Study on Antidepressant-Like Effects of Radon Inhalation on Forced Swim Induced Depression in Mice

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In this study, we aimed to find out new indications of radon therapy and examined whether radon inhalation induced antidepressant-like effects in mice. First, we investigated the effects of radon inhalation on the forced swim stress-induced model of depression. We evaluated depression-like symptoms before and after forced swim test (FST). All mice were examined the locomotor activity and the responses to novel environments by open field test, and only depression groups performed depression-like behavior by FST. Pre-treated mice inhaled radon at background (BG) level, or at a concentration of 2,000 Bq/m$^3$ for 24 h before FST, and post-treated mice inhaled similar levels of radon after the FST. Forced swim stress induced depression-like behavior, and 2,000 Bq/m$^3$-radon inhalation alleviated depression-like symptoms compared to BG level concentration. Concurrently, Swim stress induced the decrease in norepinephrine and dopamine levels in brain tissue. Furthermore, swim stress-induced depression reduced superoxide dismutase activity in blood plasma and increased lipid peroxide content in brain tissue. Treatment with radon inhalation produced antidepressant-like effects, i.e., enhanced monoamines, including Serotonin, norepinephrine and dopamine levels in brain tissue, as well as depression-like behavior. These findings indicated that radon inhalation prevented and alleviated swim stress-induced depression-like symptoms in mice.

Key Words: radon inhalation, forced swim test, open field test, monoamines, antioxidants

1. Introduction

Radon ($^{222}$Rn) is a natural radioactive, inert gaseous element that emits α-particles. Therapy using radon gas volatilized from radon-enriched water is performed for various diseases such as rheumatoid arthritis,$^{11}$ bronchial asthma,$^{2}$ hypertension, diabetes and pain, particularly osteoarthritis.$^{3}$

We have previously demonstrated that radon inhalation inhibits hepatopathy,$^{3,6}$ renal damage,$^{4,7}$ diabetes,$^{8,9}$ colitis,$^{10}$ and cerebral ischemia,$^{10}$ or alleviates paw edema$^{12}$ and inflammatory$^{13}$ and neuropathic pain$^{14}$ in mice. It is highly probable that the low-dose inhalation of radon activates defensive systems in these organs and thereby contributes to the prevention or reduction of reactive oxygen species (ROS)-related injuries, which are thought to involve peroxidation. Furthermore, the results in our experiments using intact rabbits confirmed that radon inhalation increased β-endorphin, methionine (met)-enkephalin and norepinephrine in the blood,$^{3,3}$ indicating the possibility that radon has an effect on relaxation. However, there have been no studies regarding the effects of radon on an animal model of depression-like symptoms and the mechanisms by which radon mediates relief of depression has not
been fully clarified.

Depressions are associated with a decrease in monoamines, hippocampal atrophy, inhibition of hippocampal neurogenesis, and/or reduction of hippocampal neurons e.g., brain-derived neurotrophic factor (BDNF). Ping et al. has shown that increase in BDNF levels in prefrontal cortex and hippocampus relieved depression or anxiety. Forced swim test (FST) is the most commonly used behavioral test which predicts the efficiency of antidepressant activity. Depression-like behavior has been often measured in the FST as immobility time and more recent researchers assessed the modified FST measure the swimming and climbing time. The decrease in monoamines, such as serotonin (5-HT) and norepinephrine especially in forebrain has been involved in depression, and meanwhile Cryan et al. suggested that 5-HT was activated by swimming and norepinephrine by climbing. Depression has been, moreover, related to oxidative stress and swim stress induced decrease in glutathione (GSH) and increase in catalase (CAT) levels in brain tissues of mice. Oxidative stress damaged antioxidative enzymes, such as glutathione peroxidase, CAT and superoxide dismutase (SOD). Damage can be directly linked to excessive levels of ROS, particularly superoxide (O2·−), hydrogen peroxide (H2O2), and nitric oxide (NO).

The purpose of this study was, therefore, to determine whether pre- (prevention) or post- (therapy) treatment with radon produces a remission of FST-induced depression in mice. We examined the following biochemical parameters of depression: 5-HT, norepinephrine and dopamine levels, as well as depression-like symptoms, SOD activity, total GSH and LPO contents.

2. Materials and methods

2·1 Animals and radon inhalation

Ethical approval for all protocols and experiments was obtained from the animal care and use committee of Okayama University. Male Institute for Cancer Research (ICR) mice (Charles River Laboratories Japan, Inc., Yokohama, Japan) for 8–9 weeks old were used in the protocols. The mice were housed in breeding cages (4 mice in each) for four days between receipt and the start of the experiments.

For radon inhalation, we utilized our novel radon exposure device for small animals. To generate conditions for inhalation of a specific radon concentration, the “Doll Stone” radon source (Ningyotoge Genshiryoku Sangyo, Co., Ltd., Okayama, Japan) was placed in a radon tank. The mice were separated into pre-treated (preventive) or post-treated (curative) groups that were treated before or after FST (3 min × 3 trials) respectively with radon inhalation of BG level (atmospheric air; ca. 20 Bq/m3), or at a concentration of 2,000 Bq/m3. Mice inhaled radon for 24 h. An air pump (Inno-β6000, Nisso Industry Co., Ltd., Tokyo, Japan) was used to supply mice with atmospheric air for radon at BG level. During radon inhalation, mice could move freely and had free access to food and water.

The room and cages were temperature (22±1°C) and humidity (40±4%) controlled with a 12 h light/dark cycle (lights at 8:00).

2·2 Testing procedure

All behavioral experiments were performed between 9:00 and 16:00 h.

2·3 Locomotor activity

Open field tests (OFT) assess the locomotion, exploration and anxiety. Activity monitoring was conducted in a square shaped white open-field apparatus, measuring 45×45 cm with 40 cm walls. The floor of the arena was divided into 16 equal squares. A central square (11.25×11.25 cm) was drawn in the middle of the arena. All mice were placed individually in the open-field monitored for 3 min.
by a video camera (Sony DSC-WX10). The number of crossings and time in the central area was blindly measured by observers who did not know whether the mice had inhaled radon.

2.4 Forced swim test

The modified FST was essentially performed as described by Detke et al. Depression group mice were individually placed into a transparent polymethylpentene (TPX®; Mitsui Chemicals, Inc., Tokyo, Japan) beaker (20 cm height × 14 cm diameters, filled with water to a depth of 12 cm) with temperature 25 ± 1°C and monitored for 3 min using a video camera (Sony DSC-WX10). During the test, swimming, climbing and immobility time was blindly measured by observers who did not know whether the mice had inhaled radon.

2.5 Experimental design

The OFT was conducted in all mice on the fourth day after obtaining (Pre; Fig. 1A and B).

Then pre-treated mice (Fig. 1A) inhaled 2,000 Bq/m³-radon or atmospheric air (BG level of radon) for 24 h. Immediately after radon inhalation (Post-Inh.), OFT were performed to evaluate whether radon has any negative effects on the locomotion. In the next 3 days, only the depressive group mice were tested by FST (D1–3), and then the OFT (Post-DEP) were conducted for all pre-treated mice.

Depressive groups of post-treated mice (Fig. 1B) were tested by FST for three times (D1–3) and then all post-treated mice by OFT (Post-DEP). Briefly,
mice inhaled 2,000 Bq/m³-radon or BG level of radon for 24 h and tested using the OFT (Post-Inh.). FST were performed for only depressive groups on the next day (Post-Inh.).

2.6 Biochemical assays

Two days after the end of radon inhalation of the pre-treated mice and a day after radon inhalation for the post-treated mice, biochemical analysis was performed, because on the day radon inhalation was the most effective on the depression-like behavior. Brains were quickly excised and preserved at −80°C until use.

5-HT levels in the right forebrain were measured using an ELISA kit (Labor Diagnostika Nord GmbH & Co. KG, Nordhorn, Germany) according to the manufacturer’s recommendations. Brain-tissue samples were homogenized in a 0.01 N HCl with 0.1% ascorbic acid on ice. The homogenates were centrifuged at 15,500×g for 5 min at 4°C, and the supernatants were used for the assay of 5-HT levels. Sample absorbance was read at 450 nm in a spectrophotometer and this value was subtracted from the absorbance at 620 nm.

Norepinephrine and dopamine levels in left forebrain were measured using an ELISA kit (Labor Diagnostika Nord GmbH & Co. KG, Nordhorn, Germany) according to the manufacturer’s recommendations. Mouse brains were homogenized in a 0.01 N HCl with 1 mM EDTA and 4 mM sodium metabisulfite on ice. The homogenates were centrifuged at 15,000×g for 15 min at 4°C, and the supernatants were used for the assay of norepinephrine and dopamine levels. Sample absorbance was read at 450 nm in a spectrophotometer and this value was subtracted from the absorbance at 620 nm.

Brain SOD activity was measured by the nitroblue tetrazolium (NBT) reduction method using the Wako-SOD test (Wako Pure Chemical Industry, Co., Ltd., Osaka, Japan) according to the manufacturer’s recommendations. Mouse hindbrains were homogenized in 10 mM phosphate buffer (PBS; pH 7.4) on ice. The homogenates were centrifuged at 12,000×g for 45 min at 4°C, and the supernatants were used for the assay of SOD activity. The extent of inhibition of the reduction in NBT was measured at 560 nm using a spectrophotometer. One unit of enzyme activity was defined as 50% inhibition of NBT reduction.

Brain GSH contents were measured using the Bioxytech GSH-420™ Assay Kit (OXIS Health Products, Inc., Portland, OR, USA) according to the manufacturer’s recommendations. Briefly, brain-tissue samples from hindbrain were suspended in 10 mM PBS (pH 7.4), mixed with ice-cold 7.5% trichloroacetic acid solution, and homogenized. The homogenates were centrifuged at 3,000×g for 10 min. This assay is based on the formation of a chromophoric thione, the absorbance of which can be measured at 420 nm and is directly proportional to the total glutathione concentration.

LPO content in hindbrains was assayed using the Bioxytech LPO-586™ Assay Kit (OXIS Health Products, Inc.) according to the manufacturer’s recommendations. Brain samples were homogenized in 10 mM PBS (pH 7.4) on ice. Prior to homogenization, 10 µL of 0.5 M butylated hydroxytoluene in acetonitrile was added per 1 mL of the buffer-tissue mixture. After homogenization, the homogenate was centrifuged at 15,000×g for 10 min at 4°C, and the supernatant was used for the assay. The LPO content assay is based on the reaction of a chromogenic reagent, N-methyl-2-phenylidole, with malondialdehyde and 4-hydroxyalkenals at 45°C. The optical density of the colored products was read at 586 nm in a spectrophotometer.

The protein content of each sample was measured by the Bradford method using Protein Quantification Kit-Rapid (Dojindo Molecular Technologies, Inc., Kumamoto, Japan).
Data values are presented as mean ± standard error of the mean (SEM). Each experimental group consisted of samples from five to eight animals. The statistical significance of differences was determined by Wilcoxon test for comparisons of behavior before or after inhalation, by Mann–Whitney U-test for comparisons between control without FST and animals that had inhaled radon a concentration of 2,000 Bq/m³ and depressive group (Sham) and depression with 2,000 Bq/m³ radon inhalation group (2000-DEP or DEP-2000), and by Tukey’s tests for multiple comparisons where appropriate. p values were considered significant at p<0.05.

3. Results

3.1 Effects of radon inhalation on locomotor activity, monoamines and antioxidants in mice

To evaluate the influence of radon inhalation on locomotor activity, the behavior of non-depressive mice that were tested without FST and inhaled BG level or 2,000 Bq/m³-radon was analyzed using the OFT before and after inhalation (Fig. 2; Pre and Post-Inh). No significant differences were observed in the results of the number of crossings or time in a central area in the OFT.
Additionally, monoamines, such as 5-HT, norepinephrine and dopamine in the brain, and antioxidative functions such as SOD activity, GSH content in serum and brain or LPO content in brain tissues were measured. There were no significant differences in monoamines (Table 1A), but an increase in SOD activity (Table 1B).

These findings indicated that the radon inhalation enhanced SOD activity and did not induce any negative influences on locomotor activity or monoamines.

3·2 Effect of pre-treatment with radon on FST-induced depression (preventive effects)

Mice were tested using the OFT and FST to evaluate the preventive effects of radon inhalation on depression. No significant changes in locomotor activity were observed after radon inhalation before FST (Post-Inh.) and after FST (Post-DEP) compared to pre-test value (Pre) (Fig. 3A). On the second day of FST (D2), compared to the sham group (Sham), the depression-like behavior was significantly lower ($p<0.05$) at immobility time and higher ($p<0.05$) at swimming time in the group that had inhaled 2,000 Bq/m$^3$-radon prior to FST (Fig. 3B).

The results indicated that pre-treatment with radon decreased despair and increased volition to swim. The lower depressive response of the 2,000 Bq/m$^3$-radon group tended, however, not to last up, and on the third day (D3), the depression-like behavior in sham and 2,000 Bq/m$^3$-radon inhalation groups was almost the same levels.

3·3 Effects of pre-treatment with radon on the levels of monoamines and antioxidants following FST

The levels of monoamines and antioxidants in the brain and serum were assayed in the above radon-pre-treated, depressive groups. The brain dopamine levels decreased significantly ($p<0.05$) after FST (Sham) compared to control mice without FST (Control), but 5-HT, norepinephrine and dopamine levels were increased significantly ($p<0.05$ or 0.001) by the prior inhalation of 2,000 Bq/m$^3$-radon (2000-DEP) (Table 2A). Furthermore, the decrease in brain SOD activity was significantly ($p<0.05$) inhibited by the prior inhalation of 2,000 Bq/m$^3$-radon (Table 2B).

From the results, we confirmed that the radon inhalation alleviated the depression-induced decrease in monoamines and enhanced SOD activity.

3·4 Effect of post-treatment with radon on FST-induced depression (curative effects)

To evaluate the curative effects of radon inhalation on depression, the OFT and FST were performed on mice that were treated with radon inhalation after FST-induced depression. Time in a central area in OFT was decreased by depression (Post-DEP), however, this decrease was alleviated and got closer to pre value (Pre) after 2,000 Bq/m$^3$-radon inhalation (DEP-2000) (Fig. 4A). The climbing time in FST got smaller in D2 or D3, but after radon inhalation (Post-Inh.), the time was increased significantly ($p<0.05$) compared to the third day of FST (D3) (Fig. 4B).

These findings indicated that post-treatment with radon increased volition to climb the wall of the beaker and had curative effects on depression, but the results were not very significant.

3·5 Effects of post-treatment with radon on FST-induced changes in monoamines and antioxidants

Brain norepinephrine levels in depressive mice (Sham) were significantly ($p<0.05$) lower than in control mice without FST (Control), but the levels of 5-HT and norepinephrine increased when the mice inhaled radon at a concentration of 2,000 Bq/m$^3$ after FST (DEP-2000) (Table 3A). FST-induced depression significantly ($p<0.05$) increased brain LPO
content (Table 3B) compared with controls, but the 
LPO value decreased significantly \((p<0.05)\) to the 
control level with post-depression radon treatment 
(Table 3B).

The results showed that post-treatment with radon 
increased the monoamine and antioxidative func-
tions.

4. Discussion

Radon therapy is performed for various diseases, 
particularly for ROS-related diseases such as rheu-
matic diseases in Badgastein, Austria\(^1\) and bronchial 
asthma,\(^2\) hypertension, diabetes or osteoarthritis\(^3\) 
especially at the Misasa Medical Center of Okayama 
University Hospital for a long time. Although pa-
Patients with depression have been prescribed radon therapy in Misasa 30–40 years ago, there have been no preclinical studies on the effects of radon for depression and the mechanism by which radon induces these effects remains to be clarified. We have previously demonstrated that radon inhalation increased β-endorphin and met-enkephalin in the blood, indicating the possibility that radon has an effect on relaxation. Furthermore, we have shown that radon and thermal therapy is more effective than thermal therapy. In this study, we demonstrated whether radon inhalation induced a remission of depression. To evaluate the antidepressant-like effects of radon inhalation, we used the mouse FST-induced model of depression.

Safety and adverse effects of treatments have often become major problems in the treatment of depression. Pharmacological treatment, such as antidepressants has been often prescribed for the therapy. However, in this treatment, adverse effects have been frequently pointed out. Epidemiological studies in Europe and North America indicated the risk of lung cancer due to indoor radon exposure. Adverse health effects of radon progeny that deposits in the lungs were also concerned. Some researchers said also that the lifestyle influences, e.g. smoking, affect greater negative impacts than radon exposure. In radon therapy, in Misasa, for example, patients inhale 2,080 Bq/m³ radon 9–12 times, for 40 min each time, over 3–4 weeks, in a room whose temperature is controlled at 44°C. According to the United Nations Scientific Committee on the Effects of Atomic Radiation, therapeutic effective dose within the range of ca. 63 μSv (2,080 Bq/m³, 12×40 min exposures=8 h) is lower than the average annual amount of natural radiation (2.4 mSv). The adverse effects or negative effects of radon therapy have not been reported in the past. Combination of radon therapy and antidepressants are useful in predicting some possible adverse effects or drug–drug interaction with antidepressants. Radon therapy has been drawn attention as a treatment for various diseases that works early and has long-lasting analgesic effects. The dose of radon absorbed under our experimental conditions was also quite low, according to previous reports. In this paper, mice inhaled radon in a room with controlled temperature (22±1°C) and humidity (40±4%), because mice are easily affected.

<table>
<thead>
<tr>
<th>Pre-treatment with Radon</th>
<th>Control</th>
<th>Sham</th>
<th>2000-DEP</th>
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<tbody>
<tr>
<td><strong>A) Monoamines</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Norepinephrine [ng/ml]</td>
<td>54.0±2.0</td>
<td>41.8±2.8</td>
<td>60.2±3.4*</td>
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<tr>
<td>Dopamine [ng/ml]</td>
<td>295±8</td>
<td>226±18*</td>
<td>355±23###</td>
</tr>
<tr>
<td>5-HT [ng/ml]</td>
<td>73.9±2.9</td>
<td>64.7±1.7</td>
<td>80.5±4.7*</td>
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<tr>
<td><strong>B) Antioxidative Functions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOD [U/mg protein]</td>
<td>61.7±2.7</td>
<td>49.4±11.1</td>
<td>75.8±5.3*</td>
</tr>
<tr>
<td>GSH [nmol/mg protein]</td>
<td>50.8±1.4</td>
<td>49.9±1.5</td>
<td>52.0±1.5</td>
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<td>LPO [nmol/mg protein]</td>
<td>0.38±0.11</td>
<td>0.43±0.07</td>
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Table 2: Effect of pre-treatment with Radon on depression-induced changes in monoamines in serum (A) and antioxidative functions in brain tissues (B) of depressive mice that had inhaled radon at BG level (Sham), or at a concentration of 2,000 Bq/m³ (2000-DEP) prior to FST. Each value indicates the mean±SEM. N=5–8. *p<0.05 vs. Control. **p<0.01, ***p<0.001 vs. Sham.
by heat and like dry environment, we cannot use high temperature and humidity. The results in our previous study, however, indicated that combined therapy with radon and heat is more efficient than thermal therapy without radon on humans.3)

The results indicated radon inhalation itself did not induce any negative influences on locomotor activity or monoamines and enhanced antioxidative functions. In our experiments, there were no significant changes in locomotor activity, exploration, or anxiety at OFT caused by FST-induced depression.

Depressions are associated with the decrease in monoamines, hippocampal atrophy, reduction of hippocampal neurons, and/or inhibition of hippocampal neurogenesis.19, 41, 42) Ping et al. has demonstrated that increase in BDNF levels in prefrontal cortex

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**Fig. 4** Effect of post-treatment with Radon on FST-induced depressive responses: Depression-like behavior was measured using OFT (A) and immobility (i), swimming (ii) and climbing time (iii) during FST (B) in depressive mice that inhaled radon after FST (Post-DEP) at BG level (Sham), or at a concentration of 2,000 Bq/m$^3$ (DEP-2000). Post-Inh.: After inhalation. Each value indicates the mean±SEM. $N=7$–8. $^*p<0.05$ vs. D3 of DEP-2000 mice.
Cryan et al. suggested that 5-HT was activated by swimming and norepinephrine by climbing. Stress increased glucocorticoid and suppressed the epigenetic gene expression of dopaminergic neurons. Pre-treatment with radon decreased despair and increased volition to swim, and from the results, we confirmed that the radon inhalation alleviated the depression-induced decrease in monoamines (5-HT, norepinephrine and dopamine). At the suggestion of Cryan and Lucki, these findings indicated that an increase in 5-HT was involved in swimming. This result is consistent with the results of the behavioral test that radon treatment increased the swimming time in FST. The lower depressive response of the 2,000 Bq/m³-radon group tended, however, not to last up, and, on the third day (D3), depression-like behavior in sham and 2,000 Bq/m³-radon inhalation groups was almost the same. When we consider more long effects on depressive situation, we should change the experimental design, e.g., more higher concentration of radon or longer inhalation time. Post-treatment with radon increased volition to climb the wall of the beaker and had curative effects on depression, but the results were not very significant. Monoamines and antioxidative functions were increased after radon inhalation. Increase in norepinephrine was involved in higher climbing time, indicating that these results were consistent with the results of Cryan et al. There were several differences in the inhalation methods used in those studies compared with our study. First, rabbits used were intact animals under anesthesia. Second, radon spring water was sprayed by an ultrasonic nebulizer connected to the respirator intake port for direct inhalation. Third, the radon concentration used, was relatively high (14–18 kBq/L). Therefore, these results cannot be directly compared with those of the present study. In previous studies, we have also demonstrated chronic constriction injury-induced increase in plasma norepinephrine was inhibited by radon inhalation. Furthermore, we have previously reported that radon inhalation contributed to the increase in β-endorphin and met-enkephalin in the blood of intact rabbits that have effects on relaxation.

<table>
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<tr>
<th>Post-treatment with Radon</th>
<th>Control</th>
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<th>DEP-2000</th>
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<tbody>
<tr>
<td>A) Monoamines</td>
<td></td>
<td></td>
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<tr>
<td>Norepinephrine [ng/ml]</td>
<td>37.9 ± 1.4</td>
<td>32.6 ± 1.4*</td>
<td>42.2 ± 1.5**</td>
</tr>
<tr>
<td>Dopamine [ng/ml]</td>
<td>297 ± 21</td>
<td>257 ± 21</td>
<td>342 ± 23</td>
</tr>
<tr>
<td>5-HT [ng/ml]</td>
<td>98.9 ± 6.0</td>
<td>92.0 ± 8.3</td>
<td>116.3 ± 4.0*</td>
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<tr>
<td>B) Antioxidative Functions</td>
<td></td>
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<tr>
<td>SOD [U/mg protein]</td>
<td>89.8 ± 4.8</td>
<td>87.1 ± 7.8</td>
<td>75.8 ± 4.0</td>
</tr>
<tr>
<td>GSH [nmol/mg protein]</td>
<td>51.6 ± 1.7</td>
<td>45.8 ± 2.0</td>
<td>46.7 ± 2.0</td>
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<td>LPO [nmol/mg protein]</td>
<td>0.38 ± 0.09</td>
<td>0.82 ± 0.08*</td>
<td>0.45 ± 0.10*</td>
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</table>
but we did not focus in this study.3)

Depression has been, moreover, associated with oxidative stress44–46) and swim stress induced decrease in GSH and increase CAT in brain tissues of mice.26) Oxidative stress damaged antioxidative enzymes, such as glutathione peroxidase, CAT and SOD. Because SOD detoxifies \( \text{O}_2^- \) to \( \text{H}_2\text{O}_2 \) and CAT decomposes \( \text{H}_2\text{O}_2 \) into the water and oxygen, damage can be directly linked to excessive levels of ROS, particularly \( \text{O}_2^- \), \( \text{H}_2\text{O}_2 \), and NO.27, 28) Radon inhalation enhanced SOD activity and decreased LPO content, i.e. antioxidative functions. At this point, these findings indicated that the treatment with radon had effects on depression. The results have not been replicated for GSH.

In summary, the results showed that the pre-inhalation of radon increased swimming time and decreased immobility time, and post-treatment increased climbing time. Associated with that behavioral test, monoamines and antioxidative functions were enhanced by both pre- and post-treatments. It is assumed that enhancement in antioxidative functions changed monoamine in the brain and it led to relief of depression, indicating that radon inhalation was useful as a treatment for depression.

The purpose of radon therapy in this paper is alleviating depression, i.e. we have expected to decrease in the consumption of antidepressants by using this treatment. Regardless of the fact that patients with depression have been prescribed radon therapy, there were not any clinical study reports that indicated the effects of radon therapy on depression. In this study, we have demonstrated novel scientific mechanisms of radon therapy for depression that has clinical implications. Radon therapy was meaningful from the viewpoint of reduction of depression-like symptoms and the elucidation of depression relieving mechanism.

However, the radon-mediated alleviation of depression only lasted for a short time. In future experiments, we, therefore, aim to analyze the effect of repetitive radon inhalation or combination with antidepressants in mice, to try to extend the alleviating effects of radon on depression.

The data presented in this study provide a substantial basis for future studies aimed at alleviating depression by numerous factors.

Acknowledgments

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強制水泳誘導うつ病マウスに対するラドン吸入による抗うつ効果の検討

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本研究ではラドン療法の新規適応症の探索のため，強制水泳（FST）誘導うつ病マウスに対するラドン吸入による抗うつ効果の有無について検討した。その結果，FSTに伴ううつ様行動や脳内ノルアドレナリン・ドーパミンなどのモノアミンの減少に対し，2,000 Bq/m²ラドンの24時間吸入により抑制することが示唆できた。これらの知見などから，ラドン療法の適応症の一つとして抗うつ効果の可能性のあることがわかった。