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Attractive and Aversive Response against Sodium Chloride under the Disease Conditions Including Diabetes and Chronic Kidney Disease

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Summary

Due to an aging society, the number of patients with hypertension, cardiovascular diseases and chronic kidney disease (CKD) is increasing. Epidemiological studies have shown that high blood pressure is one of the strongest predictor for developing chronic kidney disease as well as cardiovascular diseases. It is well known that excessive oral salt intake may induce high blood pressure. Thus, sodium restriction is quite a beneficial and reasonable treatment for high blood pressure; however, sodium restriction is sometimes difficult to achieve and excessive restriction affects a patient's quality of life. One candidate factor relevant to the disturbance of salt restriction is impaired sensitivity to salty taste, and previous reports showed that the CKD patient cannot sense salty taste accurately, oral sodium intake may increase. In addition, mammals exhibit sodium attraction for low to moderate sodium concentration, however, in case of higher sodium concentration, sodium attraction shifts to aversive behavior. On this basis, we hypothesized that aversive response against high sodium concentration is disturbed in CKD or diabetic patients.

In order to investigate our hypothesis, we performed the combined analyses of clinical investigation of taste tests, and experimental investigations of lick tests in murine disease models. We first performed the taste tests for healthy volunteers (n = 103, average age 40.3 y.o.) using sodium impregnated filter paper with various concentrations and found that 50% of participants exhibited the aversive response against 10% of sodium solution. In CKD patients (n = 57, average age 64.2 y.o, average Cre 3.46mg/dl), only % of CKD patients exhibited the aversive response against 10% of sodium solution. Regarding the sodium aversive test using disease murine models, we generated CKD murine model by 5/6nephrectomy and type 1 diabetic murine model by repeated low dose streptozotocin injection. We performed the sodium lick tests for these models, however, we could not find any differences in the sodium attractive and aversive responses between the wild-type control mice and various disease model mice.

In summary, we verified significant disturbance in aversive responses against higher salty taste in CKD patients, whereas it was not found in murine experiments. Further experiments and alternative interpretations to explain this inconsistency will be required.