How to Reduce Dietary Salt Intake
Just Add Spice?

Richard David Wainford

Hypertension is the single largest risk factor for multiple comorbidities, including stroke, myocardial infarction, and chronic kidney disease, and is projected to be the leading global cause of death and disability by 2020. A major risk factor for hypertension is high dietary salt intake. The salt sensitivity of blood pressure, an exaggerated pressor response to salt intake, affects ≥50% of hypertensive and ≥25% of normotensive adults and profoundly increases the risk of hypertension. Highlighting the profound impact of salt intake on global health, the World Health Organization (WHO) has proposed dietary salt reduction as a target for 2025 to reduce global mortality from noncommunicable diseases. Despite this stated WHO target, the public health impact of dietary salt intake remains significant as the vast majority of countries consume a daily salt intake far in excess of the 5 g/d recommended by the WHO. Despite multiple campaigns to increase public awareness of the potential health benefits of reducing salt intake, global salt intake remains high, and new approaches and scientific insights are required to achieve reductions in population-level salt intake.

The study conducted by Li et al, reported in this issue of Hypertension adopts an alternative approach to this issue of excess salt intake based on the hedonic properties of salty food. The authors have investigated, via clinical and basic science studies, the role of spicy taste preference on the central circuitry that responds to salt intake. The central gustatory system and mesolimbic system are vital to the processing of taste signaling and the hedonic responses to food, including the palatability of salty food. Prior investigations have determined that the individual subjective pleasantness of taste is highly associated with the orbitofrontal cortex (OFC), as such this region was a focus of the studies performed by Li et al. Further, capsaicin, the major active component creating spice in chili peppers, has been reported to influence the sensitivity of the taste of salt in human subjects and provides protection against the development of cardiometabolic disease. Based on these prior studies, Li et al1 have conducted studies to examine the impact of spicy food consumption on salty taste perception, dietary salt intake, and blood pressure.

The authors conducted a community-based observational cross-sectional study in Chinese subjects to determine the impact of the individual preference for salt and spicy flavors on dietary salt intake and blood pressure. The assessment of individual salt preference was assessed by a salt perception test, and salt tolerance was assessed by a salt super-threshold test in which patients indicated which solutions were intolerably salty. This observational study reveals a strong correlation between a preference for high salt intake and hypertension. Interestingly, the high-salt preference group exhibited a reduced perception of salt and a higher threshold for a solution to be defined as intolerably salty. Critically, salt preference had a direct impact on both patient blood pressure and daily salt intake. In terms of blood pressure, those subjects with a higher salt preference had a higher blood pressure (systolic and diastolic) and dietary salt intake than those subjects in the low salt preference group. When spicy preference (tolerability of a capsaicin solution) was assessed in this same subject population, it became apparent that a higher salt preference is associated with a reduced spicy food preference. Importantly, from a public health perspective, high spicy preference was associated with a more sensitive perception of saltiness and a lower threshold of salt intolerance. This preference for spicy food translated into reduced dietary salt intake and blood pressure versus subjects with a low spicy preference. The reduction in salt intake between high- and low-preference spicy food groups was ≥2.5 g/d—this is a potentially highly significant finding given that a reduction of salt intake by 3 g/d can protect against hypertension (Figure).

A prior study by Narukawa et al has demonstrated that 0.5 μmol/L capsaicin increased the perception of saltiness. To assess the potential effects of capsaicin on the neural perception of saltiness, the authors conducted a separate randomized, double-blind interventional study. To achieve this goal, the authors assessed metabolic activity in the insula and OFC in response to a salt stimulus via positron emission tomography/computed tomography. Using different levels of NaCl stimulation (150 and 200 mmol/L), the authors were able to detect intensity-dependent changes in metabolic activity in the insula and prefrontal cortex in response to a NaCl stimulation. Further, the authors report that capsaicin is able to increase metabolic activity in the same regions of the insula and OFC that are activated by NaCl. Critically, the authors show that the intensity-dependent metabolic changes evoked by NaCl are enhanced when capsaicin is added to the NaCl
solution. These data provide the first evidence that capsaicin can alter the neural responses to NaCl via modulation of the activation of the brain regions involved in the hedonic responses to salt.

To directly assess the role of the OFC in salt preference, further studies were conducted in mice. Using both conscious and anesthetized mice, the authors demonstrate that NaCl is able to evoke concentration-dependent neuronal population activity in the OFC (assessed by calcium waves). Supporting the data generated by the authors in human subjects, capsaicin in combination with NaCl enhanced the neuronal response to NaCl. Using a salt preference test, based on licks of standard salt solutions, the authors demonstrate that a 150 mmol/L NaCl–capsaicin solution was less preferable than a 150 mmol/L solution alone, suggesting that capsaicin is able to reduce salt intake and preference. Using an ontogenetic approach, the authors confirm a direct role of OFC neurons in salt preference in mice, in which activation of OFC neurons reduces salt preference and inhibition of OFC neurons increases salt preference.

Despite the significant advances in our understanding of salt preference that are presented by Li et al, there are several remaining questions to be addressed. This well-designed multicenter, random-order, double-blind observational and interventional study was conducted within a Chinese population. It remains to be seen if the findings in this population can be replicated and applied to other populations outside of China. To address the limitations of the current clinical data presented by Li et al, future studies that include (1) a prospective dietary interventional study of the addition of spicy food and capsaicin supplements and (2) precise measurement of individual dietary salt intake would strengthen the evidence of a role of spicy food supplements in reducing salt intake and blood pressure. Conductance of a prospective intervention study in which increased dietary spicy content or dietary spice supplementation is conducted and reductions in patient dietary salt intake and blood pressure are observed would extend the current findings beyond a correlation. Despite the complications inherent in precise assessment of dietary salt intake, this would add validity to the data set and has been achieved previously in multiple large-scale studies (eg, GenSalt, DASH-Sodium) by the provision of all meals. Additionally, further studies are required to elucidate the mechanism(s) by which capsaicin modulates neural responses to evoke potential reductions in salt intake.

What are the major insights that can be gained from this study? Despite many ongoing global public health campaigns designed to reduce dietary salt intake, including those promoted by the American Heart Association and WHO, global and Chinese daily consumption of salt continues to exceed recommended limits. This highlights the difficulty faced in encouraging reduced use of dietary sodium—who wants to reduce the pleasurable and palatable impact of dietary salt? In this study, Li et al provide compelling evidence linking the enjoyment of spiciness in food to enhanced sensitivity to central perception of salt. For the first time, these studies show that (1) both dietary salt intake and the preference to consume salt are linked to the metabolic activity of the insula and OFC and (2) that enjoyment of spicy food reduces individual salt preference, salt intake, and blood pressure through modifying the neural responses to salt intake. Given the evidence presented in both animal and human studies by Li et al in this issue of Hypertension, it is suggested that eating spicy foods or adding supplemental spicy flavor to food represents a novel lifestyle intervention that can reduce both salt intake and blood pressure, in addition to previously reported benefits of reducing cardiometabolic disease. A lifestyle intervention that adds taste to the diet, in the form of extra spice and flavor, versus reduction of the pleasure given by the salt we add to our food may have more success as a public health strategy to promote population-level dietary salt reduction.

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References
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