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The Effects of Moderate-Intensity Inhomogeneous Static Magnetic Fields on Neuromuscular Transmission

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Research Article

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Abstract

The present study focuses on the effects of moderate-intensity inhomogeneous static magnetic fields (SMF) up to 0.73 T on action potentials in Wistar rats. Thirty three animals were divided into three groups: a sham-exposed control group and two exposed groups with exposure to maximum flux densities (B_{max}) of 0.24 and 0.73 T SMF. The amplitude of the electrically evoked compound nerve action potentials (CNAP) and compound muscle action potentials (CMAP) were measured for up to 2 h. In the CNAP, the excitation of Aδ fibers was significantly enhanced by both 0.24 T and 0.73 T SMF for 2 h, relative to the sham-exposed control. Furthermore, the CMAP decrement was significantly enhanced by 0.73 T SMF for 1 to 2 h, but not by 0.24 T SMF for up to 2 h, compared with the control. These results suggest that SMF (0.24 and 0.73 T for 2 h) enhances pain perception because the Aδ fibers are responsible for pain transmission. In addition, SMF (0.73 T for 1 to 2 h) may modulate neuromuscular transmission. Thus, the magnetic force produced by SMF could affect the behavior of some types of ion channels associated with Aδ fibers, probably due to SMF-induced modulation of ion/ligand binding and ion transport.

Keywords: Magnetic Force; Electrical Nerve Stimulation; Compound Nerve Action Potentials; Compound Muscle Action Potentials; Ion Channels; Ion/ligand Binding; Ion Transport.

Introduction

Considering the widespread and rapid increase in the static magnetic fields (SMF) used in medical diagnosis and applications, various studies have investigated the effects of acute or chronic exposure to SMF on humans and animals over the past 30-40 years. A number of neuro- and electrophysiological studies on SMF effects, including or focusing on less than 1 T, have been well-reviewed elsewhere [1-3]. Several studies have reported on significant neurophysiological effects of moderate-intensity SMF ranging from 1 mT to 1 T with exposure duration from 100 sec to 40 days [4-44]. However, only a few studies have reported on the effects of moderate-intensity SMF on action potentials in vivo, probably due to SMF-induced modulation of ion/ligand binding and ion

transport [4,8,22]. For example, a spatially homogeneous SMF of 0.65 T suppressed the temporal decrease of the muscle tension induced by electrical stimulation of the sartorius muscle in the neuromuscular preparation of the bullfrog [22]. Four possible biochemical mechanisms for the SMF effect on muscle tension were proposed: (i) change of acetylcholine release from presynaptic terminals; (ii) sensitivity change of acetylcholine receptors at the endplate; (iii) change of Ca^{2+} dynamics; and (iv) change of large molecules and enzymes, e.g. calmodulin molecules, myosin light chain kinase, and ATP molecules [22].

These studies, however, mainly focused on isolated skeletal muscles and nerve fibers in vitro, and almost none on neuromuscular transmission in vivo. Therefore, this study focuses on the in vivo effects of moderate-intensity SMF up to 0.73 T on the rat sciatic nerve fibers of the sartorius muscle.

Materials and Methods

Animals and Groups

Thirty three adult male Wistar rats (body weight 250–300 g) were used in this study. Wistar rats were purchased from Charles River Laboratories Japan. The animals were housed individually in the same room, with a 12-h light/dark cycle (lights on: 7 a.m.) at a temperature of 25±0.5°C, and a relative humidity of 50±5%. Animals were fed standard rodent chow and tap water *ad libitum*. All experimental procedures performed on the animals were in strict accordance with the Guide for the Care and Use of Laboratory Animals (7th ed. 1996, US National Academy Press, Washington, DC, USA) and approved by the Animal Ethics Committee in Chiba University in Japan. The animals were divided into three groups: I) sham-exposed control group (control group); II) SMF-exposed group with inhomogeneous exposure to maximum flux densities (B_{max}) of 0.24 T (0.24 T-exposed group); and III) SMF-exposed group with B_{max} of 0.73 T (0.73 T-exposed group), which were further subdivided into six subgroups for measuring either kind of action potentials (each subgroup had 5-6 animals): Ia) control group for measuring compound nerve action potentials (CNAP); IIa) 0.24 T-exposed group for measuring CNAP; IIIa) 0.73 T-exposed group for measuring CNAP; Ib) control group for measuring compound muscle action potentials (CMAP); IIb) 0.24 T-exposed group for measuring CMAP; IIIb) 0.73 T-exposed group for measuring CMAP. The electrical stimulation and recording of both action potentials was performed for approximately 5 minutes at 1-h and 2-h exposure time in the SMF-exposed group under SMF exposure and in the sham-exposed group under non-SMF exposure (except for the Earth's magnetic field).

Magnetic Field

The SMF was generated by two neodymium–iron–boron (NdFeB) magnet assemblies (TDK, Japan), detailed specifications have been described elsewhere [42]. One magnet assembly was constructed of a pair of rectangular NdFeB magnets (magnet dimension L ×W × D = 15 × 15 × 2.4 cm; B_{max} 0.26 T on the surface of the magnet). The upper and lower magnetic plates, with oppositepolarities vertically attracting each other through a 5 cm air gap, were fixed parallel to both sides of the stainless frame. In the other magnet assembly, a pair of stronger NdFeB magnetic plates (L ×W × D = 15 × 15 × 6 cm; B_{max} 0.75 T) was used with the same air gap of 5 cm. The magnet assemblies in the sham-exposed control group consisted of the same material but were not magnetized.

The rear part of the body of the anesthetized animal, which was placed on an animal bed holder (L ×W × D = 30 cm × 10 cm × 0.5 mm), was located on the lower magnetic plate (North seeking pole) inside either type of a magnet assembly (Figure 1). The front part of the body, which was placed on a supporting box, was located outside the magnet assembly. The direction of long axis of the body (their body length of about 30 cm) was oriented orthogonal to the attracting force of magnetic plates. The spatial distribution of the SMF was measured along the *y*-axis at the animal site using a magnetic field meter (model 4048 with a Hall probe sensor A-4048-002, Bell Technologies, USA). The whole body was exposed to spatially inhomogeneous SMF (Figure 1a,b). The distance between the magnet surface and the body surface was 0.5 mm due to the depth of the animal bed holder. The B_{max} *applied to the* body was 0.24 T (Figure 1a) or 0.73 T (Figure 1b).

The gradient in the whole *body* was calculated on the basis of measured field strengths (B) as:

$$G = \partial B / \partial y \quad (1)$$

The force product (FP) was defined as:

$$FP = BG \quad (2)$$

In the magnet assembly of B_{max} = 0.24 T, the maximum values of magnetic gradient (G_{max}), and force product

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(FP_{max}) were 12.53 T m^{-1} and 0.97 T^2m^{-1}, respectively (Figure 1a). In the magnet assembly of B_{max} = 0.73 T, the G_{max}, and FP_{max} values were 26.73 T m^{-1} and 7.23T^2m^{-1}, respectively (Figure 1b). In both magnet assemblies the G_{max}, and FP_{max} values were located near the edge of the magnet. The *anesthesia was maintained* during the entire experimental period for at least 2 h and the animal was restrained in the magnetic assembly. The ambient temperature in the magnet was maintained at 25±0.5°C with the relative humidity of 50± 5%.

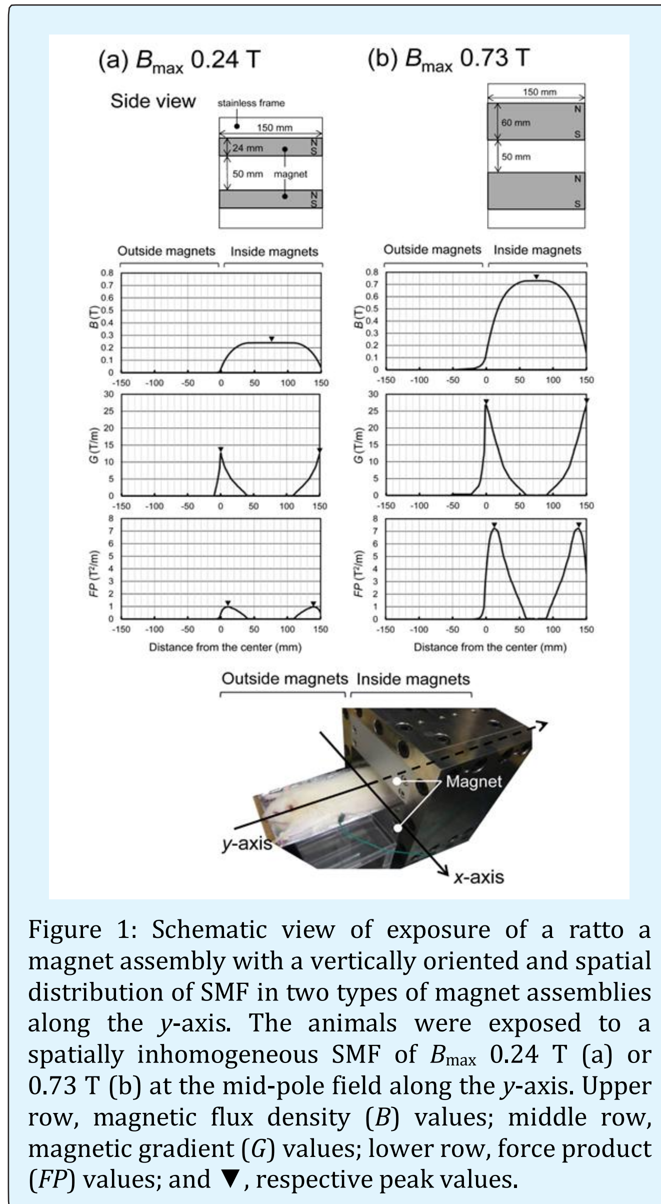

Figure 1: Schematic view of exposure of a ratto a magnet assembly with a vertically oriented and spatial distribution of SMF in two types of magnet assemblies along the y-axis. The animals were exposed to a spatially inhomogeneous SMF of B_{max} 0.24 T (a) or 0.73 T (b) at the mid-pole field along the y-axis. Upper row, magnetic flux density (B) values; middle row, magnetic gradient (G) values; lower row, force product (FP) values; and ▼, respective peak values.

Compound Nerve Action Potentials (CNAP)

Wistar rats were anesthetized with urethane (1.0 g kg^{-1}, i.p.; ethyl carbamate; Wako Pure Chemical, Japan). The rats were placed in prone position, a lateral skin incision was made on the dorsal side of the right hind limb, and then a sciatic nerve and a gastrocnemius nerve were exposed. One of a bipolar electrode was placed on the sciatic nerve for applying repetitive electrical nerve stimulation and the other bipolar electrode was attached to the medial gastrocnemius nerve for measuring compound nerve action potentials (CNAP). The distance between the stimulating and recording electrodes was approximately 3 cm. A reference ground electrode was attached to the body of each animal. The reference ground electrode was connected to the earth terminal of the power source to eliminate stray current interference. All electrodes were made of pure platinum, which is inert and non-ferromagnetic material (molar magnetic susceptibility χ_{mol} (cgs) = 193 ×$10^{-6}cm^3mol^{-1}$ at 295 K) [46] and, therefore, is apparently neither attracted nor repelled by a magnet.

After attaching the electrodes to the nerves, the nerves were covered with liquid paraffin, and were sealed with Para film (Bemis Flexible Packaging, USA) to prevent desiccation. In each animal, the four limbs and the lead wires were tightly fixed to an animal bed holder using strings in order to avoid motions associated with muscle contractions during the repetitive electrical nerve stimulation. The anesthesia lasted for at least 2 h during the measuring experiment.

The sciatic nerve was electrically stimulated during exposure to a non-homogeneous SMF of B_{max} 0.24 T or 0.73 T. Except for a strong SMF (2-8 T) generated by a superconducting magnet, a similar procedure has been described elsewhere [47]. Briefly, a measurement instrument (Neuropack MEB-2200, Nihon Kohden, Japan) was used to stimulate the nerve bundle and to record the CNAP. Repetitive electrical nerve stimulation was applied with intensities ranging from 1, 3, 5 and 7 mA, with a pulse width of 0.1 ms and a pulse repetition rate of 3 Hz. The signal-to-noise ratio (SNR) was improved by averaging 20 repetitive recordings.

Data were collected from the medial gastrocnemius nerve in the right side of 15 animals for approximately 5 minutes at 1-h and 2-h exposure time, in which stability was sufficient to allow detailed analysis. The animals were randomly divided into the above mentioned three subgroups: Ia) control group (n = 5); IIa) 0.24 T-exposed

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group (n = 5); and IIIa) 0.73 T-exposed group (n = 5) for up to 2 h. The values of CNAP were measured for these three groups.

Compound Muscle Action Potentials (CMAP)

The animals used in CMAP recordings were different individuals from those used in CNAP recordings. With the anesthetized rat in a prone position, the left sciatic nerve was exposed through a lateral skin incision on the dorsal side of the left mid-thigh. A measurement instrument (Neuropack MEB-2200, Nihon Kohden, Japan) was also used to stimulate the sciatic nerve and to record the compound muscle action potentials (CMAP). For stimulation, a bipolar electrode was attached to the sciatic nerve. The sciatic nerve was electrically stimulated during exposure to a non-homogeneous SMF of B_{max} 0.24 T or 0.73 T, using 10 repetitive pulses of 8 mA, 0.5 ms and 3 Hz, as a supramaximal stimulus. The CMAP was recorded from the left gastrocnemius muscle using a platinum concentric needle electrode (NM-030T, Nihon Kohden). The distance between the stimulating and recording electrodes was approximately 6 cm. The SNR was improved by averaging 10 repetitive recordings. All other procedures were almost the same as for the experiment of CNAP.

We calculated the values of "the relative average amplitude" and "the decrement rate" of CMAP. The values of the relative average amplitude were determined by signal averaging the successive responses elicited by repetitive ten pulses and were calculated relative to the corresponding pre-exposure values (pre-exposure baseline value = 100%). The CMAP decrement rate (%) was simply calculated as follows:

$$\text{Decrement rate (\%)} = \left(1 - \frac{P_{min}}{P_1}\right) \times 100 \qquad (3)$$

Where P_1 is the first pulse stimulus-induced amplitude and P_{min} is the minimum amplitude induced by the following pulse stimulus (Figure 2).

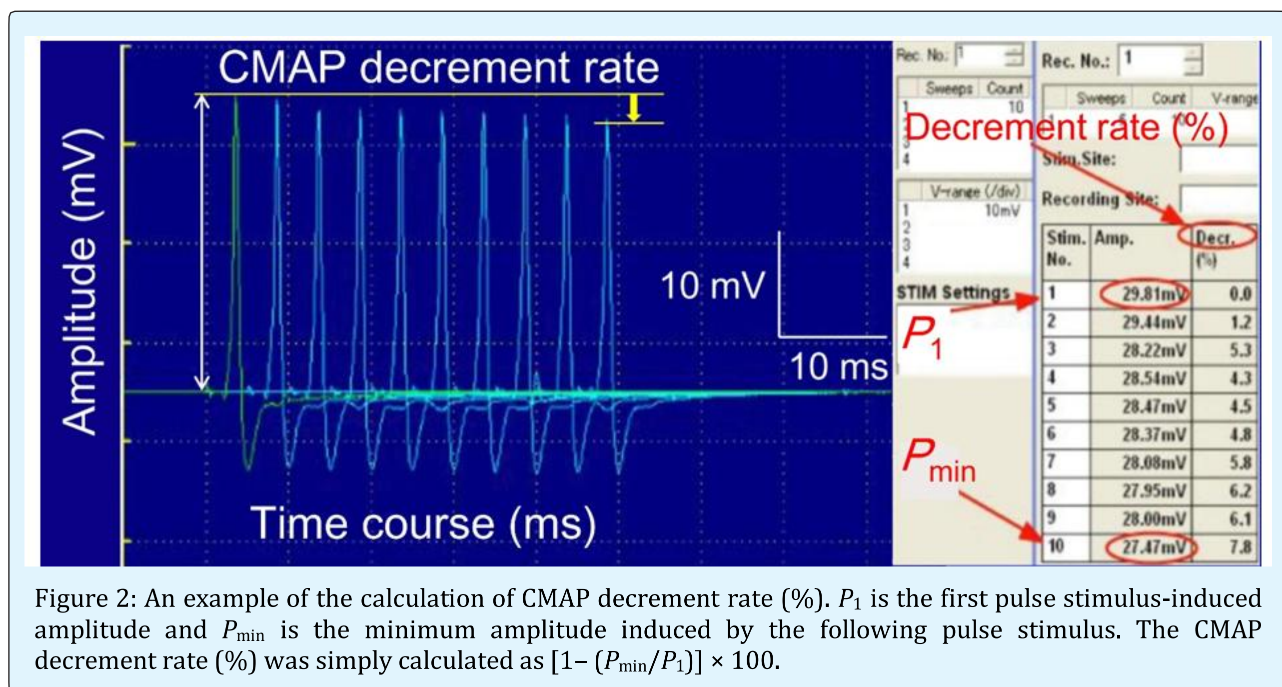

Figure 2: An example of the calculation of CMAP decrement rate (%). P_1 is the first pulse stimulus-induced amplitude and P_{min} is the minimum amplitude induced by the following pulse stimulus. The CMAP decrement rate (%) was simply calculated as $[1-(P_{min}/P_1)] \times 100$.

Data were collected CMAP from the gastrocnemius muscle in the left side of 18 animals for approximately 5 minutes at 1-h and 2-h exposure time, in which stability was sufficient to allow detailed analysis. The animals were randomly divided into the above mentioned three subgroups: Ib) control group (n = 6); IIb) 0.24 T-exposed group (n = 6); and IIIb) 0.73 T-exposed group (n = 6) for up to 2 h. The values of CMAP were measured for these three groups.

Data Processing

The results are expressed as mean ± standard error of the mean (SEM). Comparisons between groups over time

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were made using two-way analysis of variance with repeated measures, followed by the Wilcoxon rank sum test for pairwise comparisons. Significance was set at $P < 0.05$.

Results

Multiple peaks were observed in the recorded CNAP (Figure 3). Nerve fibers were classified into several types (Aα, Aβ, Aγ, Aδ, B, and C) according to their conduction velocities and functions. We identified three peaks corresponding to the Aδ, B, and C fibers (Figure 3). The respective conduction velocities of the Aδ, B, and C fibers were 13.6, 3.8 and 0.5 ms^{-1}. To investigate the SMF effects on pain-related nerve fibers, we focused on two kinds of sensory nerve fibers, that is, Aδ and C fibers, and analyzed their relative peak amplitude. Myelinated Aδ fibers respond to stimuli such as cold and pressure, and as a nociceptor, Aδ fibers convey fast pain information [48]. Slowly-conducting, unmyelinated C fibers, by contrast, carry slow pain [48]. The values of "the relative peak amplitude" of Aδ and C fibers were calculated as the relative change in the peak amplitude, relative to the corresponding peak pre-exposure values (pre-exposure baseline value = 100%).

Significant results of SMF effects on the relative peak amplitude of Aδ fibers were obtained in the range of moderate-intensity electric stimulation applied (3 and 5 mA). At 2-h exposure, both B_{max} 0.24 T and 0.73 T SMF caused significant increase in the relative peak amplitude of Aδ fibers at 3 mA stimulation (Figure 4). In addition, at 2-h exposure, B_{max} 0.73 T SMF significantly elevated the relative peak amplitude of Aδ fibers at 5 mA stimulation (Figure 4). Neither B_{max} 0.24 T nor B_{max} 0.73 T SMF exposure for up to 2 h induced any significant changes in the relative peak amplitude of C fibers in response to any electrical stimulation used in this study (Table 1).

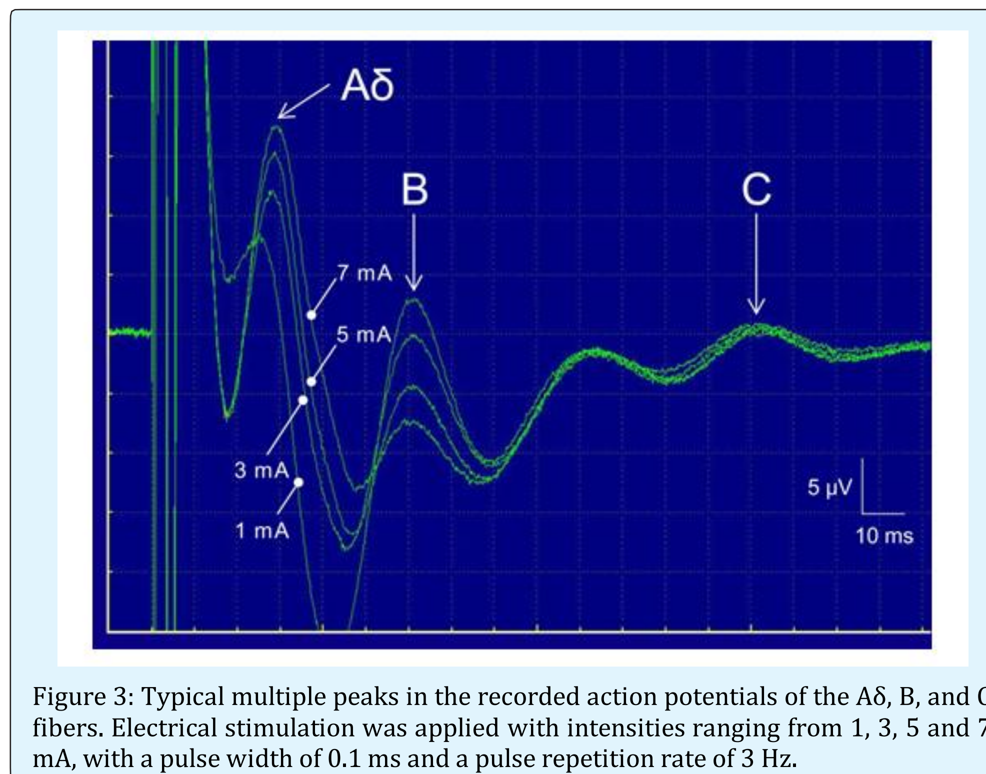

Figure 3: Typical multiple peaks in the recorded action potentials of the Aδ, B, and C fibers. Electrical stimulation was applied with intensities ranging from 1, 3, 5 and 7 mA, with a pulse width of 0.1 ms and a pulse repetition rate of 3 Hz.

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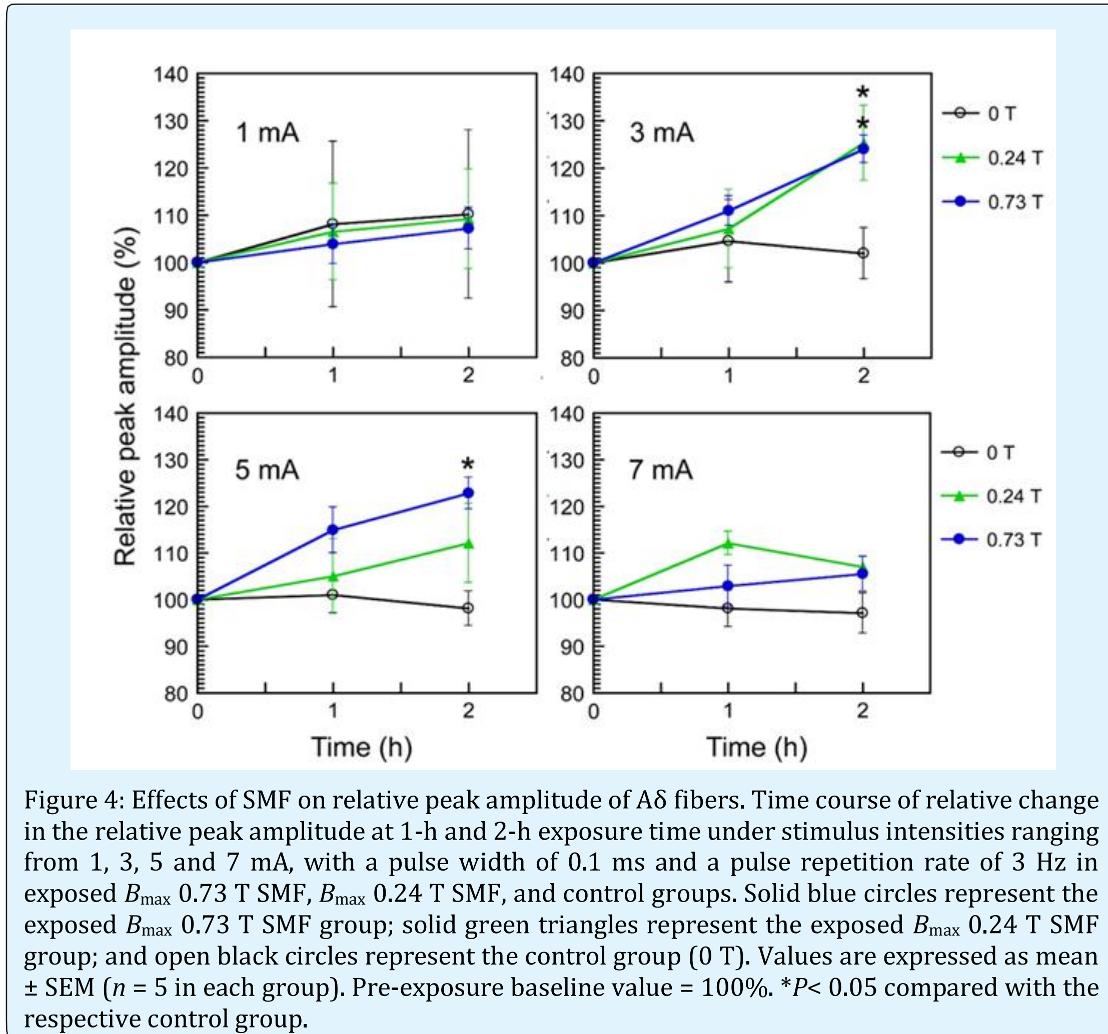

Figure 4: Effects of SMF on relative peak amplitude of Aδ fibers. Time course of relative change in the relative peak amplitude at 1-h and 2-h exposure time under stimulus intensities ranging from 1, 3, 5 and 7 mA, with a pulse width of 0.1 ms and a pulse repetition rate of 3 Hz in exposed B_{max} 0.73 T SMF, B_{max} 0.24 T SMF, and control groups. Solid blue circles represent the exposed B_{max} 0.73 T SMF group; solid green triangles represent the exposed B_{max} 0.24 T SMF group; and open black circles represent the control group (0 T). Values are expressed as mean ± SEM (n = 5 in each group). Pre-exposure baseline value = 100%. *P< 0.05 compared with the respective control group.

Exposure	Electrical stimulus intensity	Exposure duration		
		0 h	1 h	2h
0 T (Control)	1 mA	100.0 ± 0.0	104.8 ± 13.8	109.5 ± 13.8
	3mA	100.0 ± 0.0	129.2 ± 18.6	137.5 ± 20.5
	5mA	100.0 ± 0.0	117.0± 11.8	128.3 ± 13.5
	7 mA	100.0 ± 0.0	125.8 ± 3.4	134.9 ± 3.4
0.24 T	1 mA	100.0 ± 0.0	110.3 ± 19.5	97.7 ± 17.7
	3mA	100.0 ± 0.0	120.4 ± 10.1	134.7 ± 22.8
	5mA	100.0 ± 0.0	123.1 ± 9.6	120.0 ± 8.9
	7 mA	100.0 ± 0.0	117.1 ± 8.7	112.2 ± 8.8
0.73 T	1 mA	100.0 ± 0.0	108.7 ± 16.5	110.9 ± 17.5
	3 mA	100.0 ± 0.0	131.5 ± 12.4	135.2 ± 12.4
	5 mA	100.0 ± 0.0	130.8 ± 8.3	132.3 ± 8.3
	7 mA	100.0 ± 0.0	131.3 ± 2.3	129.9 ± 8.1

Table 1: Changes in the relative peak amplitude (%) of C fibers in response to SMF exposure
Values represent mean ± SEM of five animals per group.
P > 0.05, not significant (ns) in all instances compared with the respective control group (0 T).

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The values of the response latency from stimulus to the peak amplitude of Aδ fibers (Table 2) and C fibers (Table 3) were also analyzed. No significant results of SMF effects on the latency of Aδ and C fibers were obtained in any case (Tables 2 & 3).

Exposure	Electrical stimulus intensity	Exposure duration		
		0 h	1 h	2h
0 T (Control)	1 mA	17.9 ± 0.1	17.8 ± 0.1	17.8± 0.2
	3mA	17.8 ± 0.1	17.7 ± 0.1	17.8 ± 0.1
	5 mA	17.8 ± 0.2	17.9 ± 0.2	17.8± 0.2
	7mA	17.7 ± 0.2	17.8 ± 0.1	17.7 ± 0.2
0.24 T	1 mA	17.8 ± 0.1	17.8 ± 0.1	17.8 ± 0.1
	3mA	17.8 ± 0.2	17.7 ± 0.2	17.8± 0.1
	5 mA	17.7 ± 0.1	17.8 ± 0.1	17.7 ± 0.1
	7mA	17.8 ± 0.2	17.9 ± 0.2	17.8± 0.1
0.73 T	1 mA	17.8 ± 0.1	17.8 ± 0.1	17.9 ± 0.2
	3mA	17.9 ± 0.2	17.8 ± 0.2	17.8± 0.1
	5 mA	17.8 ± 0.1	17.9 ± 0.1	17.7 ± 0.1
	7 mA	17.8 ± 0.1	17.7 ± 0.1	17.8± 0.2

Table 2: Changes in the latency (ms) of AS fibers in response to SMF exposure.
Values represent mean ± SEM of five animals per group.
$P > 0.05$, not significant (ns) in all instances compared with the respective control group (0 T).

The CMAP decrement was significantly enhanced by B_{max} 0.73 T SMF during 1- to 2-h exposure period, but not by B_{max} 0.24 T SMF during the entire exposure period of 2 h, compared with the unexposed control (Figure 5). The relative average amplitude of CMAP was not affected by both SMF exposures (Table 4).

Exposure	Electrical stimulus intensity	Exposure duration		
		0 h	1 h	2h
0 T (Control)	1 mA	122.2 ± 0.2	122.1 ± 0.2	122.2 ± 0.2
	3mA	122.1 ±0.2	122.2 ± 0.2	122.2± 0.1
	5 mA	122.2 ± 0.2	122.2 ± 0.2	122.3 ± 0.2
	7 mA	122.3 ± 0.1	122.2 ± 0.2	122.2 ± 0.1
0.24T	1 mA	122.2 ± 0.2	122.3 ± 0.2	122.2 ± 0.2
	3mA	122.1 ±0.2	122.2 ± 0.1	122.2 ± 0.2
	5 mA	122.2 ± 0.2	122.1 ± 0.2	122.3 ± 0.2
	7 mA	122.1 ±0.2	122.2 ± 0.2	122.2 ± 0.1
0.73 T	1 mA	122.3 ± 0.2	122.2 ± 0.2	122.1 ± 0.2
	3mA	122.1 ±0.2	122.1 ±0.2	122.2± 0.2
	5 mA	122.2 ± 0.1	122.2 ± 0.2	122.1 ±0.2
	7 mA	122.3 ± 0.2	122.2 ± 0.2	122.1 ± 0.2

Table 3: Changes in the latency (ms) of C fibers in response to SMF exposure.
Values represent mean ± SEM of five animals per group.
$P > 0.05$, not significant (ns) in all instances compared with the respective control group (0 T).

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Exposure duration			
Exposure	**0 h**	**1 h**	**2h**
0 T (Control)	100.0 ± 0.0	112.7 ± 14.9	108.2 ± 17.7
0.24 T	100.0 ± 0.0	108.9 ± 15.9	106.9 ± 12.7
0.73 T	100.0 ± 0.0	115.2 ± 12.3	113.7± 12.1

Table 4: Changes in the relative amplitude (%) of CMAP in response to SMF exposure.
Values represent mean ± SEM of six animals per group.
$P > 0.05$, not significant (ns) in all instances compared with the respective control group (0 T).

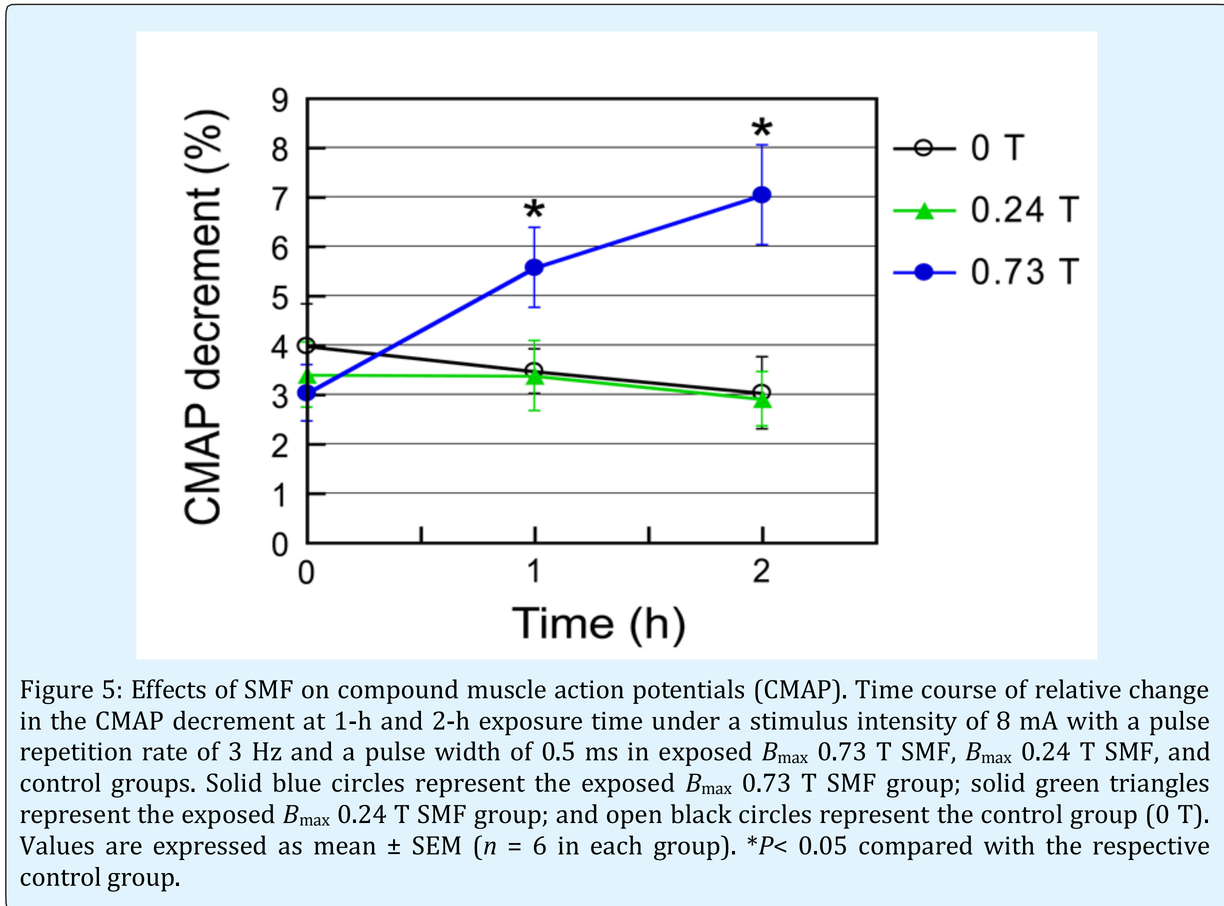

Figure 5: Effects of SMF on compound muscle action potentials (CMAP). Time course of relative change in the CMAP decrement at 1-h and 2-h exposure time under a stimulus intensity of 8 mA with a pulse repetition rate of 3 Hz and a pulse width of 0.5 ms in exposed B_{max} 0.73 T SMF, B_{max} 0.24 T SMF, and control groups. Solid blue circles represent the exposed B_{max} 0.73 T SMF group; solid green triangles represent the exposed B_{max} 0.24 T SMF group; and open black circles represent the control group (0 T). Values are expressed as mean ± SEM (n = 6 in each group). *$P< 0.05$ compared with the respective control group.

Discussion

The major finding of this study is that excitation of Aδ fibers was significantly enhanced by both 0.24 T and 0.73 T SMF for 2 h, relative to the sham-exposed control. These results in vivo implies that exposure to moderate-intensity inhomogeneous SMF enhances pain perception, through the reduction of pain threshold, because Aδ fibers are responsible for pain transmission. In contrast, our previous results in vitro (excised frog sciatic nerve preparation) suggested that B_{max} 0.70 T SMF could increase pain threshold by decreasing nerve conduction velocity of C fibers alone, but not of Aδ fibers [42].

In the current study we used urethane as an anesthetic agent because urethane is widely used to investigate neurovascular coupling due to its balanced effect on neurotransmitters [49], although the effects on neurotransmitter-gated ion channels, including nicotinic acetylcholine receptors, were reported [50]. Ideally, if possible, the experiment should be performed in conscious animals without the interference of anesthetics.

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Anesthesia by itself can modulate not only pain perception but also probably excitation of Aδ fibers. However, the finding that SMF increases nerve fibers excitability and modulate neuromuscular transmission has more important potential implication than other pain perception processes.

Another study in vitro (excised adult guinea pig spinal cords) showed that exposure to a homogeneous SMF of 0.5 T induced a decrease in the amplitude of CNAP without a change in the response latency during SMF exposure [23]. A maximum effect was evident 1–2 min after the SMF was applied, with a return to baseline within 1 min after the SMF was removed. The results were explained by a conduction block in the small axon subpopulation owing to the SMF effect on voltage-activated Na^+ channels. The relative selectivity of the SMF was believed to occur because of the relatively greater density of Na^+ channels present in smaller axons. These results in vitro are consistent with our previous results on the SMF effect on nerve conduction in vitro [42], but are inconsistent with our present results on the SMF effect on neuromuscular transmission in vivo.

It has been reviewed that in vivo nerve conduction studies have failed to establish a link between in vitro effects and the analgesic responses observed in pain studies [51]. It seems likely that the SMF effects on pain perception in vitro are often different from those in vivo, depending on the physiological conditions of the nerve membrane excitation. Although the mechanistic reasons for this difference in the threshold have yet to be clarified, SMF could affect the behavior of some types of ion channels associated with Aδ and C fibers.

The other significant finding is that the CMAP decrement was significantly enhanced by 0.73 T SMF for 1 to 2 h, compared with the control. From the viewpoint of the electrophysiological diagnosis, the enhanced CMAP decrement in repetitive electrical nerve stimulation is related to dysfunction of neuromuscular transmission [52]. This implies that SMF may cause dysfunction of neuromuscular transmission. More specifically here, the CMAP changes roughly indicate the ratio of "the number of acetylcholine (ACh) receptor responded to Ach release from presynaptic terminals" to "the amount of ACh release" [53]. Therefore, the SMF-enhanced CMAP decrement implicates that SMF may increase the ACh release from presynaptic terminals and/or decrease the sensitivity of ACh receptor because the ACh release from nerve terminals is the cause of muscle contraction. As we mentioned in the introduction, the effects of a moderate-intensity homogeneous SMF on muscle tension were found using in vitro neuromuscular preparation [22]. In considering the biochemical mechanisms, our results might be in accordance with the mechanism(s) that modulation of muscle tension appears to be a pathway(s) through which (i) ACh release from presynaptic terminals and/or (ii) sensitivity change of ACh receptors at the endplate can influence CMAP. Additional experiments with the pharmacological agents (for instance, ACh release inhibitors) and muscle tension measurements are needed to make it clear.

Despite the pain-related response induced by moderate-intensity heterogeneous SMF [16,17,28,30,31,37,39,42,43], however, there has been little documented on the evident effects of SMF on neuromuscular transmission, except for the present study. Our findings indicate that exposure to moderate-intensity inhomogeneous SMF could transiently affect such aspects of the neurophysiological response as enhanced excitation of Aδ fibers and enhanced CMAP decrement, resulting in increased pain perception. Furthermore, SMF (0.73 T for 1 to 2 h) may modulate neuromuscular transmission. Thus, SMF could affect the behavior of some types of ion channels associated with Aδ fibers.

Several studies have tested whether activation or inactivation of excitable tissues and cells by moderate-intensity SMF [5-45] and their theoretical models for the action of SMF on excitable tissues and cells have been proposed [14,54-57]. To date, however, there is insufficient direct experimental evidence pertaining to these theoretical models and the discrepancy of our present results with other studies cannot yet be explained by theoretical models. Further studies are required to better understand the underlying mechanisms of SMF effects on neuromuscular transmission and pain perception.

Conclusion

Both 0.24 T and 0.73 T SMF for 2 h significantly enhanced the excitation of Aδ fibers in the CNAP, compared with the sham-exposed control. Furthermore, 0.73 T SMF for 1 to 2 h significantly enhanced the CMAP decrement, but 0.24 T SMF for up to 2 h did not change it significantly, compared with the control. These results suggest that SMF (0.24 and 0.73 T for 2 h) enhances pain perception because the Aδ fibers are responsible for pain

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transmission. In addition, SMF (0.73 T for 1 to 2 h) may modulate neuromuscular transmission. Thus, SMF could affect the behavior of some types of ion channels associated with Aδ fibers, probably due to SMF-induced modulation of ion/ligand binding and ion transport.

Conflicts of Interest

The authors declare that we have no conflicts of interest on submission of manuscript for publication.

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