteen experimental runs (one experiment daily) were performed using adult Japanese domestic white male rabbits, weighing 3.5–4.2 kg (Nihon Ikagaku Shizai, Tokyo, Japan) with sinocarotid baroreceptors subjected to exposure with SMF. The rabbits were given free access to laboratory chow (RM4; Funabashi Nohjoh, Chiba, Japan) and tap water, and were housed in a room with a 12-h light/dark cycle at a temperature of $22.5 \pm 0.5^\circ\text{C}$ and a relative humidity of $50 \pm 5\%$. All the procedures conform with the “Guide for the Care and Use of Laboratory Animals” published by the US National Institute of Health (NIH publication no. 85-23, revised 1996) and Japanese National Ethics Committee guidelines. The rabbits were anesthetized with sodium pentobarbital (Nembutal Sodium Solution; Abbott Laboratories Co., Ltd., Chicago, IL, USA), 30 mg/kg, i.v., supplemented later as needed to maintain deep anesthesia. For mean arterial blood pressure (MAP), heart rate (HR) and arterial baroreflex monitoring, a polyvinyl catheter was introduced into the femoral artery. The catheter was tunneled subcutaneously to the back of the animals, filled with 0.9% NaCl solution containing heparin 2,000 U/ml, and plugged with a polyvinyl plug. Every day the rabbits were brought to the laboratory for flushing the catheter. The time of the experiments was chosen randomly from 10 a.m. to noon local time.

Baroreflex assessment

BRS testing was performed using the method of intravenous bolus injections of a small dose of vasoactive drug (Parati et al. 2000). To elicit reflex changes in HR in response to changes in blood pressure, bolus injections of sodium nitroprusside (1.0, 3.0, 10.0, and 30.0 $\mu\text{g}/\text{kg}$, sodium pentacyanonitrosylferrate (III) dihydrate; Wakopure

Chemical Industries Co., Ltd., Japan) and phenylephrine (0.3, 1.0, 3.0, and 10.0 $\mu\text{g}/\text{kg}$); (Neo-Synesis; Kowa Inj. Co., Ltd., Japan) were alternatively injected intravenously in increasing doses (Hof et al. 1991). Nitroprusside was administered first, followed by phenylephrine. The injection technique was strictly standardized. The active drug was first instilled into the catheter and then flushed in as a single bolus with 1.0 ml isotonic NaCl solution. Pressure ramps were applied at 3-min intervals for all doses, except for the last interval between nitroprusside (30.0 $\mu\text{g}/\text{kg}$) and phenylephrine (10.0 $\mu\text{g}/\text{kg}$), when the interval was 5 min. After each bolus, arterial blood pressure was allowed to return to its previous resting level before the next dose was given.

Data were used only when animals were calm, resting, and undisturbed. Peak responses of MAP and HR to each dose were measured. A regression analysis of the HR effects induced by the MAP changes was carried out for each dose–response curve separately for both drugs (BRS for nitroprusside, BRS_{Ni} and BRS for phenylephrine, BRS_{Ph}) (Guo et al. 1982; Hof et al. 1991), yielding the slope (beats/min/mm Hg) of each response. The slope of the linear regression line comparing two variables (regression coefficient) represents the gain in BRS expressed as beats/min/mm Hg (Korner et al. 1972; McDowell et al. 1994). Average correlation coefficients were >90%. To minimize the possible sources of variation during the entire experiment, (1) fluctuations in responsiveness within the same animals (e.g. modulated by the magnitudes of the resting blood pressure and HR baseline preceding the first, control and the second BRS test after SMF exposure), and (2) systemic differences in the responses of the various rabbits in a group, the gain from percentage changes of the MAP and HR was calculated. Peak responses of MAP and

HR were expressed as percentages of the resting values preceding each pair of pressure and depressor drug injections. The gain of the HR response was calculated as $\Delta\text{HR}/\Delta\text{MAP}$, where HR and MAP are percentages of resting and plateau values (Korner et al. 1972).

Measurement of the skin microcirculatory blood flow

For microcirculatory research, intravital microscopy by Rabbit Ear Chamber (REC) and microphotoelectric plethysmography (MPPG) were used.

The REC is a transparent round table chamber (diameter=6.4 mm) made of a disk of acrylic resin with a fully ingrown subcutaneous tissue with microvascular net, which is the subject of research. The methods for installation of REC have been published in detail (Okano et al. 1999).

MPPG is a simple noninvasive technique for the study of relative changes in peripheral circulation. MPPG is a modification of a noninvasive technique of photo(electric) plethysmography. MPPG was developed to monitor temporal changes in the microvascular blood flow in various cutaneous tissues by microscopic observation of intravital microcirculatory images displayed on a video monitor and on a photoconductive cell (Fig. 1). Its principle is based on the amount of light absorption by the hemoglobin content through transparent microvascular net ingrown in the REC detected directly by a photoconductive cell. The microvascular alternations are then transformed into an electrical signal and traced as MPPG dc profiles with a data recorder/analyzer (Asano and Brånemark 1972). The MPPG can be focused repeatedly on the whole image of a microcirculation or on a single vessel for the identical microscopic

Fig. 1 General setup of the experiment for exploring the SMF effect on baroreflex-mediated microcirculatory responses in rabbit ear lobe skin microcirculation using the microphotoelectric plethysmography (MPPG) system for intravital microscopy through a rabbit ear chamber. *MIC*, the objective of the microscope; *L*, light, halogen lamp; *C*, camera; *Polygraph*, biological amplifier and polygraph; *TV*, TV monitor with video tape recorder; *PC*, data analyzer; *MAP*, mean arterial blood pressure; *HR*, heart rate

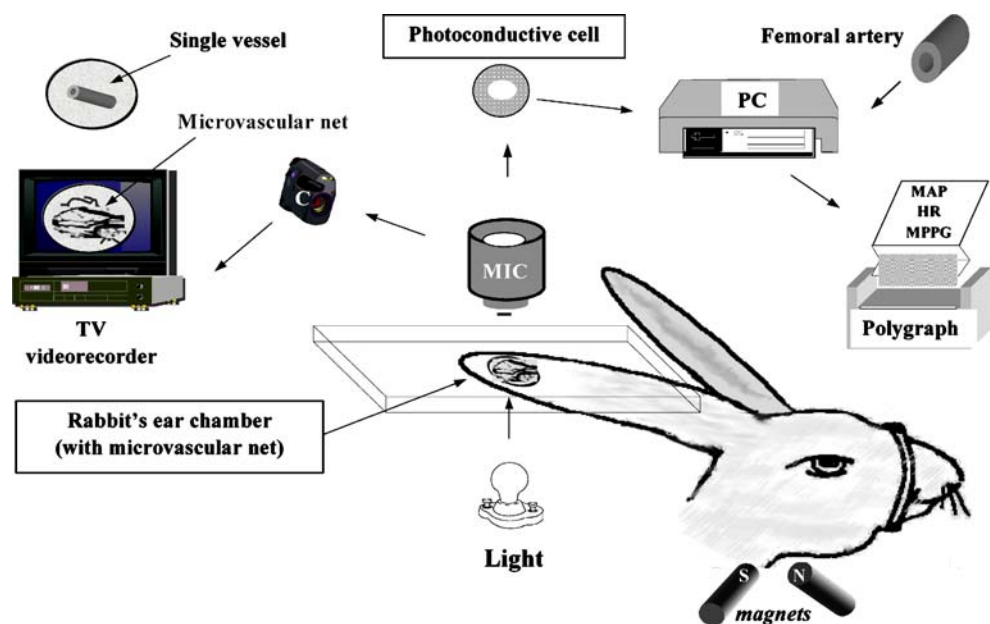


image. Therefore, MPPG mean dc levels can plot even very delicate rhythmic fluctuations in microcirculation (Okano and Ohkubo 2001; Gmitrov et al. 2002) more accurately and precisely. Close positive correlations have been found between MPPG profiles and a cross-sectional view of an artery (Okano and Ohkubo 2001). The MPPG profiles were registered continuously for the whole image of a microcirculation with the same microscopic magnification (100 \times) for all experiments. The temperature was monitored by a thermistor (MGA-III-219, Nihon Kohden Co., Tokyo, Japan) placed in close proximity to the REC, and was held constant at 23°C during the entire experiment. The registration of the MPPG was accompanied by simultaneous intravital microscopy of the explored microvascular networks (Figs. 1 and 2).

The methods of BRS testing and the MPPG technique have been published in detail (Okano and Ohkubo 2001; Gmitrov et al. 2002, Gmitrov and Ohkubo 2002a,b).

Experimental procedure

Rabbits were carefully conditioned to avoid any reaction of fear during the actual experiment, and lay prone in a specially constructed metal drum. The upper part of the nose and the upper and lower jaws were rigidly inserted into a small ring attached to the anterior part of the drum to stabilize the head, which was out of the drum (Fig. 2). The rabbits in the drum were wearing an eye mask, excluding as much light as possible, to calm them (Gmitrov and Ohkubo 2002a,b). To minimize the influence of discomfort and immobilization stress on BRS, rabbits were sedated by infusion of pentobarbital (5 mg/kg/h) during the entire 120-min experiments. The ear lobe was attached to the acrylic observing stage of the microscope, using plastic surgical adhesive tape strips to prevent any changes in the position of the REC during the entire experiment. Mean femoral artery blood pressure, HR and the blood flow in skin microvascular network of the ear lobe (estimated by MPPG) were simultaneously recorded with a polygraph (Nihon Kohden Corp., Tokyo, Japan) (Figs. 1, 3) and calculated using a data analyzer (DAA-110B; Kyowa Electronic Instruments Co., Ltd., Tokyo, Japan), with a sampling time of 200 ms. Blood pressure and heart rate variability were quantified electronically from femoral artery blood pressure fluctuations as the standard deviation (SD) of the average MAP and HR.

The first measurement of BRS was made 15 min after the beginning of the experiment (Fig. 3). At 50 min in a cylindrical Nd₂-Fe₁₄-B alloy magnets (8 coin-shaped magnets stuck together, Neomax, PIP Tokyo Ltd., Tokyo, Japan), 23 mm in diameter and 4 cm in length with flux density of 500 mT in the middle of the pole face surface, were carefully positioned with opposite poles under the

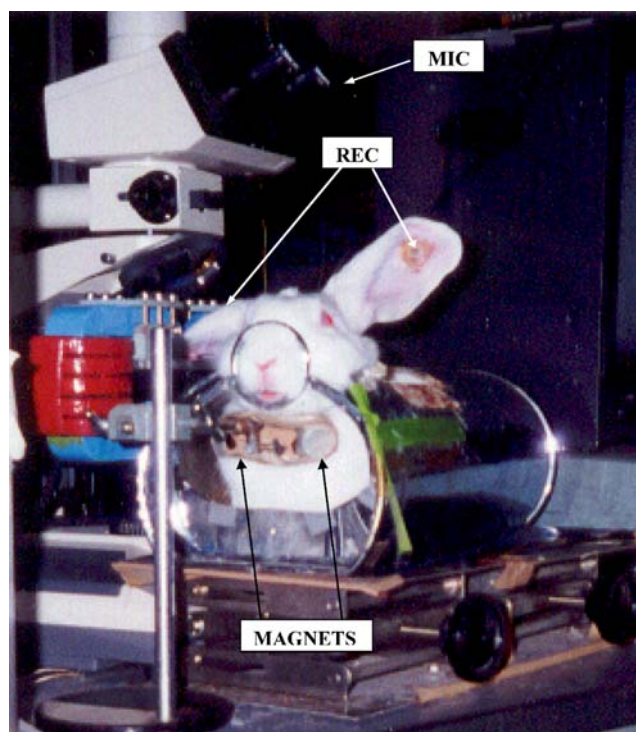


Fig. 2 A photograph of the experimental setup. The rabbit, trained to accept restraint calmly, was inserted into a metal drum with its neck and head out. The head was fixed between the metal ring and the drum, and then NdFeB magnets with opposite poles hold by manipulators were carefully positioned under sinocarotid baroreceptors in the sinocarotid triangle of the rabbit's neck. The right ear with a rabbit ear chamber (REC) (REC is visible on the left free ear) was positioned under the objective of the microscope (MIC) for simultaneous intravital observation of the microvascular networks and for MPPG registration during the entire experiment

right and left carotid sinus. To avoid any pressure on the rabbit's neck, magnets were held by manipulators at an angle of 110° to each other, just touching the closely trimmed hair of the neck under the sinocarotid baroreceptors, and were directed apart from the location of the heart or the brain (Figs. 1, 2). The field at the site of the baroreceptors, which were situated about 0.5 cm from the pole faces, was 350 mT. SMF gradient was 30 T/m. The field intensity in the heart and brain was almost the same as the background GMF intensity at the laboratory. After 40 min of SMF exposure (90 min into the experiment), a second measurement of BRS was made (Fig. 3). A comparison of BRS before and after 40 min of SMF exposure was then made. The analysis of MAP, HR and MPPG followed. To exclude the direct effect of nitroprusside and phenylephrine on MAP, HR and skin microvascular blood flow, hemodynamic measurements preceded BRS testing. The 0–15 min of the experiment was considered as a control value, and was compared with data during SMF exposure (50–90 min) (Fig. 3).

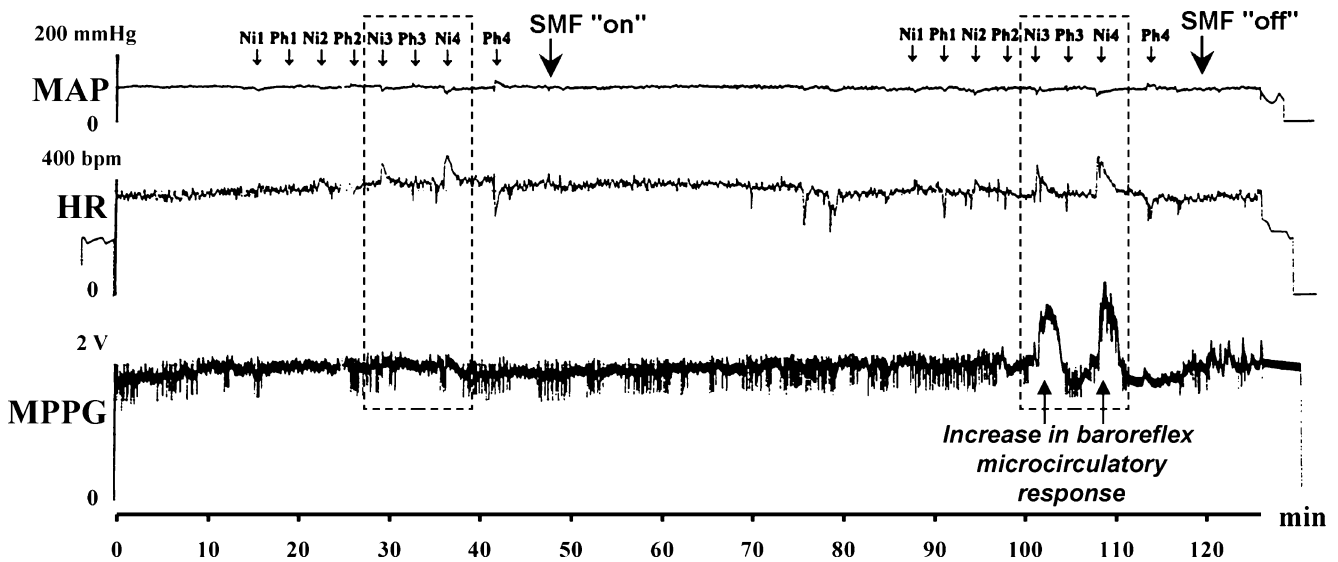


Fig. 3 Recordings following local action of 350 mT static magnetic field (SMF) on sinocarotid baroreceptors. MAP, mean arterial blood pressure; HR, heart rate; MPPG, microphotoelectric plethysmography; SMF "on", onset of SMF exposure; SMF "off", cessation of SMF exposure. (Ni1, 1.0; Ni2, 3.0; Ni3, 10.0; Ni4, 30.0), (Ph1, 0.3; Ph2, 1.0; Ph3, 3.0; Ph4, 10.0), doses of nitroprusside and phenylephrine ($\mu\text{g}/\text{kg}$) respectively, given by bolus injection for BRS testing. After SMF exposure baroreflex mediated HR increase, on response to the same dose and hypotensive with control - pre SMF exposure bolus

injections of nitroprusside (Ni3, Ni4), was significantly larger, indicating the increment in BRS_{Ni} for nitroprusside. In addition a notable rise of microvascular blood flow (MPPG) was observed, copying HR swing out, responding to equal-hypotensive with pre SMF exposure nitroprusside (Ni3, Ni4). This indicates the increment of the baroreflex stimulus-induced microcirculatory response for nitroprusside. There was no significant change in baroreflex-mediated HR or microcirculatory response after bolus injections of phenylephrine

The flux density of the magnetic field was measured with a gauss/tesla meter (Model 4048; F.W. Bell, Division of Bell Technologies, Orlando, FL, USA). The accuracy of the Gaussmeter probe ($4 \times 1 \times 30$ mm) indicated by the manufacturer was 0.01 mT. The field intensity without magnetic field exposure did not differ from the background intensity of the geomagnetic field at the laboratory. The values of GMF disturbance as reflected by K and K_p were kindly supplied by the nearby Kakioka Magnetic Observatory. The ambient DC GMF in the laboratory was

46–47 μT , assessed from the International Geomagnetic Reference Field (IGRF) 1995 model (Data Analysis Center for Geomagnetism and Space Magnetism, Graduate School of Science, Kyoto University, Kyoto, Japan) Table 1.

Statistical analysis

A paired t -test or Wilcoxon signed rank test was used, as required, to estimate changes in measured parameters before and after SMF exposure (Table 2).

Table 1 Variable definitions

Variable	Definitions
BRS	Baroreflex sensitivity, the measure of the arterial baroreceptor functional state; = change in HR/change in MAP after challenge
BRS_{Ni}	Baroreflex sensitivity for nitroprusside; = increase in HR/decrease in MAP after i.v. nitroprusside bolus, represents prevalingly sympathetic branch of the baroreflex heart rate response
BRS_{Ph}	Baroreflex sensitivity for phenylephrine; = decrease in HR/increase in MAP after i.v. phenylephrine bolus, represents prevalingly vagal branch of the baroreflex heart rate response
GMF	Geomagnetic field
HR	Number of heart beats each minute
K, K_p	The indices of the GMF activity
MAP	Mean arterial blood pressure, the average pressure exerted by the blood on the arterial walls
MPPG	A noninvasive technique for the study of relative changes in microcirculatory blood flow based on the amount of light absorption by the hemoglobin content throughout transparent microvascular net measured by a photoconductive cell
REC	A transparent round table chamber (diameter = 6.4 mm) made of a disk of acrylic resin with a fully ingrown subcutaneous tissue with microvascular net, which is the subject of MPPG measurements
SMF	Static magnetic field

Table 2 Static magnetic field effect on hemodynamics

Parameters	MPPG (V)	BRS _{Ni} (bpm%/mmHg%)	MAP (mmHg)	MAP SD (mmHg)	HR (bpm)	HR SD (bpm)
Control (n=14)	1.52±0.13	0.94±0.15	107±4.2	2.6±0.18	284±9.8	9.9±0.89
SMF exposure (n=14)	1.9±0.21; <i>p</i> <0.022	1.6±0.28; <i>p</i> <0.002	100±3.6; <i>p</i> <0.007	3.5±0.3; <i>p</i> <0.036	293±6.2; <i>p</i> <0.28	12±1.1; <i>p</i> <0.07

MPPG, microcirculatory blood flow measured by microphotoelectric plethysmography; BRS_{Ni}, arterial baroreflex sensitivity for nitroprusside; MAP, mean arterial blood pressure; HR, heart rate; MAP SD, blood pressure variability measured by mean arterial blood pressure standard deviation; HR SD, heart rate variability measured by mean HR standard deviation

The relationship between arterial baroreflex and microcirculation was analyzed estimating the association between SMF induced change in baroreflex sensitivity ($\Delta\text{BRS}=\text{BRS}_{\text{afterSMF}}-\text{BRS}_{\text{priorSMF}}$) and in microcirculatory blood flow ($\Delta\text{MPPG}=\text{MPPG}_{\text{afterSMF}}-\text{MPPG}_{\text{priorSMF}}$), using Pearson product moment correlation (Table 3, Fig. 4).

To measure GMF impact on the SMF-evoked microcirculatory effect, we analyzed the association between SMF-induced change in microvascular blood flow (ΔMPPG) with actual geomagnetic activity reflected by *K* indices, using the Spearman rank order correlation (Table 3).

To estimate GMF influence on the SMF-induced microcirculatory effect in conjunction with arterial baroreflex, we analyzed the interaction between BRS, blood pressure variability (MAP SD) and microcirculatory blood flow (MPPG), before and after SMF application, in the condition of low and high geomagnetic activity. A repeated measures multifactorial ANOVA was used, followed by a multiple pair-wise comparison procedure (Tukey Test) (Fig. 5). The section of the experimental run was determined as the first factor with levels: (a) control, prior and (b) exposure, measurements after SMF application. The second factor consisted of GMF activity with levels: (a) measurements in the condition of low GMF activity, and (b) high GMF activity. Low GMF activity was defined with actual *K* index below its median (1.5) (*K*=1), high geomagnetic activity above the median (*K*=2–5). The third factor consisted of the types of interacting parameters during corresponding control (prior SMF) or SMF exposure conditions (Fig. 5).

Data are presented as mean ± standard error of the mean. A *p* value<0.05 was considered as statistically significant.

Results

We found that 350 mT SMF local exposure to sinocarotid baroreceptors significantly decreased blood pressure, and increased microcirculatory blood flow (MPPG), BRS for nitroprusside and blood pressure variability (MAP SD) (Table 2). We did not find a significant change in BRS after SMF exposure when it was measured by the phenylephrine method (BRS_{ph}, prior to SMF, 0.81±0.09 vs BRS_{ph} after SMF exposure, 0.90±0.13 bpm%/mmHg%, *p*=0.24).

A significant positive correlation was found between the degree of the SMF-induced increase in BRS_{Ni} and the increment in MPPG ($\Delta\text{BRS}_{\text{Ni}}$ with ΔMPPG), (Table 3, Fig. 4). This was opposite to BRS for phenylephrine ($\Delta\text{BRS}_{\text{ph}}$) and to SMF-induced change in blood pressure (ΔMAP), which did not correlate significantly with change in microvascular blood flow (ΔMPPG) (Table 3).

We also found a significant inverse correlation between the degree of the SMF-induced microcirculatory effect and increasing geomagnetic activity (*K* index with ΔMPPG), (Table 3). Furthermore, a significant interaction was found between microcirculation (MPPG), BRS_{Ni}, blood pressure variability (MAP SD), SMF exposure and the condition of low GMF or high GMF activity (Fig. 5).

Discussion

This study provides evidence that arterial baroreflexes participate in the regulation of the microcirculation of the skin (Bernardi et al. 1997; Szili-Torok et al. 2002), comprising a sophisticated “heart beat to heart beat” sensitive regulatory mechanism to adjust microcirculatory

Table 3 Correlation of the SMF-induced changes in microcirculation with actual geomagnetic activity, with SMF-induced changes in baroreflex sensitivity, and with SMF-induced changes in mean arterial blood pressure

Parameters	<i>N</i>	<i>K</i>	<i>K_p</i>	$\Delta\text{BRS}_{\text{Ni}}$ (bpm%/mm Hg%)	ΔMAP (mmHg)
ΔMPPG (V)	14	$r_s=-0.55, p<0.041$	$r=-0.49, p<0.069$	$r=0.7, p<0.009$	$r=-0.39, p<0.16$

ΔMPPG , SMF induced increment in microcirculatory blood flow; *K* and *K_p*, indices of geomagnetic activity; $\Delta\text{BRS}_{\text{Ni}}$, SMF induced increment in BRS; ΔMAP , SMF induced decrease in mean arterial blood pressure; *r_s*, correlation coefficient for Spearman rank order correlation; *r*, correlation coefficient for Pearson product moment correlation

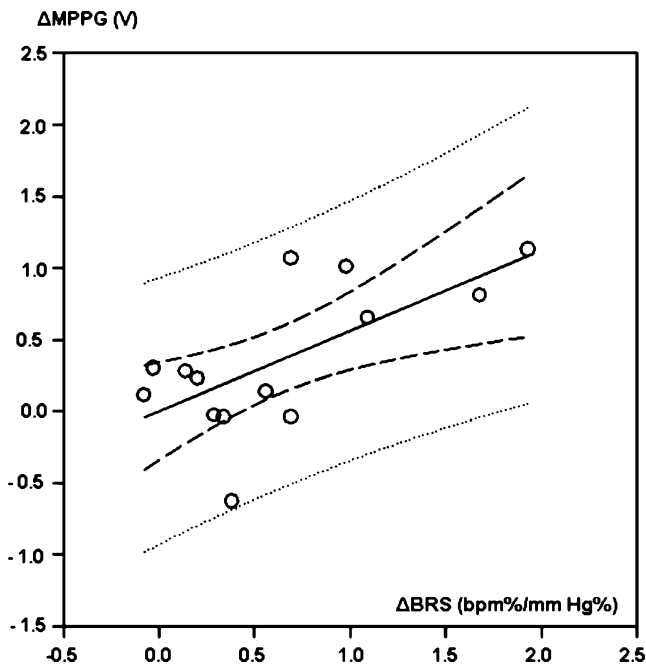


Fig. 4 The analysis of the relationship between baroreflex sensitivity and microcirculatory blood flow after SMF exposure. ΔBRS_{Ni} , SMF-induced increase in baroreflex sensitivity; $\Delta MPPG$, SMF-induced increase in microcirculation. A significant positive correlation between ΔBRS_{Ni} and $\Delta MPPG$ was found, which indicated the increment of the baroreflex-mediated microcirculatory response after SMF exposure

blood flow to actual metabolic demands. The principal finding of our study is that artificial SMF and natural GMF contrarily affect this important regulatory mechanism (Fig. 5). SMF local exposure at 350 mT to sinocarotid baroreceptors increased microcirculatory blood flow (MPPG) and BRS, as opposed to geomagnetic disturbance, which decreased both parameters (Fig. 5). Furthermore, a significant interaction was found between both magnetic fields regarding their effect on microcirculation and on BRS, modifying the final hemodynamic effect. Increased geomagnetic activity significantly attenuated SMF effect on microcirculatory blood flow and on arterial baroreflex (Table 3, Fig. 5).

We concluded that GMF probably affected central baroreflex pathways (Gmitrov and Ohkubo 2002a,b; Gmitrov and Gmitrova 2004) and interfered with SMF local stimulatory effect on sinocarotid baroreceptors diminishing SMF-evoked baroreflex-mediated microcirculatory response.

Possible interpretations

Modification of the baroreflex mediated microcirculatory response A significant positive correlation between SMF-induced increase in BRS for nitroprusside (ΔBRS_{Ni}) and increment in microvascular blood flow ($\Delta MPPG$) indicated an increase of the baroreflex-mediated microcirculatory response, reflecting the participation of the arterial barore-

flex in the regulation of the microcirculation and its enhancement after SMF exposure (Table 3, Fig. 4). Pentobarbital infusion did not participate in this effect because, as opposed to SMF, i.v. pentobarbital did not change (Gmitrov and Ohkubo 2002b) or even decrease BRS (Morita et al. 1987; Yang et al. 1996; Wuliya et al. 2004).

We did not find significant association between SMF-induced change in microvascular blood flow and MAP, indicating that the fluctuations in skin blood flow are more likely the result of the skin baroreflex-mediated vascular resistance than a direct blood pressure–flow relationship (Bernardi et al. 1997) (Table 3).

The absence of significant correlation between BRS for phenylephrine (ΔBRS_{Ph}) and SMF-induced change in microvascular blood flow ($\Delta MPPG$) is explained by differential excitation of the baroreflex response. The phenylephrine test represents the prevailingly vagal branch of the baroreflex heart rate response, whereas the nitroprusside BRS test employs prevailingly the sympathetic branch of the baroreflex response. The differential baroreflex control of heart rate and vascular resistance in rabbits was found previously, and must be due in large part to the fact that heart rate responses are modulated by vagal as well as sympathetic neurons, whereas vascular resistance is

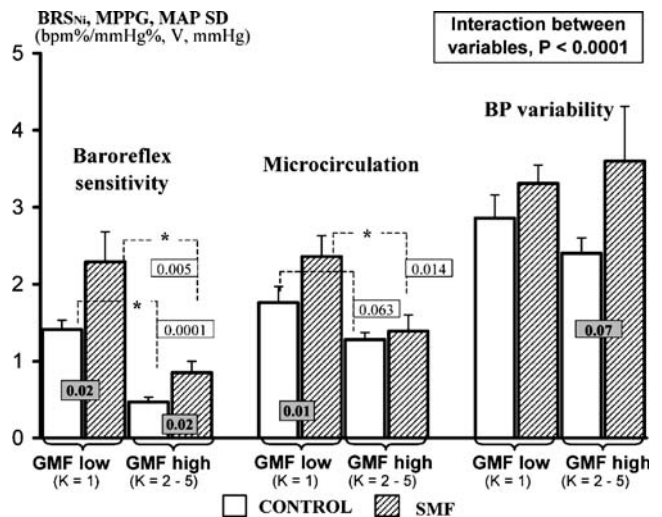


Fig. 5 SMF and GMF interrelated effect on arterial baroreflex sensitivity (*BRS*), microcirculatory blood flow (*MPPG*) and on blood pressure (*BP*) variability (*MAP SD*). *Control*, control measurements prior to SMF exposure, open bars; *SMF*, after static magnetic field exposure, hatched bars; *GMF low*, hemodynamic parameters during days with low geomagnetic activity; *GMF high*, hemodynamic parameters during days with high geomagnetic activity; * statistical significance with *p* values in the rectangles. High GMF activity compared with low GMF activity significantly decreased BRS_{Ni} and microcirculation both prior and after SMF exposure. SMF, as opposed to GMF, significantly increased BRS_{Ni} in conditions of low and high geomagnetic activity. SMF also increased microcirculatory blood flow, but only with a background of low GMF activity. A significant interaction between all variables indicates SMF and GMF interrelated impact on baroreflex-mediated microcirculatory response

predominantly regulated by sympathetic outflow (Guo et al. 1982). This may explain why BRS tested by nitroprusside, representing the sympathetic branch, displayed a larger association with SMF-induced microvascular effect than did phenylephrine, employing prevalently the vagal branch of the baroreflex response. In addition, even in the absence of hemodynamic load induced by i.v. bolus of nitroprusside and phenylephrine, SMF evoked significant change only in blood pressure and in microcirculation predominantly regulated by sympathetic outflow, and had no bradycardiac effect on heart rate, predominantly initiated by vagal outflow (Table 2). This, with regard to the fact that the modulation of the arterial baroreflex may evoke asymmetric autonomic response, and does not always in the same strength involve sympathetic and vagal efferents (Koizumi and Kollai 1981; McDowell et al. 1994; Guo et al. 1982), supported our conjecture that SMF exposure to sinocarotid baroreceptors in larger extent affected the sympathetic branch of the autonomic response.

A significant negative correlation between the increase of the microcirculatory blood flow and an increment in geomagnetic activity (K index) (Table 3) demonstrated the GMF suppressive effect on SMF-induced microcirculatory response. The significant interaction between MPPG, BRS and MAP SD with reference to control and SMF exposure conditions in high and low GMF environments (Fig. 5) pointed to the arterial baroreflex mechanism as being responsible for the GMF suppressive effect on microcirculation. SMF increased BRS during both high and low geomagnetic activity, as opposed to microcirculation, which was affected by SMF only in the condition of low geomagnetic activity (Fig. 5). This indicated the weakening of the SMF influence on baroreflex-mediated microcirculatory response in the condition of high geomagnetic activity. The consistency of the results, when analyzed in different ways (Spearman correlation and ANOVA), leads us to believe that the association found between BRS, microcirculation, SMF and GMF reflects a real effect.

There was no time during the course of our study when there were unusually geomagnetic conditions reflected by the K index ($K=0$ or 6–9). Perhaps one might expect an even larger association if the microcirculatory changes were followed over a greater range of K values occurring during geomagnetic storms with intense geomagnetic disturbance. Most likely increased geomagnetic activity suppressed brain stem and higher baroreflex regulatory centers (Gmitrov and Gmitrova 2004), counteracting SMF local stimulatory effect on arterial baroreceptors and on baroreflex-mediated microcirculatory response. The stimulatory effect of the sinocarotid baroreceptors was recognized in our previous experiments with weaker SMFs, generated by much smaller SmCo magnets (cross-sectional area 23 mm², 200 mT), positioned precisely under visual control over

operatively approached glomus caroticus in the condition of total pentobarbital anesthesia (Gmitrov et al. 1990; Gmitrov and Gmitrova 1994), and in conscious rabbits (without pentobarbital sedation, 240 mT) (Gmitrov et al. 1995). Similarly as in conscious animals, in the condition of pentobarbital anesthesia, GMF disturbance reduced SMF evoked sinocarotid baroreceptor-mediated hemodynamic response (Gmitrov and Gmitrova 1994).

We cannot also exclude the direct effect of magnetic fields on the vascular bed. The local application of SMF to the sinocarotid region probably improves sinocarotid artery stretch properties, which for imbedded baroreceptors serve as a mechanical filter that determines both the magnitude and rate of strain of the baroreceptor membrane, importantly affecting the process of the baroreceptor sensory transduction (Honig 1981). We demonstrated the SMF effect on the vascular wall previously when flux density of even lower intensity (250 mT) induced vasodilatation in rabbit-ear microvascular networks (Gmitrov et al. 2002).

As opposed to SMF, the direct effect of GMF on microcirculatory networks is less probable because of its much weaker intensity. Central arterial baroreflex regulatory mechanisms are most likely being employed here.

Relationship with other microvascular beds The relationship between cutaneous microcirculation and baroreceptor function cannot be directly translated into a broader association with other microvascular beds because the baroreflex differently modulates the sympathetic drive to different organs (Malpas 2002). Probably the effect depends on the density of the arterioles and/or the arteriovenous anastomoses, i.e. structures rich in sympathetic innervation, the main determinants of the baroreflex-mediated microvascular fluctuations (Bernardi et al. 1997) being larger for lungs and kidney, which are highly baroreflex-sensitive in contrast to the skin, which is only weakly regulated by baroreceptor activity (Malpas 2002). Probably other key organs myocardium and brain even in larger extent “baroreflex and GMF-SMF sensitive” (compared to skin) due to their larger metabolic demands, more intense blood flow by denser microvascular net with richer sympathetic innervation.

This study complements our previous research pointing to the fact that in addition to the general hemodynamic (Gmitrov and Ohkubo 2002a,b; Gmitrov and Gmitrova 2004), SMF and GMF modulate microcirculation, affecting the entire cardiovascular system through the baroreflex control mechanism; and that the actual geomagnetic background significantly modulated the 350 mT SMF cardiovascular effect. This is in accordance with previous observations on the level of cardiovascular physiology (Gmitrov and Gmitrova 1994; Gmitrov and Ohkubo 2002a,b) and on tissue and cellular level (Blackman et al. 1985; Liboff 1985) that geomagnetic activity modifies the

biological effect of artificial magnetic fields. We concluded that actual geomagnetic activity is an important modifying factor of the reproducibility of the magnetobiological experiments, and should be considered when assessing the biological effect of artificial magnetic fields.

Possible implementation

This study provides evidence concerning the impairment of cardiac autonomic regulation on days with intense solar activity, and could partially explain the adverse effect of GMF disturbance on the cardiovascular system, pointing to worsened arterial baroreflex sensitivity as the underlying physiological mechanism. Decreased BRS was found to be the most important cardiovascular risk factor associated with sympathetic activation, arterial hypertension (Malpas 2002) and increased cardiovascular mortality (La Rovere et al. 1998). The coupling of the macro- (Gmitrov and Ohkubo 2002a,b; Gmitrov and Gmitrova 2004) and microcirculatory consequences of the decreased BRS during geomagnetic disturbance may comprise an additional cardiovascular risk.

GMF activity was found earlier to decrease heart rate in adults (Otsuka et al. 2000; Cornélissen et al. 2002). A decrease in heart rate variability had been also associated with exposure to a magnetic storm in space in a transverse study on cosmonauts (Baevsky et al. 1997). These, considering that heart rate variability is closely linked with arterial baroreflex cardiovascular regulatory mechanism and its decrease is coupled with the decrease in BRS (La Rovere et al. 1998), support our results. We speculate that probably the arterial baroreflex microcirculation regulatory mechanism may participate in the previously reported modulatory effect of geomagnetic activity on capillary blood flow in IHD patients (Gurfinkel et al. 1995) suggesting human studies in the line of magnetic field arterial baroreflex-microcirculation relationship. Our results demonstrate that even during moderate “normal” fluctuations in GMF activity (a “Solar Quiet” period) the autonomic nervous system and its important constituent the arterial baroreflex are sensitive to delicate variations in GMF. A very risky period may come during the peak of each sunspot cycle when the sun goes through violent activity, resulting in long-lasting large autonomic fluctuations, with a corresponding potential clinical impact and prophylactic measures in high-risk cardiovascular conditions.

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