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Clarification of Regulatory Mechanisms of Visceral Fat Accumulation and Ectopic Fat Deposition Induced by Excessive Salt Intake

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Summary

The direct effects of excessive salt intake on the pathogenesis of metabolic diseases remain unknown. Using a mouse model of diet-induced obesity, we have reported that excessive salt intake in combination with excessive fat intake causes visceral fat gain, decreased liver weight, and decreased insulin secretion, despite suppression of body weight gain. In this study, we aimed to clarify how excessive salt intake affects visceral fat accumulation and ectopic fat deposition and contributes to the pathogenesis of metabolic diseases.

Male C57BL6 mice were fed a high-fat diet (60% fat calorie ratio, 0.38% salt concentration) or a high-fat, high-salt diet (60% fat calorie ratio, 2.0 or 4.0% salt concentration), and epididymal white adipose tissue and liver were removed and analyzed at 21 weeks after loading. Gene expression of Cd11c, TNF-α, and MCP-1 in epididymal white adipose tissue was significantly decreased in the high-fat, high-salt diet (HFHS) group compared with the high-fat diet (HF) group. The size and the number of adipocytes and shape of crown-like structures formed by F4/80-positive cells was not different between the two groups. In the liver, there was no significant difference in gene expression of inflammatory cytokines between the two groups, but fat deposition was reduced in the HFHS group compared to the HF group. The HFHS group had higher levels of urinary catecholamines than the HF group.

The differences in gene expression between the HFHS and HF groups suggest that the pathways for M1 macrophage migration, inflammatory cytokine expression, and fibrosis progression, which induces and exacerbates inflammation, were attenuated in the HFHS group. We hypothesized that lipid spillover may be less likely to occur when fat intake is accompanied by excessive salt intake. In addition, the results showed that excessive salt intake accompanied by fat intake causes sympathetic activation, suggesting that sympathetic activation may have a role in the pathogenesis.

Type 2 diabetes mellitus in Asians, including Japanese, is characterized by impaired insulin secretion that does not fully compensate mild insulin resistance caused by visceral fat accumulation. We further investigate the role of excessive salt intake in the pathogenesis of Type 2 diabetes or metabolic diseases.