Salt and Sensitivity

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Almost 110 years ago, Ambard and Beaujard were the first to systematically explore the association between salt intake and blood pressure. They start their article with the following statement (translated from French): “It seems to us that one can say that each individual who is able to retain chloride is, by that very fact, apt to develop arterial hypertension.” They go on by describing several patients in whom an increase in salt intake was associated with retention of sodium (or rather chloride) and a rise in pressure. Interestingly, they also observed that in a few patients blood pressure did not increase despite massive salt loading, and they wondered whether there would be an internal mechanism that would serve to keep arterial pressure constant. It is clear that these investigators are to be credited for their discovery of the phenomenon of salt-sensitivity. Nevertheless, it took another 75 years before the terms salt-sensitive and salt-resistant became familiar in the literature.

An important question is whether salt-sensitivity is a fortuitous phenomenon that may or may not be found on a certain occasion or that it is a trait that will be repeatedly demonstrable in the same person. To answer this question, we first need to address how we should define salt-sensitivity. Unfortunately, there is no consensus in the literature, and one can find almost every possible definition that one can think of. Both the amount of salt administered and the magnitude of the response above which pressure is considered to be salt-sensitive vary enormously among studies. Therefore, it is unlikely that all these studies have identified the same type of individuals as being more or less sensitive to salt. In addition, it has become customary to make an absolute distinction between salt-sensitive and salt-resistant people. The reason for this lies, of course, in our incorrigible tendency and wants to categorize people into very specific groups. But just as it is impossible to draw an undisputable, dividing line between normotension and hypertension, there is no justification to prefer 1 particular threshold above another when it comes to separating sensitive from resistant individuals on the basis of their responses to salt.

Indeed, when one plots the changes in pressure as a frequency diagram, a unimodal (Gaussian) distribution emerges. Thus, it would be much better to abandon the dichotomous approach and consider the degree of salt-sensitivity as a continuous variable. If we do so, the second issue to think about, and one that has not been addressed properly so far, is the time course of blood pressure changes after a sudden change in salt intake. In the literature, one can find salt challenges that lasted anywhere from a few days to a few weeks. However, it is conceivable that some people respond swiftly with a rise in pressure when their salt intake is increased, whereas in others the changes in pressure may follow a more sluggish course. Therefore, the term salt-sensitivity should imply not only the magnitude of a response but also the time during which that response has been attained. In other words, by using different time frames one may not identify the same people as being more or less sensitive to salt. An illustration of this view is given in the Figure. Let us assume that the 2 patients A and B are on balance on a low-salt diet at time zero, and that both are subjected to the same dietary salt load. Let the responses R1 and R2 be 2 different levels above which we define the blood pressure as being salt-sensitive. If the assessment takes place at time T1, we will label patient A as sensitive and B as resistant, irrespective of which threshold we have chosen. However, at time T2, patient B would still be considered resistant with threshold R2 but sensitive with threshold R1. As a corollary, it may be better to look at the tangent of the angle that describes the pressure changes over time rather than at the response, per se. Of course, when the time frame is similar for all the patients in a particular study, one may argue that it does not matter but that argument would be based on the premise that pressure responses are linear over time and we do not know whether that is truly the case (patient C in the Figure).

Based on the above reasoning, we propose that the degree of salt-sensitivity be expressed as the pressure change per unit change of salt (or sodium) intake over time. Only then can the results of different studies be compared with each other. It also implies that >2 time points are required to evaluate blood pressure responsiveness.

A third element that needs discussion is the reproducibility of the responses. Does someone express the same degree of sensitivity at various points in time? It is surprising how few data are available on this issue. Inasmuch as this problem has been addressed, results are variable and there is certainly no stone-hard evidence that the phenomenon is reproducible. However, the studies that have been done have included only a small number of individuals and spanned a relatively short period of time. Therefore, it is very fortunate and timely that this issue of Hypertension features a study by Gu et al’ on the long-term reproducibility of salt-sensitivity testing. In 487 Chinese adults from rural areas, the investigators found moderate, yet highly significant correlations between the blood pressure responses to low- or high-salt intake at 2 time periods...
4.5 years apart. Interestingly, the reproducibility of blood pressure changes in response to potassium supplementation was also tested. Unfortunately, however, no 24-hour ambulatory blood pressure measurements were performed, so that the results rely on only a small number of readings. In addition, close examination of the data reveals (and this is mentioned appropriately by the authors) that the correlation coefficients for the pressure changes at the beginning and the end of the study were seemingly low. In fact, results from the initial test can explain only ≈20% of the results from the retest. Thus, to conclude that “blood pressure responses to changes in dietary sodium and potassium are not random phenomena but stable and reproducible human characteristics over a relatively long time period” is perhaps a little overstated. On the contrary, with so many potential mechanisms involved, it would be surprising to find a much greater concordance. Moreover, whether the results in the Chinese population can be extrapolated to, for instance, Europeans or blacks is not clear either.

Nevertheless, it is fair to conclude that the degree to which blood pressure is sensitive to alterations in salt intake may well vary around a certain setpoint but is certainly not fixed in time. Thus, it may well be that good reproducibility of a salt-sensitivity test only reflects the relative constancy of the compensating mechanisms. However, the setpoint may change over time. If we consider a greater degree of salt-sensitivity as a relative failure of compensating mechanisms to keep the pressure constant, probably the best we can do is to direct our research efforts toward those mechanisms and to the factors, which determine the salt–pressure setpoint.

Disclosures
None.

References
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