

Niacinamide ameliorates the anxiety-like behavior induced by social defeat stress

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Objectives: In Japan, power harassment (mobbing, bullying, spitting, and moral harassment) has become a social problem. It is born out of differences in social status and causes brain dysfunction. World Health Organization reported that 280 million people are suffering from depressive symptoms. Including other mental disorders, the number of people impaired their mental health becomes enormous. Brain dysfunction is treated with medication, but the risk of recurrence is high. Hence, it is important to prevent the on- set of brain dysfunction. Several epidemiological studies reveal that vegetarian have higher risk of mental disorders compared with omnivores. These studies propose that dietary animal protein is important to maintain our mental health. Therefore, clarifying the relationships between brain dysfunction and daily diets may enable to prevent the brain dysfunction through an improvement of dietary habit. The present study employed a social defeat stress model that replicates power harassment in human society to induce the symptoms of depressive disorder. Neuroinflammation induced in this model is believed to be partly responsible for the development of brain dysfunction. Therefore, we focused on niacinamide which has anti-inflammatory effect and is contained in animal products. The purpose of the present study was to verify whether niacinamide administration in the social defeat stress model has a preventive effect on brain dysfunction.

Materials and Methods:

Social Defeat Stress Model BALB/c mice were introduced to resident ICR mice as an intruder for 3 minutes. Aggressive ICR mice (resident) were severely attacked BALB/c mice (intruder). After 3 minutes of this social conflict, BALB/c mice were rescued and placed into the other compartment of the same test cage for 24 hours. In this period, BALB/c mice were exposed to psychological stress by threat and odor from ICR mice. This stress procedure was repeated with unfamiliar aggressive ICR mouse for 10 days, resulting in the brain dysfunction.

Verification of the preventive effect of niacinamide on brain dysfunction BALB/c mice were divided into three groups: control group, stress group, and niacinamide group. For the first 14 days, distilled water was intragastrically administered to the control and stress groups, and niacinamide solution was administered to the niacinamide group. For the next 10 days, the stress and niacin- amide groups were exposed to social defeat stress. Oral administration was continued during this period in all groups, and was done one hour prior to the stress loading in the stress and niacinamide groups. At the end of stress loading period, social interaction test (26th day), elevated plus maze test (27th day) and forced swimming test (34th day) was performed to evaluate the social be- havior, anxiety-like behavior and depression-like behavior, respectively. On 35th day, the brains were collected for metabolome analysis.

Results and Discussion: In the elevated plus maze test, niacinamide administration significantly improved the reduced entries in open arms in stress group, indicating that niacinamide exerts an anxiolytic effect under stressful condition. In the social interaction test and the forced swimming test, behavioral abnormalities were alleviated by niacinamide supplementation although no significant difference was observed. In metabolome analysis of the hippocampus, N-Acetyl-L-aspartic acid increased by social defeat stress tended to be suppressed by niacinamide administration. Accumulation of N-Acetyl-L-aspartic acid is recognized as a partial pathogenesis of Canavan disease, which displays the atrophy of white matter. NAcetyl- L-aspartic acid causes neurotoxicity, which causes the loss of neurons. Therefore, we hypothesized to reduce the elevated N-Acetyl-L-aspartic acid induced by social defeat stress in preventative effect of niacinamide in brain dysfunction.

Conclusion: In the present study, niacinamide administration improved an anxiety-like behavior induced by social defeat stress, indi- cating that meat consumption may be effective in preventing brain dysfunction. Further study should be done to clarify whether di- etary meat products contained niacinamide can ameliorate the brain dysfunction under stressful condition in the future.

Key words: Niacinamide, Social defeat stress, Anxiolytic-like effect, Stress prophylaxis