

Effects of niacinamide in an animal model of motivational deficit induced by lipopolysaccharide administration

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Objectives: The World Health Organization reports that there are more than 300 million people with mental illness worldwide, and the number is increasing in recent years. Although not widely recognized, a symptom that co-occurs with various psychiatric disorders is motivational deficit. The pathological mechanism of motivational deficit remains unclear, which development of appropriate medication for that has been delayed. It is important to prevent the brain dysfunction because of the difficulty in radical care. In the present study, motivational deficit was induced by an intraperitoneal administration of lipopolysaccharide (LPS). Chronic stress has been hypothesized to induce brain dysfunction including motivational deficit mediated by an inflammatory response via TLR4, and LPS also triggers an inflammatory response via the same mechanism. Since the LPS model exhibits the motivational deficit mediated by neuroinflammation, we focused on niacinamide, which has attracted attention for its anti-inflammatory effects. Niacinamide is one of the nutritional components found in meat and other animal products. The objective of the present study was to determine whether niacinamide can ameliorate motivational deficit induced by LPS treatment.

Materials and Methods:

- i) Verification of whether motivational deficit and depressive disorders are induced by similar mechanism Imipramine, one of antidepressants, or Phosphate-buffered saline (PBS) was intraperitoneally injected 23.5 h after LPS or PBS administration. An additional 30 minutes later, a forced swim test or object exploration test was performed. Immobility time in the forced swim test and exploratory behavior in the object exploration test were measured as indices of depressive-like behavior and motivation, respectively. Immediately after the behavioral test, brains were collected for monoamine analysis by reversed-phase high performance liquid chromatography.
- ii) Evaluation for the effect of niacinamide on the animal model of motivational deficit Niacinamide was intragastric administered for 7 days and an open field test was performed on 8th day. PBS or LPS was intraperitoneally injected immediately after the open field test. An object exploration test was further performed 24 hours after the administration.

Results and Discussion:

- i) Verification of whether motivational deficit and depressive disorders are induced by similar mechanism In the forced swimming test, imipramine administration improved the increased immobility induced by LPS administration. This result indicates that the prolonged state of immobility induced by LPS administration is almost identical with the depressive state in human being. In contrast, imipramine had no effect on the exploratory behavior decreased by LPS administration in the object exploration test, indicating that the decreased exploratory behavior is not related to the depressive state in human being. These results demonstrated that motivational deficit is unrelated to depressive disorders and may be induced by completely different mechanism. Therefore, we focused on monoamines which are neurotransmitters to explore the mechanism of motivational deficit. Monoamine analysis revealed that LPS administration decreased dopamine, but not serotonin concentration in the brain. The previous study reported that the disruption of dopaminergic nervous system decreases the exploratory behavior. Thus, motivational deficit induced by LPS administration may be related to the damage of dopaminergic system in the brain.
- ii) Evaluation for the effect of niacinamide on the animal model of motivational deficit In the object exploration test, exploratory behavior which was decreased by LPS administration tended to be improved by niacinamide administration. This result suggests that the anti-inflammatory effects of niacinamide may ameliorate the motivational deficit via the suppression of neuroinflammation. Moreover, previous studies suggest that niacinamide may affect the brain dysfunction via neurogenesis. Therefore, further study should be carried out to clarify the effects of niacinamide for neuroinflammation, neurogenesis and dopaminergic neurons in the future.

Conclusion: The present results indicated that niacinamide treatment alleviated the motivational deficit induced by LPS administration in the object exploration test. The consumption of meat product rich in niacinamide may be useful for preventing the loss of motivation and maintaining the health.

Key words: Niacinamide, Motivation deficits, Lipopolysaccharide