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Static Magnetic Field Effect on Cardiovascular Regulation: A Review

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Author's contribution

The whole work was carried by the author JG.

Review Article

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ABSTRACT

Mounting evidence suggests that environmental and occupational magnetic fields affect cardiovascular system. In this review, supported by original hemodynamic recordings - direct experimental evidence of the effect - static magnetic field (SMF) effects on arterial baroreflex cardiovascular control mechanism have been summarized. Local exposure of 120 - 350 mT SMF to sinocarotid baroreceptors in rabbits and healthy volunteers exerted a stimulatory effect on arterial baroreflex - normalized arterial blood pressure in hypertensive and hypotensive conditions, significantly increased microcirculation, heart rate variability, arterial baroreflex sensitivity and sodium nitroprusside (spontaneous nitric oxide donor) microcirculatory vasodilatory effect. The improvement of the vasodilator responsiveness to nitric oxide by baroreceptor stimulation suggested to be a new mechanism in baroreflex physiology with potential implementation in a spectrum of cardiovascular diseases where endothelial dysfunction and sympathovagal imbalance that results from a loss of baroreflex control over autonomic activity increases the risk of morbidity and mortality substantially. The modulation of the baroreflex-mediated autonomic cardiovascular control is a new concept for understanding environmental magnetic fields effect on cardiovascular system and an effective strategy to prevent their potential public health hazards.

Keywords: Baroreceptor; baroreflex sensitivity; heart rate variability; Ca^{2+} channel; microcirculation; nitric oxide.

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ABBREVIATIONS

BRS *: Arterial baroreflex sensitivity*
HR *: Heart rate*
iv *: Intravenous*
MAP *: Mean femoral artery blood pressure*
MPPG *: Microphotoelectric plethysmography*
NO *: Nitric oxide*
REC *: Rabbit ear chamber*
SMF *: Static magnetic field*

1. INTRODUCTION

Mounting evidence suggests that environmental and occupational magnetic fields affect cardiovascular system with potential public health hazards [1-5]. The establishment of strong static magnetic fields (SMFs) in medicine and industry such as magnetic resonance imaging, high-energy technologies, superconducting generators, in facilities using electrolytic processes, direct current transmission lines and in different welding technologies [6,7] generates emergent need for research targeted on cardiovascular regulatory structures as potentially the most vulnerable and magneto-sensitive parts of the cardiovascular system. Magnetic field local exposure to separate parts of richly branched cardiovascular regulatory chain may have advantage to study. By this approach it is possible to discover the most magneto-sensitive parts of the regulatory circuit that trigger cardiovascular physiology opposed to whole-body magnetic field exposure technique [8].

It is widely recognized that arterial baroreceptors play a key role in the operation of cardiovascular functions and in the reflex regulation of blood pressure under normal and pathological conditions. Arterial baroreceptors located in the carotid sinuses and aortic arch, normally respond to stretch by initiating reflexes that promote parasympathetic and restrain sympathetic activities significantly modifying heart rate, peripheral vasoconstriction and cardiac output. These reflex responses result in a powerful moment-to-moment negative feedback regulation of blood pressure reducing its lability and optimizing blood flow to meet the metabolic demands of peripheral tissues. In addition, arterial baroreflex protects heart from arrhythmias by providing appropriate rapid modulation of autonomic tone and the heart rate [9].

In this review the results of the research proposing baroreflex physiology to be a transmitter of magnetic fields effects on cardiovascular system are summarized. Sinocarotid baroreceptors suggested having magneto-sensitive properties and their magnetic stimulation to be effective therapeutic tool in cardiovascular conditions where sympathovagal imbalance and endothelial dysfunction increases the risk of morbidity and mortality substantially.

2. SMF BAROREFLEX-MEDIATED CARDIOVASCULAR RESPONSE

SMF sinocarotid baroreceptor exposure research was launched in rabbits under the condition of total pentobarbital anesthesia allowing precise positioning of the magnets with opposite poles over operatively approached glomus caroticum. 200 mT SMF generated by SmCo alloy magnets exerted an outstanding homeostatic hemodynamic effect. SMF significantly decreased mean arterial blood pressure (MAP) in the condition of arterial hypertension induced by noradrenalin intravenous (iv) infusion (-10.0% decrease), but during

arterial hypotension induced by aortic depressor nerve electric stimulation raised blood pressure effectively (+14.1% increase) (Fig. 1) [10,11]. This blood pressure normalizing property indicated activation of the arterial baroreflex cardiovascular control mechanism and derives from the main physiological purpose of sinocarotid baroreceptors to stabilize blood pressure, protecting heart and vessels from pressure overloud damage [12]. The results in total anesthesia were confirmed in conscious normotensive animals where 350 mT SMF local exposure to sinocarotid baroreceptors (Fig. 2) displayed a significant hypotensive effect (-4.8%) (Fig. 3) [13]. In conscious rabbits sedated by a low dose of iv pentobarbital infusion arterial baroreceptor blood pressure buffering was directly tested and SMF homeostatic effect on hemodynamic was confirmed. SMF reduced MAP (-6.2%) and iv phenylephrine bolus injections induced abrupt elevations in blood pressure even more effectively (-21.9%) (Fig. 4) [14]. SMF blood pressure buffering effect was coupled with increase in arterial baroreflex sensitivity (+68.8) supporting it to be an indicator of autonomic cardiovascular control and a specific measure of the baroreceptor capacity to reduce high blood pressure variability efficiently [14,15]. The concomitant increase in heart rate variability, measured by heart rate standard deviation (+20.6%) (Fig. 4), confirmed the activation of the arterial baroreflex control mechanism with potential additive cardioprotective properties [16].

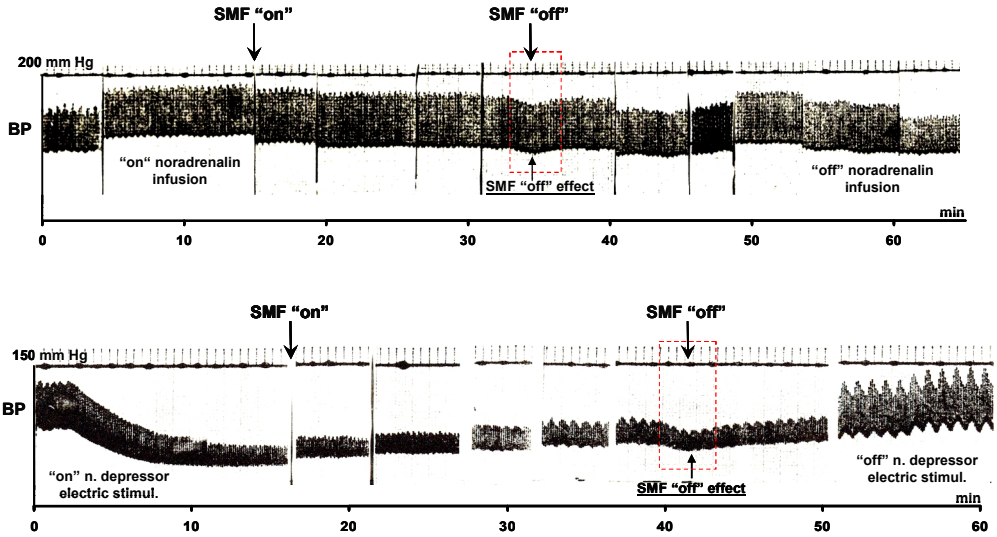

Fig. 1. ***Upper panel.*** **Example of hemodynamic recording following local action of a 200 mT static magnetic field (SMF) on sinocarotid baroreceptors under total pentobarbital anesthesia in the condition of arterial hypertension induced by noradrenalin intravenous infusion.** BP, femoral arterial blood pressure; ''on'' noradrenalin infusion, onset of noradrenalin infusion; ''off'' noradrenalin infusion, cessation of noradrenalin infusion. SMF ''on'', onset of SMF exposure; SMF ''off'', cessation of SMF exposure. A notable decrease in blood pressure after SMF exposure and a reaction on SMF removal from sinocarotid baroreceptors the "off" effect are apparent

Lower panel. **Example of hemodynamic recording following local action of a 200 mT SMF on sinocarotid baroreceptors under total pentobarbital anesthesia in the condition of arterial hypotension induced by aortic depressor nerve electric stimulation.** ''on'' n. depressor electric stimul., onset of aortic depressor nerve electric stimulation; ''off'' n. depressor electric stimul., cessation of aortic depressor nerve electric stimulation. A notable increase in blood pressure after SMF exposure and reaction on SMF removal from sinocarotid baroreceptors the "off" effect are apparent.

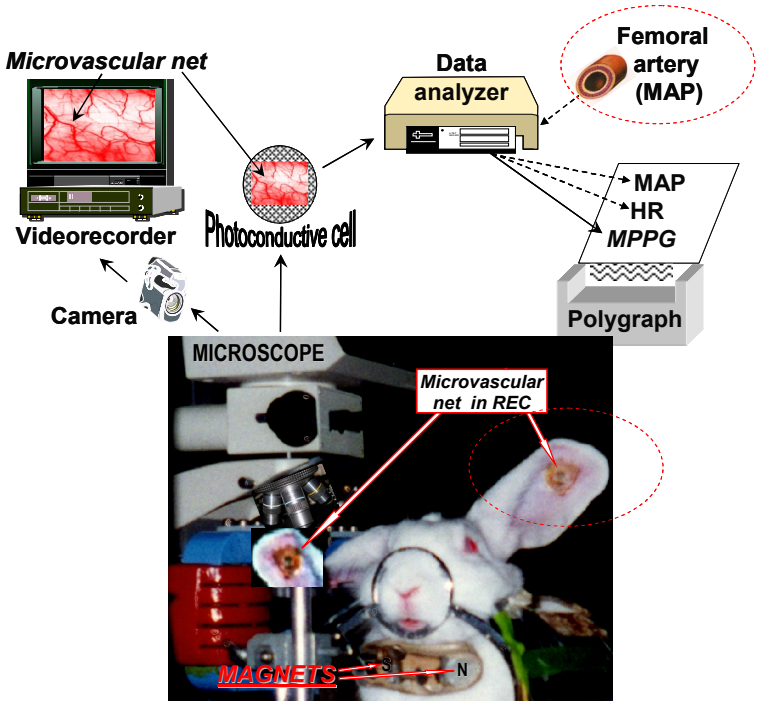

Fig. 2. Experimental set-up used to explore the effect of static magnetic field on baroreflex-mediated macro- and microcirculatory response in conscious condition. The right ear including a rabbit's ear chamber (REC) with ingrown skin micro vascular networks was positioned under the objective of the microscope for intravital observation of the microcirculation and measurement of the microcirculatory blood flow using micro photoelectric plethysmography (MPPG). Another REC is visible on the left free ear. Simultaneously with microcirculation (MPPG) mean femoral artery blood pressure (MAP) and heart rate (HR) were measured. Magnets, Nd_2-Fe_4-B alloy magnets, positioned with opposite poles under carotid sinuses; polygraph, biological amplifier and polygraph.

In some experiment in anesthetized animals a hemodynamic reaction to magnets removal from sinocarotid baroreceptors (SMF "off" effect) was observed, which manifested itself by a short term decrease in blood pressure (Fig.1). This phenomenon was also found in normotensive conscious condition where in addition to blood pressure decrease a simultaneous decrease in respiration, heart rate and cutaneous blood flow was observed (Fig. 3). This clearcut depressor and bradycardic responses are similar as those observed during sinocarotid baroreceptor direct mechanic stimulation by neck suction technique [17]. The phenomenon of SMF "off" effect profoundly supported SMF stimulatory effect on baroreceptors and indicated activation of both vagal and sympathetic components of the arterial baroreflex. Importantly, SMF stimulatory effect was confirmed in chronic experiments where a similar intensity 180 mT SMF, generated by a disc-shaped permanent $Sm_2Fe_{17}N_3$ magnet implanted in adjacent to the left carotid sinus baroreceptor region in the neck of the stroke-resistant spontaneously hypertensive rats for 5 – 8 weeks, significantly increased baroreflex sensitivity and suppressed or retarded the development of the arterial hypertension [18] (Table 1).

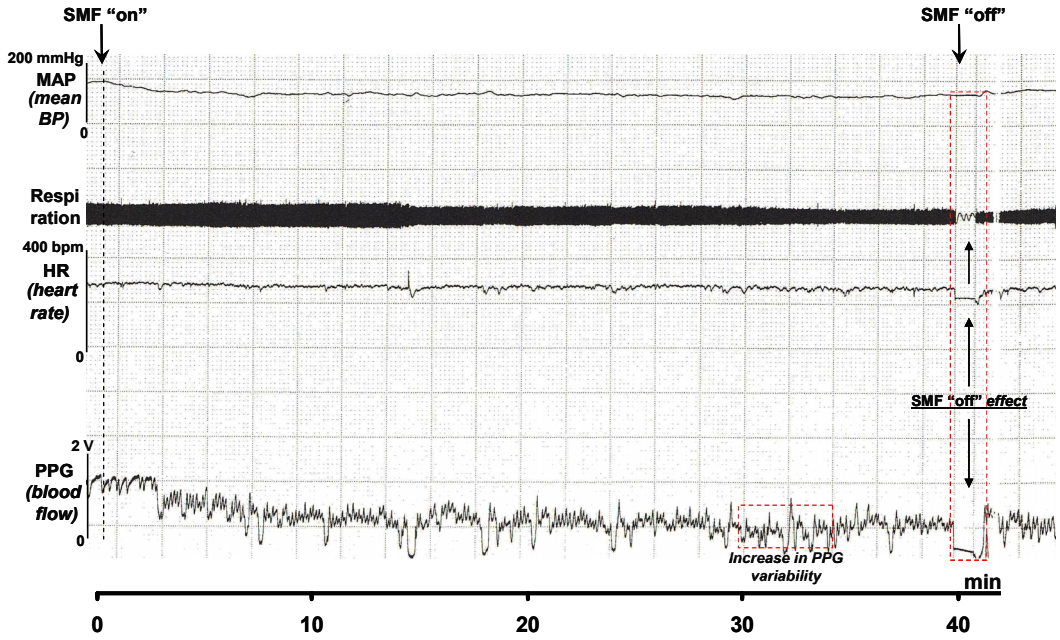

Fig. 3. Example of hemodynamic recording following local action of a 350 mT static magnetic field (SMF) on sinocarotid baroreceptors under conscious condition without pentobarbital sedation. MAP, mean ear arterial blood pressure; Respiration, respiration monitoring; HR, heart rate; PPG, photoelectric plethysmography; SMF ‘‘on’’, onset of SMF exposure; SMF ‘‘off’’, cessation of SMF exposure. A notable fall in blood pressure accompanied by increase in cutaneous blood flow (PPG) variability (reflected vasomotion) is apparent. A reaction on SMF removal from sinocarotid baroreceptors the “off” effect is obvious.

Essentially, the enhancement of the arterial baroreflex hemodynamic control extended on microcirculatory level, implementing thus the final pursuit of the cardiovascular regulatory mechanisms to improve tissues perfusion in target organs. SMF sinocarotid baroreceptor exposure evoked a significant vasodilatory effect, increasing microcirculatory blood flow (+23.0%) within cutaneous tissue of the rabbit’s ear lobe estimated by microphotoelectric plethysmography (Fig. 4). A notable increase of microvascular dilation (+163.2%) synchronized with reflex increase in heart rate in response to same dose and hypotension iv bolus of nitroprusside (Ni3, Ni4 after *versus* before Ni3, Ni4 SMF exposure) suggested baroreflex participation in microcirculatory control and its enhancement after SMF exposure (Figs. 4, 5). This was also found in steady state hemodynamic condition when a significant positive correlation between increase in baroreflex sensitivity and microcirculatory blood flow was observed [8].

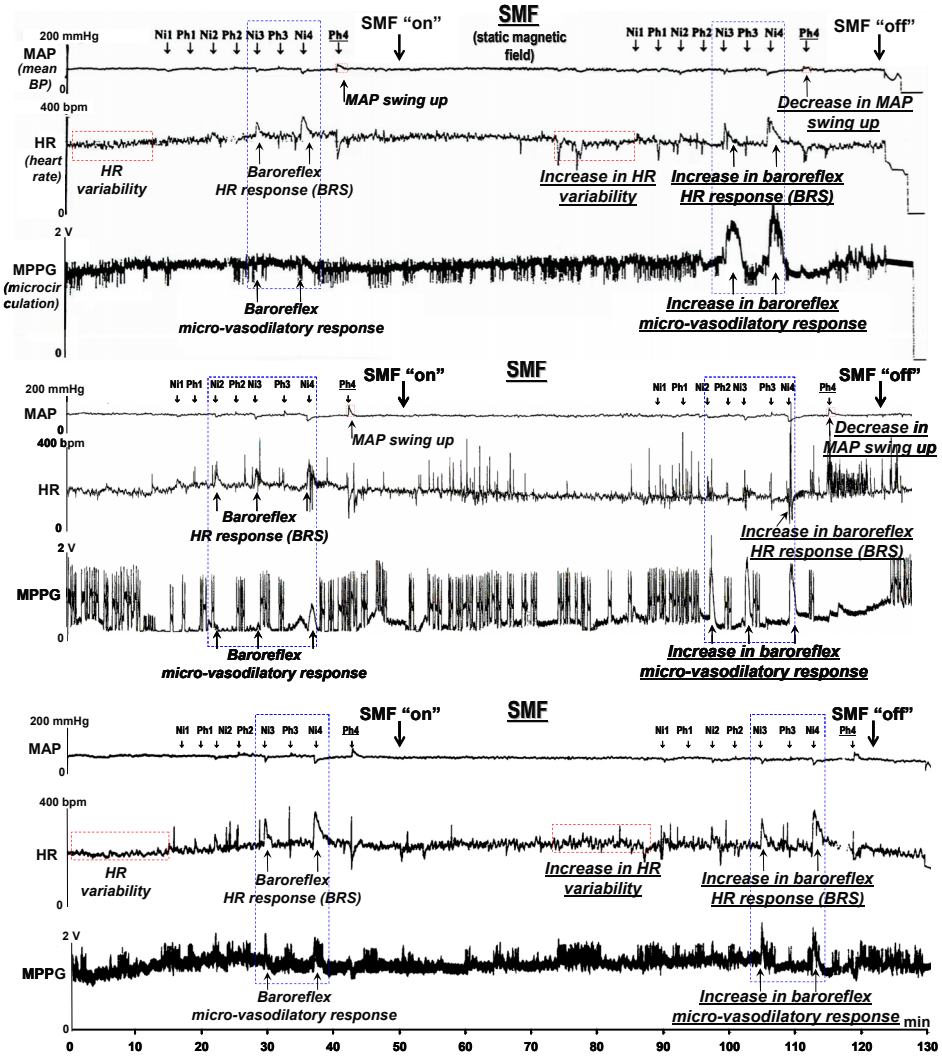

Fig. 4. ***Upper panel.*** **Example of hemodynamic recording following local action of a 350 mT static magnetic field (SMF) on sinocarotid baroreceptors under conscious condition with pentobarbital sedation.** MAP, mean femoral arterial blood pressure; HR, heart rate; MPPG, microcirculatory blood flow measured by microphotoelectric plethysmography; BRS, arterial baroreflex sensitivity; 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 sodium nitroprusside and phenylephrine (μg kg^{-1}), respectively, given by intravenous (iv) bolus injection for BRS testing. A notable increase in baroreflex heart rate and microvasodilatory response due to same dose nitroprusside on the background of gradual increase in vasodilation (MPPG) is obvious.
Middle panel. **Example for experimental run with SMF exposure.** A marcant increase in baroreflex microvasodilatory response (MPPG) after iv bolus of nitroprusside is apparent.
Lower panel. **Additional example for experimental run with SMF exposure.** A notable increase in heart rate variability is obvious.

Table 1. Static magnetic field effect on sinocarotid arterial baroreceptors

Authors	Study parameters	Experimental specimen	SMF effects
Gmitrova & Gmitrov, 1990 [10]	16 subjects, sinocarotid baroreceptors local exposure to 200 mT SMF for 30 min in the condition of arterial hypertension induced by noradrenalin intravenous (iv) infusion	Rabbits under pentobarbital anesthesia	Decrease in arterial blood pressure
Gmitrov et al., 1990 [11]	15 subjects, sinocarotid baroreceptors local exposure to 200 mT SMF for 35 min in the condition of arterial hypotension induced by right aortic depressor nerve electric stimulation	Rabbits under pentobarbital anesthesia	Increase in arterial blood pressure, heart and respiration rate
Gmitrov & Gmitrova, 1992 [30]	8 subjects, sinocarotid baroreceptors local exposure to 200 mT SMF for 40 min in the condition of arterial hypotension induced by verapamil iv infusion	Rabbits under pentobarbital anesthesia	No field effect on blood pressure, decrease in respiration rate
Gmitrova & Gmitrov, 1994 [51]	16 subjects, sinocarotid baroreceptors local exposure to 200 mT SMF for 30 min in the condition of arterial hypertension induced by noradrenalin iv infusion	Rabbits under pentobarbital anesthesia	GMF potentiated SMF hypotensive effect
Gmitrov et al., 1995 [13]	20 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min in the condition of arterial normotension	Conscious rabbits	Decrease in blood pressure and increase in cutaneous blood flow and heart rate variability
Gmitrov, 1996 [19]	15 subjects, sinocarotid baroreceptors local exposure to 120 mT SMF for 4-5 min in the condition of arterial normotension	Healthy volunteers	Increase in heart rate variability
Okano et al., 1999 [36]	22 subjects, ear skin microcirculatory network local exposure to 1 mT SMF for 10 min	Conscious rabbits	Increase in microvascular dilation under noradrenaline-induced high vascular tone and vasoconstriction under acetylcholine-induced low vascular tone
Gmitrov & Ohkubo, 2002 [52]	26 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min in the condition of arterial normotension	Conscious, sedated rabbits	SMF attenuated GMF-induced decrease in BRS
Gmitrov & Ohkubo, 2002 [31]	22 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min and verapamil iv infusion	Conscious, sedated rabbits	Verapamil infusion blocked out SMF and GMF effect on BRS
Gmitrov et al., 2002 [24]	20 subjects, ear skin microcirculatory network local exposure to 250 mT SMF for 40 min	Conscious, sedated rabbits	Increase in microcirculatory blood flow and vasodilation
Gmitrov & Gmitrova, 2004 [53]	132 subjects, without SMF exposure in the condition of arterial normotension	Conscious, sedated rabbits	A significant negative correlation was found between increase in GMF activity, BRS and heart rate variability. The abrupt change in GMF activity was associated with increase in MAP and MAP × HR product - measure of myocardial oxygen consumption
Okano & Ohkubo, 2005 [18]	14 subjects, sinocarotid baroreceptors local exposure to 180 mT SMF in the condition of arterial hypertension for 5-8 weeks	Spontaneously hypertensive rats	Suppressed or retarded the development of arterial hypertension together with increase in BRS. Increase in plasma NO metabolites
Gmitrov, 2007 [8]	14 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min in the condition of arterial normotension	Conscious, sedated rabbits	Decrease in blood pressure, increase in BRS, microcirculation and baroreflex microcirculatory response, reflected in increase of sodium nitroprusside (spontaneous NO-donor) vasodilatory effect
Gmitrov, 2007 [54]	14 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min in the condition of arterial normotension	Conscious, sedated rabbits	GMF attenuated SMF-induced increase in BRS and in microcirculation
Gmitrov, 2010 [14]	14 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min in the condition of arterial normotension	Conscious, sedated rabbits	Decrease in phenylephrine-induced abrupt elevation in blood pressure coupled with increase in BRS
Gmitrov, 2013 [37]	14 subjects, sinocarotid baroreceptors local exposure to 350 mT SMF for 40 min in the condition of arterial normotension 20 subjects, ear skin microcirculatory network local exposure to 250 mT SMF for 40 min in the condition of arterial normotension	Conscious, sedated rabbits	Both SMF direct application to sinocarotid baroreceptors or to microcirculatory network induced a similar significant increase in microcirculatory blood flow and vasodilation

BRS: arterial baroreflex sensitivity, GMF: geomagnetic field, NO: nitric oxide, SMF: static magnetic field

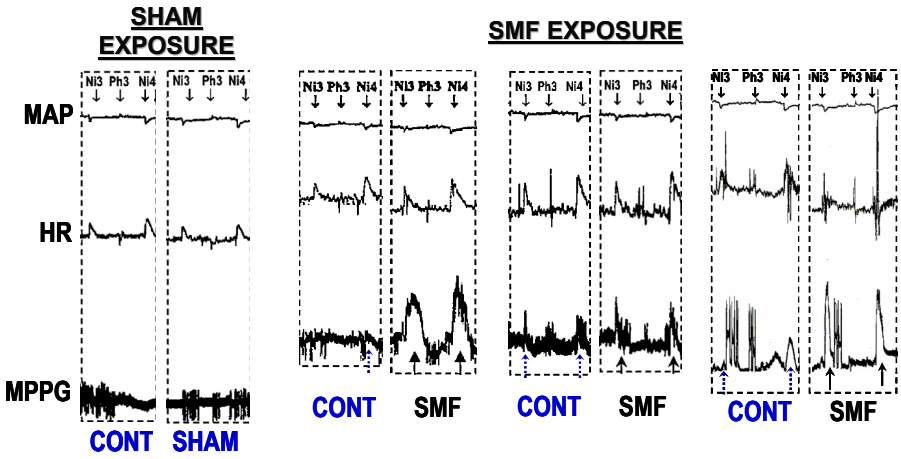

Fig. 5. Microvasodilatory response to the same dose of intravenous (iv) bolus injection of sodium nitroprusside. Segments of experimental recordings before and after local action of a 350 mT static magnetic field (SMF) on sinocarotid baroreceptors under conscious condition with pentobarbital sedation. MAP, mean femoral arterial blood pressure; HR, heart rate; MPPG, microcirculatory blood flow measured by microphotoelectric plethysmography; Ni, Ph, doses of sodium nitroprusside and phenylephrine (μg kg^{-1}) given by iv bolus injection. CONT, initial control readings; SHAM, after SHAM magnets exposure; SMF, after static magnetic field exposure. Note, the sodium nitroprusside NO-mediated vasodilatory effect (reflected by MPPG swings up) markedly increased after 40 min of a 350 mT SMF exposure to sinocarotid baroreceptors.

SMF stimulatory effect on sinocarotid baroreceptors was also confirmed in humans. In conscious healthy volunteers local application of a 120 mT SMF to the sinocarotid triangles increased heart rate variability, when it was measured both in time domain (analyzing heart rate standard deviation) (+12.0%) and frequency domain (using fast Fourier transform) (+15.2%) (Figs. 6 and 7). The increment occurred mainly in a low-frequency domain with remarkable amplitude situated in 0.1-Hz region [19], which is closely coupled with arterial baroreflex [20,21]. In addition, the low-frequency/high-frequency heart rate variability spectral component ration (Lo/Hi) increased, which reflects sympathovagal balance modulated by the gain of the arterial baroreflex [21]. The findings in healthy volunteers were confirmed in animal studies [14] where the increment in heart rate variability was coupled with increase in baroreflex sensitivity (Fig. 4). The decrease in heart rate variability was found to be a major independent cardiovascular risk factor for the onset of malignant arrhythmias in cardiac patients related to their sympathetic overactivity, and was associated with death from heart failure and recurrent myocardial infarction [16,22]. Thus, SMF by its ability to augment normal (Fig. 6) and restore lowered heart rate variability (Fig. 7) may present a significant cardioprotective potential in a range of important cardiovascular conditions, which key deleterious feature is sympathovagal imbalance and baroreflex dysfunction [12,23].

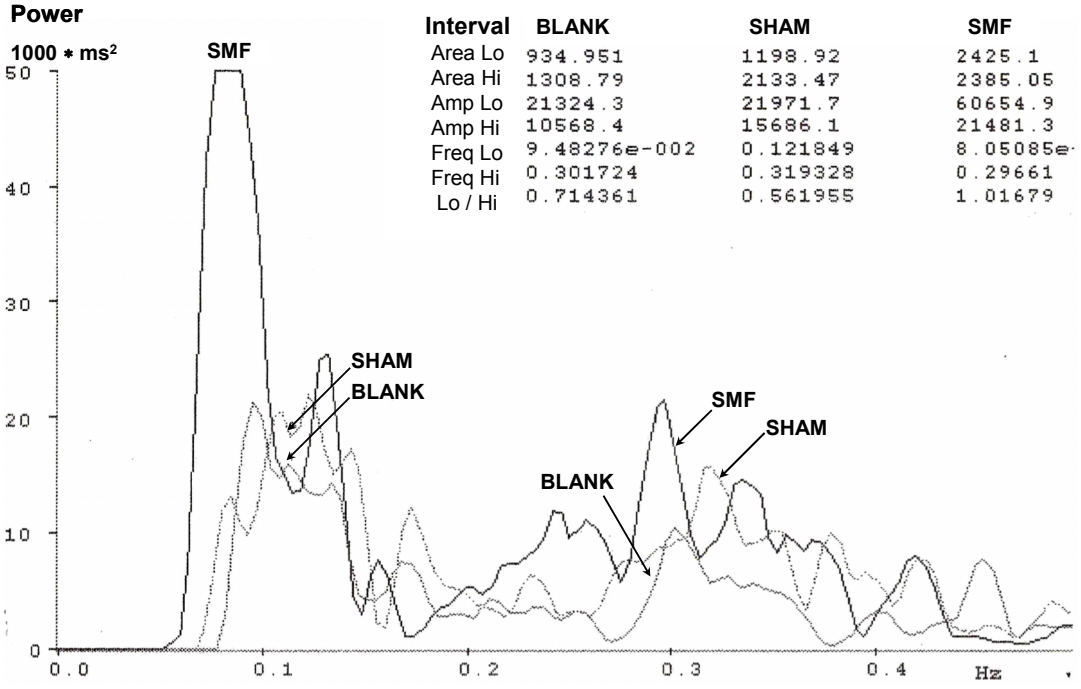

Fig. 6. A frequency domain analysis of the heart rate variability using fast Fourier transform in conscious healthy volunteer after blank control (BLANK), sham control (SHAM magnets exposure) and local exposure of 120 mT static magnetic field (SMF) to the sinocarotid triangles. Note, SMF induced a remarkable increase of power spectra area (Area) and amplitude (Ampl) in both low (Lo) and high (Hi) frequency bands with maximal increase of the Lo frequency spectral component in the 0.1-Hz frequency region, which is strongly coupled with arterial baroreflex capacity to stabilize blood pressure fluctuations.

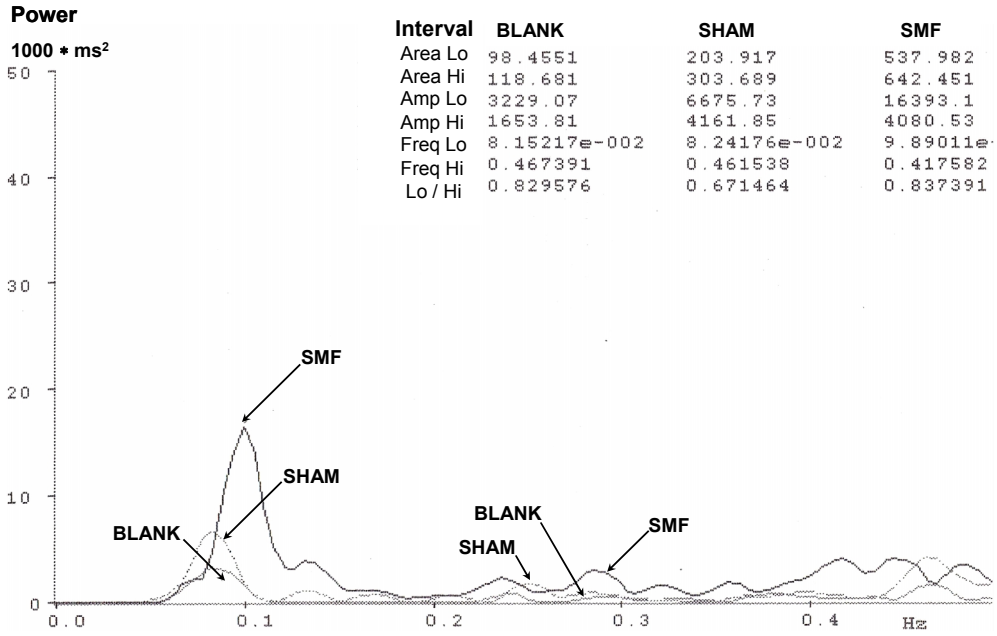

Fig. 7. Example of experimental run in conscious healthy volunteer where local application of 120 mT static magnetic field to the sinocarotid triangles restored initially decreased power spectra situated in 0.1-Hz region.

3. PROPOSED MECHANISM OF SMF EFFECT ON ARTERIAL BARORECEPTORS

There are two principal ways how SMF can affect baroreceptor mechanoelectrical transduction: by action on carotid artery wall mechanical properties and/or on functional properties of the baroreceptor cell membrane itself and attached sinocarotid nerve endings.

It is believed that the local application of an SMF to the sinocarotid triangle probably improves the elastic stretch properties of the sinocarotid artery vascular wall [8], which serves for imbedded baroreceptors as a mechanic filter that determines both the magnitude and rate of strain of the baroreceptor membrane [9]. This importantly affects the process of the baroreceptor sensory transduction reflected by alternations in arterial baroreflex sensitivity and heart rate variability. SMF effect on elastic properties of the vascular wall was demonstrated in study when a similar intensity as to sinocarotid baroreceptor exposure 250 mT SMF induced a vasodilation within the rabbit's ear microvascular networks [24] (Table 1). SMF probably modifies baroreceptor activity throughout local release from carotid artery endothelium chemical mediators, e.g. nitric oxide (NO), that increases vascular wall smooth muscles distensibility and/or acts directly on baroreceptors or sinocarotid nerve endings modulating the process of mechanoelectrical transformation [9,25,26]. This hypothesis was partly supported by increase in plasma NO metabolites during sinocarotid baroreceptor chronic SMF exposure in spontaneously hypertensive rats [18].

However, theoretical considerations suggest that SMF shows a direct stimulatory effect on the sinocarotid baroreceptor itself directly affecting magneto-sensitive structures [14] or by magnetically induced blood flow potential modulated by carotid artery pulsations [11,14,27,

28] and magnets removal generating SMF "off" effect. SMF may enhance Ca^{2+} dependent mechanoelectrical transformation that occurs in baroreceptors membrane spike-initiating zone near sinocarotid nerve terminals [8].These areas are rich in voltage-gated Ca^{2+} channels and more sensitive to electrical charge, which can result in the generation of action potentials [29]. A high efficiency of the voltage-gated Ca^{2+} channel blockade with verapamil to impede SMF baroreceptor stimulatory effect [30,31] indirectly supported this idea.

A growing body of evidence suggests that mechanosensitive ion channels play a key role in magnetoreception. Hughes et al. [32] found that SMF modulated a mechanosensitive ion channel activity in artificial liposomes and supported previous studies showing that the effects of SMFs on ion channels may be mediated by changes in membrane properties due to anisotropic diamagnetism of lipid molecules. Petrov and Martinac [33] supported the above research and found that 400 mT SMF (similar intensity as used in baroreceptor SMF exposure) could reverse gadolinium (Gd) block of the bacterial mechanosensitive channel of large conductance, suggesting that the effect of SMFs may result from changes in physical properties of the lipid bilayer due to diamagnetic anisotropy of phospholipid molecules, which under influence of SMFs could cause displacement of Gd^{3+} ions from the membrane bilayer and remove the mechanosensitive channel block. However, gadolinium is widely used in baroreceptor research as a non-specific blocker of their activity preventing non-voltage-gated Ca^{2+} influx through mechanosensitive ion channels in baroreceptor neurons during their membrane deformation and the process of the mechanoelectrical transduction [12]. These findings, taking into account that arterial baroreceptors typically belong to the family of mechanoreceptors, highly support results with SMF baroreceptor exposure giving them a molecular basis of the mechanism of the effect. In addition to direct Ca^{2+} influx, mechanosensitive ion channels indirectly activate voltage-gated Ca^{2+} channels causing depolarization [34,35], enabling SMF to modulate intracellular Ca^{2+} influx by both cooperative Ca^{2+} channel systems.

It is hypothesized, that SMF modulates blood pressure pulsatory changes in lipid bilayer of the baroreceptor cell membrane affecting mechanically-gated Ca^{2+} influx, the process of depolarization and its encoding into action potential discharge resulted in improvement of the mechanosensory transduction and the carotid sinus baroreflex hemodynamic responses. The similar mechanosensory mechanism is probably participates in SMF vasodilatory effect [8,24,36]. SMF may promote endothelial shear stress signal transduction and NO-dependent vasodilation [37] by activation of the gadolinium inhibited stretch activated Ca^{2+} channels, which are similarly to baroreceptors rich in vascular endothelial cell membranes [38,39]. Therefore, it is not excluded that SMF improves carotid artery compliance and baroreceptor mechanoelectrical transduction by both baroreceptor and endothelial gadolinium-dependent mechanosensory systems. Further research is needed, however it seems that SMF effect on cellular membrane mechanosensitive structures, including Ca^{2+} channels, progressively gaining confidence to be a universal mechanism of SMF effect in different tissues and organs.

4. POTENTIAL CLINICAL IMPLEMENTATION OF THE BARORECEPTORS MAGNETIC STIMULATION

Arterial baroreflex dysfunction has become a key issue in cardiovascular physiology, with respect to its role in the pathogenesis of essential hypertension [40]. However, a large amount of evidence suggests that even in absence of arterial hypertension a decreased baroreflex sensitivity is considered as an independent risk factor for greater vascular and target organ damage [16]. Low baroreflex sensitivity and heart rate variability are coupled

with increased risk of developing a reduced survival from coronary heart disease, heart failure, diabetes and aging [12,16,23]. The results presented here demonstrate that a local exposure of the sinocarotid baroreceptors to SMF increases baroreflex sensitivity and heart rate variability. These effects may synergistically reinforce the main pursuit of the arterial baroreflex control mechanism, to protect cardiovascular system from lethal consequences of the pronounced sympathovagal imbalance results in large part from high blood pressure variability and cardiac arrhythmias [12,16]. A larger vasodilatory effect of a sodium nitroprusside, a spontaneous NO donor [41], coupled with increase in baroreflex sensitivity suggests augmentation of the arterial baroreflex capacity support NO-dependent vasodilation to be a new mechanism in baroreflex physiology [37]. Arterial baroreflex modulating intrinsic fluctuations in sympathetic outflow may dynamically sensitize vascular smooth muscles to NO, restoring the balance between endothelium-derived relaxing and contracting factors, suggested to be the hallmark of arterial wall integrity and a decisive mechanism of endothelial and microvascular dysfunction [42,43,44]. The failure of the baroreflex-mediated NO-derived vasodilation may have etiopathogenetic significance in a spectrum of cardiovascular and metabolic conditions such as arterial hypertension, coronary heart disease, diabetes and insulin resistance one of which key feature and causing factor is NO deficit and baroreflex dysfunction [42,45,46] both appearing in preclinical stages of the disease [47,48]. On the other hand the enhancement of the same mechanism is probably participate in high efficiency of sinocarotid baroreceptor electric stimulation in drug resistant arterial hypertension and heart failure [29,49]. The concurrent increase in baroreflex sensitivity and plasma NO metabolites during sinocarotid baroreceptor chronic SMF exposure [18] supports our results and the cross talk connection between NO metabolism and arterial baroreflex function [50].

5. CONCLUSION

For the first time it was shown that a dynamic physiological regulatory system responded to magnetic field in consequence of its peripheral receptor activation. SMF exerted stimulatory effect on sinocarotid arterial baroreceptors improving global neuro-autonomic regulation both on macro- and microcirculatory level: normalized blood pressure, increased heart rate variability, arterial baroreflex sensitivity, microcirculatory blood flow and NO dependent vasodilation. Further research is needed to support the relevance of the proposed mechanisms and potential therapeutic implications. However, the improvement of the vasodilator responsiveness to NO by baroreceptor stimulation seems to be a new universal mechanism and therapeutic strategy to stabilize blood pressure, ameliorate autonomic, endothelial and vascular dysfunction [37] in cardiovascular diseases where sympathovagal imbalance that results from a loss of baroreflex control over autonomic activity increases the risk of morbidity and mortality substantially [12]. The modulation of the baroreflex-mediated autonomic cardiovascular control is a new concept for understanding environmental and occupational magnetic fields effect on cardiovascular system and an effective key to develop preventive measures against their potential public health hazards [1-5, 51-54].

CONSENT

Not applicable.

ETHICAL APPROVAL

The author hereby declares that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

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COMPETING INTERESTS

The author has declared that no competing interests exist.

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