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Research report

Lowering barometric pressure aggravates depression-like behavior in rats

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ABSTRACT

Weather change has been known to influence the condition of patients with mood disorder. However, no animal studies have tested the influence of climatic factor on emotional impairment. In this study, we examined the effect of lowering barometric pressure (LP) in a climate-controlled room on immobility time in the forced swim test in rats, which is considered to be an index of behavioral despair (helplessness). When the rats were exposed to daily repeated forced swim, the immobility time gradually increased. This increment was inhibited by repeated administration of the antidepressant imipramine, suggesting that the immobility is an anxiety/depression-like behavior. LP exposure (20 hPa below the natural atmospheric pressure) further increased immobility time in rats submitted to repeated forced swim. In another series of experiments, we examined the effect of daily repeated LP exposure on the maintenance of immobility after withdrawal from 6-day repeated forced swim. When the rats were challenged with forced swim under natural atmospheric pressure on day 14 after the withdrawal, immobility time was significantly longer than in non-conditioned rats. These findings demonstrated that LP in the range of natural weather change augmented the depression-like behavior in rats.

1. Introduction

Mood disorders such as depression, anxiety, obsessive–compulsive disorder and post-traumatic stress disorder are serious problems in today's society. Various animal models have been developed based on the hypothesis that mood disorders are caused by stressors (e.g., the chronic variable stress model) or neuronal deficits (e.g., the olfactory bulbectomy model), and utilized widely for evaluating novel compounds with respect to mood disorders in preclinical settings [1]. Chronic stress can accelerate disease processes, cause neural degeneration, and lead to depression or other mood disorders [2–4]. It has been reported that repeated forced swim stress, which is one of the models of human mood disorders, causes the loss of adult neural stem cells and that antidepressant drugs reverse this disorders [4]. We have demonstrated that changes in social environment, such as social isolation stress, induced behavioral abnormality, and animals reared in social isolation exhibited increased vulnerability to swim stress and increased anxiety to elevated open-arm [5].

Climate has been long suspected to play a role in the onset and development of depression, and the seasonality in the evolvement of depressive symptoms [which are not part of seasonal affective disorder] has been reported for both unipolar and bipolar patients [6–8]. In fact, the admission rates of bipolar depressed patients increase during spring/summer and correlate with maximal environmental temperature [9] and cold, darkness and low barometric pressure have been associated with increased onset rates of depressive episodes in patients [10], suggesting climatic relationships with depression. Moreover, it has been reported that physiological disorders such as headaches [11] and neuropathic pain [12,13], are aggravated by changes of the weather, and a variety of causes have been claimed, e.g., barometric pressure, humidity and temperature. We have demonstrated that experimentally lowering barometric pressure (LP) intensifies pain-related behaviors in rats with chronic constriction injury on the sciatic nerve [12,13]. These reports suggest a climatic relationship with physiological and psychological disorders, and we hypothesized that climatic variables may be associated with onset rates of some specific clinical subtypes of depression. However, there are no data from basic research on the relationship between climatic factor and depression-like behavior in animals.

In the present study, we examined whether LP in a climate-controlled room affects the immobility time in the forced swim test in rats, which is considered to be an index of behavioral despair (helplessness).

Abbreviation: LP, lowering barometric pressure.

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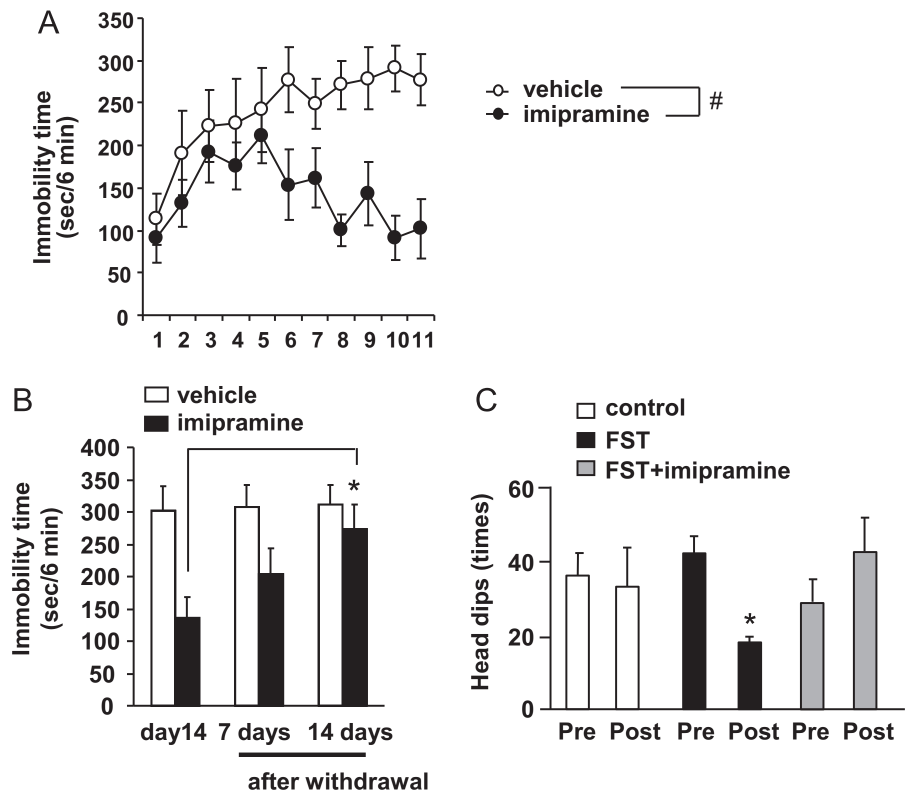

Fig. 1. Effects on behavior of repeated forced swim as chronic stress. A Rats were subjected to repeated forced swim for 11 days. Rats were given imipramine (10 mg/kg, i.p.) or vehicle (saline) after each forced swim for 11 days. Values indicate the mean ± S.E.M. ($n = 6$). #$p < 0.05$ vs the vehicle-treated group. B Rats were subjected to repeated forced swim for 14 days. At 7 and 14 days after the withdrawal of repeated forced swim, rats were exposed to forced swim for 6 min again. Values indicate the mean ± S.E.M. ($n = 5$–6). *$p < 0.05$ vs day 14 on the imipramine-treated group. C Head dip activity was measured as helplessness in response to mild stress after repeated forced swim for 14 days, compared with that before forced swim. Values indicate the mean ± S.E.M. ($n = 4$–6). *$p < 0.05$ vs pre-value in the imipramine-treated group.

2. Materials and methods

2.1. Animals

Male Sprague–Dawley rats, 250–300 g (Japan SLC), were used. The animals were housed two or three per cage under controlled temperature (24 °C) and a 12 h light/dark cycle, and were given free access to food and water. All the experiments were conducted according to the Regulations for Animal Experiments in Nagoya University, and the Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Academic Research Institutions in Japan.

2.2. Repeated forced swim stress

The forced swim test (FST) was carried out as described previously with minor modifications [4,5]. Rats were subjected to daily forced swim stress for 6–14 days. Rats were placed in a glass cylinder (35 cm high × 24 cm diameter) filled to a depth of 25 cm with water (25 ± 1 °C). A 3- or 6-min test was repeated each day. Immobility time (floating) was measured. A rat was judged to be immobile if it ceased struggling and remained floating motionless in water making only those movements necessary to keep its head above water.

Rats were given imipramine (10 mg/kg) or vehicle (saline) intraperitoneally after each forced swim for 11–14 days. After the withdrawal of repeated forced swim, imipramine was no longer applied. At 7 and 14 days after the withdrawal of repeated forced swim, the rats were exposed to forced swim again.

2.3. Elevated open-platform test

An elevated open-platform test was performed in accordance with previous reports [14], with minor modifications. The experiment was conducted in a room illuminated by white fluorescent light (100 lx). A transparent acrylic cylinder (56.5 cm high × 14 cm diameter) was placed upside-down and rats were placed individually on the top (open-platform) for 6 min. When a rat slipped off the platform, it was immediately replaced on the open-platform and the measurement was continued. Head dips (exploratory movement of head/shoulders beyond the edge of the open-platform), a risk assessment behavior, were defined as behavioral activity in response to mild stress, and measured. The total number of times that an animal showed this behavior was recorded.

2.4. Low-pressure exposure

The barometric pressure of the climate-controlled room was lowered by 20 hPa below the atmospheric pressure, which is the type of change often observed when a typhoon passes. This was accomplished over 10 min. The pressure was maintained at this level for 6 min, and then returned to the baseline pressure over 10 min. The ambient temperature was controlled at 24 °C [12,13].

2.5. Statistical analysis

All data were expressed as the mean ± standard error of means (S.E.M.). Statistical significance was determined by Mann–Whitney *U*-test for two group comparisons, and one or two-way analysis of variance (ANOVA) for multigroup comparisons in the experiments, and by a repeated measures ANOVA. Fisher's LSD test was used for post hoc comparisons when the *F* value was significant ($p < 0.05$).

3. Results

3.1. Effects of repeated forced swim as chronic stress on behavior

Rats were subjected to the forced swim stress repeatedly. They exhibited longer immobility in a time-dependent manner (Fig. 1A), and high levels remained even after 14 days (Fig. 1B) which may be explained by either helplessness or habituation to the stress. Imipramine treatment significantly inhibited the increase in immobility time induced by the forced swim stress, although its inhibitory effect was not evident on day 1–5 (Fig. 1A, drug, $F_{(1,10)} = 6.46$, $p < 0.05$; day, $F_{(13,130)} = 5.71$, $p < 0.05$; interaction, $F_{(13,130)} = 4.64$, $p < 0.05$ by repeated two-way ANOVA). Next, at 7 and 14 days after the withdrawal of repeated forced swim for 14 days, rats were exposed to forced swim again. Immobility in the vehicle-treated group remained for at least 14 days, even after the forced swim withdrawal ($F_{(2,8)} = 0.18$, $p > 0.05$ by repeated one-way