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Exploring How Salt Loading Affects Kidney Damage via Neuro-Immune Interactions

Shinji Tanaka [1], Chikara Abe [2]

[1] The University of Tokyo Hospital, Division of Nephrology and Endocrinology,
[2] Gifu University Graduate School of Medicine

Summary

We previously reported that stimulation of vagal afferent fibers or restraint stress can activate the C1 neurons -> sympathetic nervous system -> splenic nerve -> spleen axis, resulting in the protection against acute kidney injury. On the other hand, it was demonstrated that elevated blood Na^+ concentrations induced by the administration of hypertonic saline activated OVLT -> PVN -> C1 neurons -> sympathetic nervous system, resulting in an elevation of blood pressure. Based on these findings, we hypothesized that elevated blood Na^+ concentrations induced by the administration of hypertonic saline activates the OVLT -> PVN -> C1 neurons -> sympathetic nervous system -> splenic nerve -> spleen pathway, resulting in the altered phenotype of the splenocytes and kidney protection against acute injury. First, we confirmed that serum Na^+ concentrations were significantly elevated by hypertonic saline administration (orally or by intraperitoneal injection), which is consistent with the previous study. Then we explored whether the elevated blood Na^+ concentrations resulted in kidney protection against acute injury using the bilateral renal ischemia-reperfusion model and cisplatin nephropathy model. Oral administration of hypertonic saline did not reduce plasma creatinine levels (a representative marker of kidney function) in the bilateral renal ischemia-reperfusion model. Furthermore, intraperitoneal administration of hypertonic saline did not affect kidney injury in either model. It is possible that the C1 neurons -> sympathetic nervous system axis was not activated in our mice. We need to confirm the activation of this axis by investigating cFos in C1 neurons and renal sympathetic nerve activity. We are also planning to test other kidney disease models (e.g., folic acid administration, unilateral renal ischemia-reperfusion, cecal ligation and puncture).