Five-tesla Static Magnetic Fields Suppress Food and Water Consumption and Weight Gain in Mice

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Abstract: In this study, the effects of 5-tesla (T) static magnetic fields (SMFs) on food and water intake in BALB/c mice were examined. We also examined body weight changes, organ weights and some serum biochemical parameters to evaluate the physiological changes resulting from changes in food and water intake.

Mice were exposed to 5-T SMFs for 24 h and 48 h. Food intake, water intake and the mean body weight of mice tended to decrease after 24 h of exposure to SMFs (p = 0.054, p = 0.119, p = 0.107, respectively). Those parameters decreased significantly after 48 h of exposure (p = 0.039, p = 0.0003, p = 0.009, respectively). These results suggested a positive relationship between the duration of exposure, and the responses, represented by food intake, water intake, and body weight of the mice. However, the weights of brain, lungs, heart, liver, spleen, and kidneys did not change after 48 h of exposure. The blood urea nitrogen (BUN) levels and blood glucose levels increased significantly after 48 h of exposure (p = 0.03, p = 0.005, respectively). The BUN-to-creatinine (BUN/Cr) ratio tended to increase after 48 h of exposure (p = 0.07).

We conclude that exposure to 5-T SMFs for 48 h suppresses eating and drinking behavior. We considered that the decreased body weight, increased BUN levels and slightly increased BUN/Cr ratio after 48 h of exposure to 5-T SMFs were due to body fluid loss resulting from decreased food and water intake.

Key words: Static magnetic fields — Water intake — Food intake — Body mass — Rodent — Blood chemistry

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INTRODUCTION

In recent years, the development of magnetic resonance technology has created the possibility of exposing people to strong static magnetic fields (SMFs). Nowadays, 1.5-tesla (T) nuclear magnetic resonance imaging (MRI) machines are widely used for medical diagnosis, with small numbers of 2-T machines also being used and 4-T machines being installed to achieve improved scanner performance\(^1\). There is little doubt that the areas in which MRI can be applied will continue to expand, since magnetic resonance technology offers not only structural information (by means of MRI), but also chemical information (by means of magnetic resonance spectroscopy) and functional information (by means of functional MRI)\(^2\). Moreover, nuclear magnetic resonance spectroscopy machines with more powerful SMFs (6–12 T) are being used to conduct chemical research in research laboratories\(^3\), which means that workers may be frequently exposed to strong SMFs.

Research on the safety of SMFs has yielded no direct experimental evidence of any acute adverse effects of exposure to SMFs up to about 2 T in humans\(^3\). Millions of MRI scans performed in the last decade have confirmed that MRI scans are not harmful to patients\(^5\). The National Radiological Protection Board (NRPB) has recommended 2-T SMFs as a ceiling value for acute whole-body exposure, and 5-T SMFs for acute limb exposure\(^3\). The American Conference of Governmental Industrial Hygienists (ACGIH) has published the following threshold limit values for SMFs: routine occupational exposure should not exceed 60 mT and a flux density of 2 T is recommended as the ceiling value\(^4\). Many researchers have reported that SMFs with a field strength of 50 mT to 1.6 T affect behavior such as motor activity, the operant responding, and irritability in animals\(^5\)–\(^9\). However, some researchers have concluded that SMFs with a field strength of 150 mT and 1.5 T had no effects on animal behavior, such as motor activity and passive avoidance\(^10\), \(^11\). Thus, although SMFs above 2 T may affect animal behavior, to date there have been few reports on the effects of SMFs above 2 T.

Neurobehavioral tests such as the measurement of physiological-consummatory behavior, the open field test, the passive avoidance learning test, and other tests have been used to evaluate the effects of chemical and physical agents on rodents\(^12\), \(^13\). It has been known that changes in those behavioral tests may occur on the dose-response curve of toxic effects at lower doses than required to produce other changes such as morphological changes\(^12\). Therefore, evaluation of the effects of strong SMFs above 2 T on animal behavior is urgently needed to assess the safety of strong SMFs from the standpoint of both clinical medicine and occupational health.

The aim of our study was to detect behavioral changes induced by 5-T SMFs. We evaluated physiological-consummatory behavior by measuring food and water intake and changes in the body weight of mice exposed to 5-T SMFs. We also examined body weight changes, organ weights and serum biochemical parameters to evaluate any physiological changes associated with the behavioral changes.
Animals
Eight-week-old male BALB/c CrSlc mice (22.0–25.0 g) were obtained from Japan SLC, Inc. (Hamamatsu, Japan). Four mice were housed in a polycarbonate cage and kept in an animal room (constant temperature 21–23°C, humidity 45–55%, lights on 0600 to 1800 h) under specific pathogen-free conditions. The mice were given chow (Funabashi Farm, Japan) and tap water ad libitum. The cages were 110 mm high, 200 mm deep, and 125 mm wide with an open tray where food and water were provided.

Magnetic field exposure system
A superconducting magnet (SCM) (JS 500, Toshiba Corporation, Japan) was used to generate the SMFs (Fig. 1). The cylinder bore of the SCM was 200 mm in diameter and 1475 mm long. The magnetic flux density was measured with a gaussmeter (FW Bell, U.S.A.). A uniform magnetic flux density was produced in a 200-mm long space at the center of the cylinder bore (Fig. 2). The magnetic flux density at the center of the cylinder was 4.88 ± 0.03 T.

Fig. 1. View of experimental equipment showing an animal cage in the bore of the superconducting magnet (JS 500).
The SCM system was placed in a room with temperature controlled at 21–23°C (Sanyo Electric, Inc., Japan). Humidity in the room was maintained at 45–55%. The air in the cylinder bore was circulated by an air compressor. The temperature at the center of the cylinder bore was also maintained at 21–23°C. Light in the room was controlled with a 24-h cycle of ON at 0600 and OFF at 1800. Light intensity at the edge of the cylinder bore was 250–300 lux, while that inside the cylinder bore was low. However, it was impossible to measure the light intensity of the area where the animals were placed because a photocell illuminometer could not work inside 5-T SMFs. Light intensity in a room was measured using a photocell illuminometer (SPI-1, Toshiba Corporation, Japan).

Static magnetic fields exposure

After handling the animals for seven days, a pair of cages, each containing four mice, was used for each experiment. Four mice were housed in a polycarbonate cage (110 mm in height, 200 mm in depth, 125 mm in width), and given chow and tap water ad libitum during exposure. One cage was placed in the center of the cylinder bore and exposed to 5-T SMFs for 24 h and 48 h. During the same period, another cage was placed in the center of another cylinder bore, resembling the bore of the SCM cylinder, which was outside the shield, under the same

Fig. 2. Static magnetic flux-density distribution inside JS 500.
Origin of x-axis is in the geometrical center of the exposure area.
STATIC MAGNETIC FIELDS SUPPRESS FEEDING AND DRINKING

All animals were weighed before and after exposure to the SMFs. At the end of the exposure period, the amounts of food and water consumption were measured. Immediately after exposure to SMFs for 48 h, blood samples were collected by cardiac puncture under ether anesthesia. Eight out of twenty-four mice from each 48-h exposure group were chosen, and the following organs were sampled and weighed after blood sampling: brain, heart, lungs, liver, spleen, kidneys. Blood samples were rapidly centrifuged and the serum was stored at -80°C until it was analyzed for total osmolality, blood urea nitrogen (BUN), serum creatinine (Cr), blood glucose, total protein (TP), sodium (Na), chlorine (Cl), potassium (K), glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), and lactate dehydrogenase (LDH). The total osmolality values were determined by the freezing-point method in an Osmotoron-5 (Orion Riken Inc., Japan). BUN (urease ultraviolet method), Cr (Folin-Wu method), blood glucose (glucose dehydrogenase method), TP (Biuret method), GOT (ultraviolet method), GPT (ultraviolet method), and LDH (ultraviolet method) were measured in an automatic analyzer (Model 736-40, Hitachi Inc., Japan) by SRL Inc. Japan. Na (Flame photometry), K (Flame photometry) and Cl (chloridemeter) were measured in an automatic electrolyte analyzer (Model 710, Hitachi Inc., Japan) by SRL Inc. Japan. The amount of serum per mouse was limited and it could only be used to measure one or two indices.

BUN and Cr levels were measured in the same animals.

Data analysis

Experimental results were analyzed by use of Student's t-test.

RESULTS

Immediately after the start of the exposure, the animals gathered in a corner of the cage and crouched down. The activity of the mice exposed to the SMFs appeared to be suppressed during the exposure period.

The amounts of food and water consumed by exposed and sham-exposed animals during the exposure period were compared (Fig. 3). The mean food and water intake in the 24-h exposed group tended to decrease (p = 0.054, p = 0.119, respectively). Food intake by the exposed group decreased significantly after 48 h of exposure to SMFs (p = 0.039), and water intake also decreased significantly (p = 0.0003) compared with the sham-exposed group. The mean body weight changes in the exposed groups and sham-exposed groups are shown in Table 1. Exposure to the 5-T SMFs for 24 h tended to decrease the body weight of mice (p = 0.107), although exposure for 48 h did significantly decrease it (p = 0.009).

The organ weights of the brain, lungs, heart, liver, spleen, and kidneys of mice exposed to 5-T SMFs for 48 h are shown in Table 2. The weights of those organs
Fig. 3. Effects of 5-T SMFs on food consumption and water consumption.
A cage containing four mice was exposed to 5-T SMFs for 24 h and 48 h. Food consumption (A) and water consumption (B) per four mice were measured during 24-h and 48-h exposure to 5-T SMFs: exposed group, ■; sham-exposed group, □. Results show mean ± S.D. for 4–6 experiments. # p < 0.1, * p < 0.05, ** p < 0.001 by Student’s t-test.

Table 1. Body weight changes of mice exposed to 5-T SMFs.

<table>
<thead>
<tr>
<th></th>
<th>24 h exposure</th>
<th>48 h exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham</td>
<td>Exposed</td>
</tr>
<tr>
<td>Pre exposure body weight (g)</td>
<td>24.87 ± 1.32</td>
<td>24.93 ± 1.19</td>
</tr>
<tr>
<td>Post exposure body weight (g)</td>
<td>25.03 ± 1.41</td>
<td>24.73 ± 1.30</td>
</tr>
<tr>
<td>Post exposure body weight - Pre exposure body weight (g)</td>
<td>0.16 ± 0.54</td>
<td>-0.20 ± 0.91</td>
</tr>
<tr>
<td>n</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

Results show mean ± S.D., ** p < 0.01 by Student’s t-test.
Table 2. Effects of SMFs on body weight and organ weight of mice.

<table>
<thead>
<tr>
<th></th>
<th>Absolute weight (g)</th>
<th>Relative organ weight (percentage of body weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham exposed (n = 8)</td>
<td>Exposed (n = 8)</td>
</tr>
<tr>
<td>Pre exposure body weight</td>
<td>24.1 ± 0.9</td>
<td>24.0 ± 0.5</td>
</tr>
<tr>
<td>Post exposure body weight</td>
<td>24.6 ± 1.0</td>
<td>23.7 ± 0.6'</td>
</tr>
<tr>
<td>Brain</td>
<td>0.44 ± 0.02</td>
<td>0.42 ± 0.02</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.16 ± 0.01</td>
<td>0.17 ± 0.01</td>
</tr>
<tr>
<td>Heart</td>
<td>0.13 ± 0.01</td>
<td>0.13 ± 0.01</td>
</tr>
<tr>
<td>Liver</td>
<td>1.04 ± 0.07</td>
<td>0.99 ± 0.08</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.09 ± 0.02</td>
<td>0.07 ± 0.01</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.36 ± 0.02</td>
<td>0.36 ± 0.01</td>
</tr>
</tbody>
</table>

Mice were exposed to 5-T SMFs for 48 h.
Results show mean ± S.D., * P < 0.05 by Student’s t-test.

in the exposed animals did not change after 48 h of exposure.

The data obtained from serum biochemical analyses after 48 h of exposure are shown in Table 3. The BUN levels and the mean blood glucose values were significantly higher in the exposed group than in the sham-exposed group (p = 0.03, p = 0.005, respectively). The BUN/Cr ratio in the exposed group tended to be higher than in the sham-exposed group (p = 0.07).

DISCUSSION

We concluded that exposure to the 5-T SMFs for 24 h tended to suppress food intake, water intake and body weight gain, while exposure for 48 h suppressed them significantly. Thus, the results of our study revealed a positive relationship between the duration of exposure, and the responses, represented by food intake, water intake and the body weight of the mice.

The changes in body weight may be a reflection of changes in tissue mass or body fluid content, while changes in body weight of short duration may be due to fluid shifts. Plasma creatinine levels and BUN levels are usually a reflection of the glomerular filtration rate, and BUN levels are more sensitive than creatinine. The BUN/Cr ratio has been used as a sensitive clinical index of very moderate or prodromal hypohydration. It is inferred that the decreased body weight, increased BUN level, and slightly increased BUN/Cr ratio after 48 h of exposure to 5-T SMFs were due to body fluid loss resulting from decreased food and water intake.
Reviewing the studies on the effects of SMFs on the eating and drinking behavior in animals, some studies have shown that the amount of food intake was increased in animals exposed to SMFs with the field strength 20 mT, 30 mT or 110 mT, although one study showed that exposure to 60-mT SMFs did not affect food intake. Concerning the effects of SMFs on the water intake of animals, several studies showed the water intake of animals increased after exposure to SMFs with field strengths of 20 mT to 600 mT. Concerning the effects of SMFs on body weight, Nahas et al. showed that exposure to 20-mT and 120-mT SMFs increased the body weight of rats, whereas Bellossi et al. did not find any changes in the body weight of rats exposed to 400-mT and 800-mT SMFs. Barnothy showed that the body weight of mice decreased on the second day of continuous exposure to 420-mT and 940-mT SMFs. He thought the decrease in body weight on the second day was due to a “shock” induced by the magnetic field.

These studies suggest that exposure to SMFs, from 20 mT to 600 mT, increases food and water intake by animals, while exposure to SMFs, from 20 mT to 120 mT, increases the body weight of animals. These findings are the opposite of ours. Such conflicting findings indicate that SMFs of 5 T might affect animals in a different way than SMFs of less than 600 mT.

The mechanism underlying the effect of 5-T SMFs on the eating and drinking behavior of mice can be explained in several ways. The first possible explanation is that the mice exposed to 5-T SMFs felt discomfort that led to reduced food and water intake. Weiss et al. revealed that the mice preferred the non-magnetic

<table>
<thead>
<tr>
<th></th>
<th>Sham exposed</th>
<th>Exposed</th>
<th>Number</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>BUN (mg/dl)</td>
<td>16.5 ± 3.4</td>
<td>22.0 ± 3.8</td>
<td>7</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Cr (mg/dl)</td>
<td>0.4 ± 0.1</td>
<td>0.4 ± 0.1</td>
<td>7</td>
<td>N.S.</td>
</tr>
<tr>
<td>BUN/Cr</td>
<td>40.7 ± 13.6</td>
<td>53.0 ± 9.2</td>
<td>7</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Na (mEq/l)</td>
<td>147.9 ± 1.8</td>
<td>149.0 ± 3.2</td>
<td>7</td>
<td>N.S.</td>
</tr>
<tr>
<td>K (mEq/l)</td>
<td>4.6 ± 0.6</td>
<td>4.2 ± 0.4</td>
<td>7</td>
<td>N.S.</td>
</tr>
<tr>
<td>Cl (mEq/l)</td>
<td>109.0 ± 2.4</td>
<td>107.4 ± 1.8</td>
<td>7</td>
<td>N.S.</td>
</tr>
<tr>
<td>TP (g/dl)</td>
<td>5.0 ± 0.2</td>
<td>4.9 ± 0.2</td>
<td>6</td>
<td>N.S.</td>
</tr>
<tr>
<td>Blood glucose (mg/dl)</td>
<td>153.0 ± 25.1</td>
<td>199.3 ± 18.6</td>
<td>6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>GOT (IU/l)</td>
<td>194.6 ± 73.2</td>
<td>206.4 ± 106.6</td>
<td>5</td>
<td>N.S.</td>
</tr>
<tr>
<td>GPT (IU/l)</td>
<td>81.6 ± 81.5</td>
<td>73.0 ± 71.2</td>
<td>5</td>
<td>N.S.</td>
</tr>
<tr>
<td>LDH (IU/l/37°C)</td>
<td>532.3 ± 156.2</td>
<td>368.3 ± 96.5</td>
<td>6</td>
<td>N.S.</td>
</tr>
<tr>
<td>Osmotic Pressure (mOsm/l)</td>
<td>347.0 ± 5.2</td>
<td>348.7 ± 5.9</td>
<td>6</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* Student’s t-test, N.S.: non-significant
area to the magnetic area with 4-T SMFs using a simple T-maze but they did not find any differences between 1.5-T SMFs and the non-magnetic area\textsuperscript{24}. It has been reported that people exposed to 4-T SMFs experienced vertigo and nausea during rapid head movement, but that these responses did not occur in subjects lying stationary in the fields\textsuperscript{2, 25}. Head movements can produce small magnetohydrodynamic forces in the semicircular canals of the inner ear\textsuperscript{21}. Accordingly, the animals exposed to strong SMFs over 1.5 T may feel discomfort such as vertigo and nausea, and their behavior is depressed. This hypothetical mechanism can explain the suppressive effect of 5-T SMFs on the eating and drinking behavior of animals.

The second possible explanation is that 5-T SMFs may affect the circadian rhythms of mice. Melatonin, a ubiquitously acting hormone secreted by the pineal grand, shows a significant circadian rhythm in mammals, and melatonin levels in the blood of mammals are high at night and low during the day\textsuperscript{26}. Recently, many researchers have shown that melatonin, as well as the enzyme involved in its synthesis serotonin-N-acetyltransferase (NAT)\textsuperscript{27, 28} and cyclic adenosine monophosphate\textsuperscript{29} were reduced by SMFs in the geomagnetic range during the dark phase. The drinking and eating behavior of rodents synchronizes with light-dark alternation and exhibits a regular 24-h rhythm\textsuperscript{30}. The changes in circadian rhythms produced by magnetic fields may affect drinking and eating behavior. However, these studies were concerned with the effects of SMFs in the geomagnetic range and 140-mT SMF had no significant effect on nocturnal pineal melatonin synthesis in rats\textsuperscript{31}. The effects of SMFs up to 5 T on the circadian rhythm of animals have not been investigated.

Finally, we cannot exclude the possibility that 5-T SMFs acted directly on the central nervous system of mice. Eating and drinking behavior are regulated by complex mechanisms, and there are several neural centers for appetite and thirst\textsuperscript{32, 33}. However, the effects of 5-T SMFs on such neural centers have not been revealed.

Blood glucose levels in the exposed group were higher than in the sham-exposed group. A temporary diabetic-like response with an increased level of cortisol was reported in rats exposed to 1 or 10 mT SMFs\textsuperscript{34}. This phenomenon was explained as a response to stress produced by SMFs. The magnetic fields we tested were 5-T SMFs and this field strength should be strong enough to produce stress in animals. Thus, the elevation of blood glucose can also be explained by the “stress” of exposure.

In the near future, there is no doubt that the chances of exposure to powerful SMFs in our daily lives will increase. Our results, which showed that 5-T SMFs affect animal behavior, should be kept in mind when we evaluate the safety of SMFs. Further studies are needed to clarify the mechanism underlying the effects of strong SMFs on animal behavior from the standpoint of clinical medicine and occupational and environmental health.
ACKNOWLEDGMENTS

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