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Original Research Article

Sodium, Blood Pressure, and Ethnicity: What Have We Learned?

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ABSTRACT An enormous amount of research has yielded significant knowledge about ethnic differences in sodium homeostasis and blood pressure regulation. Consistent findings such as greater sodium-sensitivity, lower potassium excretion and high higher serum sodium levels in African Americans need further exploration to define more precise physiological mechanisms. The genetic alleles associated with sodium homeostasis in relation to blood pressure have accounted for only a small proportion of the variance in blood pressure. Several allelic variants differ in frequency among ethnic groups and heat-adapted genetic variants have a high prevalence in low latitudes and hot, wet climates which lends support to the "sodium retention" hypothesis. The blood pressure disparities between African Americans and whites may, in part, be due to different allelic frequencies of genes associated with sodium homeostasis. However, with advances in genomics, environmental factors tend to be neglected in research. Better measures of environmental stress have recently been developed by anthropologists and should be included in research designs by investigators in other disciplines. Public health efforts should encourage food producers to reduce sodium content of its products, and physicians should encourage patients to reduce consumption of high sodium packaged and fast foods. Am. J. Hum. Biol. 21:679–686, 2009. © 2009 Wiley-Liss, Inc.

Sodium intake had been alleged to be associated with essential hypertension since the beginning of the 20th century, but no careful research was carried out until the 1950s. During the 1950s–1960s, Dahl published numerous articles presenting evidence for a positive correlation between dietary sodium and blood pressure. In a pilot study subjects were divided into two groups: those who were classified as having had a low salt intake throughout their lives, and those classified as having been high salt ingestors (Dahl and Love, 1957). This latter group had significantly more hypertension than the former. Dahl astutely surmised that not all subjects with a high salt intake would develop hypertension due to the variability in individual biological response.

Following this study, Dahl (1960) turned to an exploration of salt intake among populations. Using 24 h urine sodium measurements, he and his colleagues examined the prevalence of hypertension across five geographical populations. There was a clear correlation between increasing daily sodium intake and prevalence of hypertension among Eskimos in Alaska, Marshall Islanders in the Pacific, Americans in the northern United States, as well as both Southern and Northern Japanese.

My own work was influenced by the Dahl population study. Building on Dahl's insights, in the early 1970s, I surveyed the biomedical literature and compiled data from 27 epidemiological and clinical studies that presented data for sodium intake and blood pressure levels for men and women aged 50–60 years (Gleibermann, 1973). Using linear regression analyses, I found that salt intake was significantly related to both systolic and diastolic blood pressure ($P < 0.0005$ for both) in males. Results for females were the same as for males. The data in this article were retrospective and not all of the sodium data were collected from 24 h urine samples. Thus, although the evidence was clearly suggestive of a sodium/blood pressure relationship, it was necessary for more rigorous studies to be carried out.

The remainder of this paper will discuss the major research endeavors and findings carried out during the past quarter of a century, including the Intersalt Study and the discovery of variability in human salt sensitivity. I will then consider what we have learned about ethnic disparities in the relationship of sodium to blood pressure. Two hypotheses concerning an evolutionary adaptation to low sodium have been proposed: the "sodium retention" hypothesis that was described in my 1973 paper, and the "slavery hypothesis" proposed by Grim sometime later (Gleibermann, 1973; Wilson and Grim, 1991). Because Grim's hypothesis has received so much media and critical attention, it will be helpful to consider briefly some pros and cons of his work. I will then discuss ethnic disparities observed in intermediate phenotypes related to sodium homeostasis as well as genetic variants that have been described as sodium conserving and heat adapted. Water conservation has recently been addressed as a factor in sodium homeostasis and will be discussed. Finally, I will briefly discuss the few findings regarding psychological factors and sodium homeostasis, and the new methods of measuring environmental stressors that have been introduced by anthropologists.

INTERSALT STUDY

In order to establish a link between sodium ingestion and high blood pressure, it was necessary to demonstrate an association between these factors within a population where individuals varied widely in the amount of salt ingested through their dietary habits. Thus, in 1984 the National Heart, Lung and Blood Institute initiated the INTERSALT study, with the explicit aim of providing reliable data about sodium excretion and blood pressure

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between and within cultures (Intersalt Cooperative Research Group, 1988). Over ten thousand subjects were recruited from 52 centers in 32 countries worldwide. Subjects provided a 24-hour urine sample from which dietary sodium was estimated. The data were adjusted for relevant covariates of age, sex, body mass index, alcohol consumption and potassium intake.

The results of this formidable investigation remain controversial (Taubes, 1998). For the inter-population analysis, 24-hour urinary sodium excretion was significantly related across centers to the slope of blood pressure as a function of age. However, the analysis was dominated by data from four equatorial population samples (Yanomamo and Xingu Indians from Brazil, Luo tribesman from Western Kenya, and peoples from the Asaro valley in the eastern highlands of Papua, New Guinea) all of which had extremely low median 24 h urinary sodium excretion. When these groups were removed from the analysis, there were no associations between sodium excretion and systolic or diastolic blood pressure (Intersalt Cooperative Research Group, 1988). For the intra-population analysis, only 8 of the 52 samples had a statistically significant association between 24-h urinary sodium excretion and systolic blood pressure. Two groups showed a negative correlation.

Several years later, the original data were reexamined and were presented as both corrected and not-corrected for regression dilution bias (Elliott et al., 1996). Results for the entire sample of 10,074 men and women showed, for example, age-sex adjusted increases of systolic blood pressure of 1.6 mmHg for the not-corrected data and 4.3 mmHg for the corrected data with each 100 mmol increase in 24-h urinary sodium. No statistical analyses were reported for these results. The authors claimed that the "strong, positive association of urinary sodium with systolic pressure of individuals concurs with Intersalt across population findings and results of other studies" (Elliott et al., 1996, p 1249). The controversy over the interpretation of the results was rampant. A more recent statement by the National Heart, Lung, and Blood Institute suggests that there remain statistical issues which still underlie the interpretation of these data (Chobanian and Hill, 2000).

SALT SENSITIVITY

The idea that individuals might be "salt-sensitive" or "salt-resistant" arose from the differential responses to alterations in dietary sodium in interventional experimental studies. The definition of and the methods of testing for salt sensitivity can be attributed to Weinberger and his group (Weinberger et al., 1986). Sodium was manipulated rapidly from a high to a low salt intake on a sample of normotensive and hypertensive subjects, From the results, Weinberger arbitrarily defined salt sensitivity as a decrease in mean arterial pressure greater than or equal to 10 mmHg and salt resistance as a decrease less than or equal to 5 mm Hg. Those with a blood pressure decrease of 6–9 mm Hg were labeled indeterminate. These authors found that the hypertensive patients were significantly ($P < 0.001$) more salt sensitive than the normotensive subjects. In a longitudinal study of one year, Weinberger and Fineberg (1991) found blood pressure responses to salt to be reproducible.

Evidence for several physiological factors associated with salt sensitivity has been described (Weinberger, 1996). Renal function and the renin-angiotensin-aldosterone (RAAS) system have been identified as being related to salt sensitivity. Other factors have been suggested including atrial natriuretic factor, the sympathetic nervous system, adrenergic receptors, endothelin and nitric oxide, ion transport, and insulin but these mechanisms are unproven (Weinberger, 1996).

ETHNIC DIFFERENCES IN SODIUM HOMEOSTASIS

African Americans provide a natural experiment for examining differential aetiologies in simple and complex diseases. The higher prevalence of essential hypertension was discovered through comparative studies of whites and blacks beginning about three-quarters of a century ago (Adams, 1932). These two ethnic groups, residing for millennia in starkly different ecological niches, allow the principles of Darwinian medicine to be applied to mainstream medical research (Nesse and Williams, 1994). African Americans are not a homogenous genetic population in the United States. Rather, they represent subsets which are geographically distinct with respect to white admixture and thus can yield clues about genetic diseases in terms of proportions of European-derived and African-derived variants (Chakraborty et al., 1992).

Starting in the 1960s, the prevalence of hypertension was regularly observed to be almost twice as high in African Americans as in whites with an earlier onset and more severe sequelae (Nesbitt and Victor, 2004). Several hypotheses were proposed to explain these differences and included dietary differences in sodium and potassium intake, racial prejudice resulting in severe psychological stress, and less access to health care. At the present time, it is most reasonable to suggest that African Americans have elevated blood pressure owing to complex gene by environment interactions.

Intermediate phenotypes related to sodium homeostasis

One of the earliest consistently replicated differences between African-Americans and whites with respect to sodium homeostasis was the lower plasma renin activity (PRA) observed in both normotensive and hypertensive African-Americans (Adlin et al., 1982; Channick et al., 1969; Creditor and Loschky, 1968; Helmer, 1965). Plasma renin activity represents one step in the pathway of RAAS, the major mechanism for maintaining sodium and potassium homeostasis in the body. PRA is a bioassay which measures generation of angiotensin I in the presence of excess substrate. Renin, released from the kidney, combines with the substrate angiotensinogen to produce angiotensin I. When sodium intake is high, PRA is low permitting sodium excretion; when sodium intake is low PRA is high allowing the body to retain sodium and come into balance with dietary sodium intake. The lower PRA observed in approximately half of the African Americans studied remains unexplained.

One of the most fascinating field studies carried out by medical researchers was that conducted among the Yanomamo Indians of northern Brazil and southern Venezuela, a group of tropical rain forest Indians who had only recently begun consuming salt. Oliver et al. (1975)

collected 24-h urine samples as well as blood samples on a small number of Yanomamo Indians. Results indicated that the mean urinary sodium excretion in adult males was 1 mEq (23 mg). Oliver et al. (1975) suggest that the sustained sodium intake of the Yanomamo is probably lower than any previously recorded for man. This population appears to have no difficulty in carrying out daily human activities with this minimal sodium intake. For the Yanomamo Indians (Oliver et al., 1975), the efficiency of this pathway is indicated by the observation that all subjects excreted aldosterone in excess of the upper limit of normal for Caucasians on a general diet. All plasma renin levels were within or exceeded the range seen in North Americans ingesting short term low 10 mEq sodium diets. The Yanomamo Indians, described as a "no-salt" culture by these authors, can maintain normal activities on the minutest amounts of sodium. Plasma sodium concentrations of several selected Yanomamo males had a mean of 140 mEq/L which is identical to individual values in modern Western countries.

In addition to PRA a number of other phenotypes have been described wherein African Americans and whites have consistent significant differences relating to sodium homeostasis: African Americans take longer to excrete a sodium load (Luft et al., 1979); they have higher red blood cell sodium levels, as well as differences in sodium, potassium-ATPase, sodium-potassium cotransport, and lithium-sodium countertransport (Aviv and Gardner, 1989). After the concept of sodium sensitivity was established investigators began to examine ethnic differences in this regard. It was soon apparent that African Americans had a greater proportion of sodium sensitive individuals than whites, both among normotensives and hypertensives (Sowers et al., 1988; Zemel et al., 1987). Numerous clinical studies involving electrolytes and neurotransmitters have been carried out in an effort to understand the mechanisms underlying this pattern of response to high levels of sodium ingestion. The research is ongoing and no clear understanding of sodium sensitivity, either in African Americans or whites has been yet achieved.

In addition to clinical and experimental studies, many epidemiological investigations examined dietary intake and excretion of sodium and potassium in African Americans compared with whites. For example, Frisancho et al. (1984) examined the NHANES 1 (1971–1974) data based on dietary recall and found that African Americans consumed less sodium and less potassium than whites. Urinary sodium/potassium ratios were higher in Africans Americans because their potassium intake was reported as much lower. Other similar studies, but with different designs and samples led to no definite conclusions. A consistent observation, however, indicates that blacks excrete less potassium than whites (for review, see Aviv and Aladjem, 1990). Whether this is from lower dietary intake or physiological mechanisms determining potassium homeostasis is not known, although African Americans have been observed to have higher total body potassium content (primarily muscle mass) than whites (He et al., 2003). One recent hypothesis to explain sodium sensitivity in blacks, based on complex physiological reasoning, proposes an augmented activity of the sodium-potassium-chloride cotransport by a consideration of the lower potassium excretion in this ethnic group (Aviv et al., 2004).

The "sodium retention" hypothesis and the "slavery hypothesis"

In 1973, when I published my paper on cross-cultural evidence for a relationship between sodium and blood pressure, I also proposed the following which in time came to be referred to as the "sodium retention" hypothesis (Hancock and Di Rienzo, 2008; Weder, 2007).

> During the Pleistocene, Africa was a homogeneous economy; its inhabitants all hunted on the savannah. Man's sodium intake was most likely comparable to what Bushmen obtain today from their natural diet [about 175 mg Na]. Perhaps this was adequate for early man most of the time. However, it is reasonable to postulate a small but constant selection pressure from sodium depletion heat exhaustion against those individuals who lost more sodium in their sweat during a hunt. Selection would be more intense during sudden, sporadic heat waves, before the homeostatic salt-saving mechanisms could be mobilized to their maximum Women would be particularly stressed during periods of pregnancy and lactation (Gleibermann, 1973, p 151).

Years later, Wilson (1986), an African historian, also suggested that Africans had a long term history of selection for efficient salt retaining mechanisms; however, he distinguished between the salt poor interior of West Africa and the salt producing areas of the coast and desert. Thus, he further suggested that this selection pressure resulted in populations of sodium sensitive individuals in the interior of West Africa, but not in the coastal areas. Finally, he suggested that slaves from the coastal areas would have suffered from higher blood pressure once they reached North America because the diet of slaves was high in sodium—salt allowances for slaves could be as high as one pint a week and admixture with European genes was minimal in those years (Wilson, 1986).

Still later, Wilson and Grim worked together and put forth what came to be known as the "slavery hypothesis," most frequently now associated with Clarence Grim. This hypothesis was first formally stated in a peer-reviewed journal in 1991 (Wilson and Grim, 1991), although the ideas had been presented at meetings and in abstracts previously. At this time, Wilson's hypothesis had been revised: according to these authors there were two temporally-distinct parts to the "slavery hypothesis": (1) selection during the "middle passage," and (2) selection while working as slaves in North America. The selection pressure was the same: slave ship mortality was high because of acute heat stress in overcrowded quarters, dehydration due to lack of adequate water supplies, and electrolyte depletion from vomiting and diarrhea associated with communicable diseases such as dysentery. It was also suggested that the same selection pressures operated during centuries of slavery in North America with the major cause of death on plantations being dehydration from epidemics such as cholera without adequate water replacement given to correct the condition. The result of these conditions was proposed to have selected for a population of efficient salt retainers vulnerable to the hypertensionogenic effects of present-day high salt diets (Wilson and Grim, 1991).

Kaufman has vehemently criticized the "slavery hypothesis" in a number of publications (Kaufman, 2008; Kaufman and Hall, 2003). He is concerned that a biological disparity between racial groups may be considered a "deformity rather than a mere divergence" (Kaufman and Hall, 2003, p 115). However, he conflated his criticisms of media hype and the unfortunate use of terms such as "defective gene" with his evaluation of the scientific legitimacy of the hypothesis. Kaufman's scientific criticism of the "slavery hypothesis" relies on the reasoning of Jackson (1991), a biological anthropologist. In this paper, Jackson critiqued the "slavery hypothesis" essentially by interpreting the events during the "middle passage" (the crossing of the Atlantic) as bringing about a bottleneck effect and consequently a constriction of genetic variability in the surviving slave population. She then proceeded to explain why such events could not reasonably occur. However, nowhere do Grim and Wilson (1991) reason in this manner; they merely imply that natural selection occurred at a number of genetic loci associated with sodium homeostasis. In effect, with very high mortality, there need only be a shift in gene frequencies at a number of loci. Variants for sodium sensitivity could have increased and variants for sodium resistance could have decreased. Owing to constant gene flow, these different variants could likely have been present over the entire African continent and were reasonably present in the huge numbers of people who were forcibly sent to North America to live as slaves. Should either the "slavery hypothesis" or the "sodium retention" hypothesis be shown to be valid, the variants at the loci of importance are not likely to have become fixed: not every African American develops high blood pressure owing to a genetic predisposition, nor are whites all immune to developing hypertension. Later, Grim stated that the "slavery hypothesis" could be tested by comparing frequencies of genetic variants for salt sensitivity between Western hemisphere descendants of Africans with these same genotypes in populations in Africa (Grim and Robinson, 2003). (Below, in the section entitled "Sodium conserving and heat adapted genes," I will present some evidence relating to gene frequency differences between Africans and African Americans for a locus associated with sodium homeostasis.)

Weiss, in discussing this issue, has pointed out:

> There are many ways to design studies to determine whether genetic susceptibility variants are present in New World African-derived populations, so long as the studies are adequately designed ... Clearly this would have to include a serious attempt to account for environmental factors, something geneticists too often find inconvenient. But linkage-mapping studies in appropriately ascertained families could be designed (2003, p 123).

Weder (2007) also believes the "slavery hypothesis" is testable and useful in that future studies of recent selection may contribute to understanding the genetic basis of sodium sensitivity.

Sodium conserving and heat adapted genes

A number of genetic variants have recently been shown to be involved in sodium homeostasis; these variants have been described as sodium conserving or heat adapted, and include AGT (angiotensinogen) and CYP3A5 (cytochrome P450 3A5). In both of these genes, single nucleotide polymorphisms (SNPs) have been identified that impact sodium retention and blood pressure (Young, 2007). Other variants which increase water retention and cardiovascular reactivity have been considered heat-adapted alleles and have been shown to have a high prevalence at low latitudes and in hot, wet climates (Young, 2007). These include GNB3 (G protein beta3 subunit) C825T, ADRB2 (beta2 adrenergic receptor) G47A and G79C, ENaCalpha (epithelial sodium channel alpha) A-946G, and ENaC-gamma (epithelial sodium channel gamma) A-173G. Young (2007) suggests that populations from hot environments are more likely to develop high blood pressure than those from cold environments owing to a history of adaptation to climate.

TABLE 1. Ethnic allele frequencies of the M235T variants of the AGT gene

Ethnicity	Allele frequency (%) T	M
Nigerian	91	9
African-American	87	13
African-Caribbean	81	19
Caucasian U.S.	42	58
Caucasian France	45	55
Japanese	83	17

Adapted from Rotimi et al., 1996.

The CYP3A5 gene has two variants: an expressor (*1) and a reduced-expressor(*3). Among a sample of 89 African Americans, the allele frequency of (*1) was 0.7 which is greater than all other ethnic populations studied (Givens et al., 2003). In a sample of 25 African Americans, systolic blood pressure, mean arterial pressure, pulse pressure and creatinine clearance was significantly higher in those with the *1*1 genotype compared to those with *1*3 and *3*3 genotypes. Systolic blood pressure was 16 mmHg higher in the *1*1 group when compared to the *3*3 group.

The A(−6) promoter variant of AGT is in close linkage disequilibrium with T235 and both are associated with an increased risk of essential hypertension and with higher levels of plasma angiotensinogen (Jeunemaitre, 1992) although not all studies have reported this (Forrester et al., 1996). Both variants have a higher frequency in African populations compared with non-African populations (Nakajima et al., 2004; Rotimi et al., 1996). These variants are fixed in chimpanzees and other nonhuman primates and therefore are considered ancestral (Inoue et al., 1997). Several years ago (Gleiberman, 2001) I pointed out that the difference in frequencies between African Americans and Caucasians for the angiotensingen variants support the "sodium retention" hypothesis. The T variant (Table 1) is associated with higher levels of angiotensinogen and higher blood pressure; the frequency in Nigerians is 91% and in U.S whites it is only 42%. In African Americans, the allele frequency is 87% and this is most reasonably accounted for by admixture with whites. This would suggest that selection for a salt retaining genotype would have occurred slowly during most of the pleistocene and not in the recent history of the African slave trade (Gleiberman, 1973; Jackson, 1991).

With recent advances in genomics, more complex analyses of the angiotensinogen gene have been carried out

(Fejerman et al., 2006). Using haplotypes constructed from single-nucleotide polymorphisms of the AGT gene Fejerman et al., (2006) examined haplotype patterns in samples of Nigerians and African Americans. These authors judiciously comment that their study results are confounded by environmental factors that were not measured. In any event, they did find that haplotype H1 was associated with high AGT levels in Nigerians and in African Americans. Haplotype 1 is similar to the chimpanzee sequence; when chimpanzees were given a high salt diet their blood pressure levels increased. Thus, these authors conclude that modern humans inherited variants that are adaptive in low sodium environments.

What about water?

Sodium homeostasis has been intensively studied in relation to blood pressure because of the reasonable hypothesis that being sodium replete and consequently volume expanded impacts directly on the cardiovascular system. However, the importance of sodium intake can only be completely understood as it relates to its effect on extracellular fluid. The major ion in the extracellular fluid is sodium, and a number of transport systems act to pump sodium out of the cell into the extracellular and interstitial fluid. In contrast, potassium is the major ion in the cells. It is surprising that so much research has been carried out regarding sodium homeostasis with virtually no reference to water availability and its role in thermoregulation or heat exhaustion in different ethnic groups.

In tropical climates, particularly on the open savannah, sweating is profuse during periods of hard work, (e.g. hunting) in order to maintain thermal equilibrium. Tropical climates can be hot and dry, or wet and humid; in this discussion, only the hot, dry climate of the open savannah will be considered inasmuch as it is believed, although not certain, that hominid evolution occurred in such an environment where bipedalism for running would have been advantageous (Hanna and Brown, 1983). Thus, where temperatures are high, and evaporation can be optimally effective, sweat losses can be as high as two liters per hour (Kerslake, 1972). Water must be replaced or else events leading to circulatory failure, collapse and eventual death would occur. For women, replenishing water lost during lactation can also be a critical selective pressure. And compared with adults, children produce proportionately more metabolic heat, have a core temperature that rises faster during dehydration, and have smaller organ systems, allowing for less efficient heat dissipation (Luke and Micheli, 1999). Although diarrhea and vomiting are themselves adaptations, when the fluid losses from diseases such as dysentery and cholera are excessive and when water is not available to replenish the losses mortality can occur (Wilson and Grim, 1991). These authors were quite prescient in their understanding that diarrhea and vomiting during the "middle passage" and not just sodium depletion could lead to dehydration and ultimately death.

According to Hubbard and Armstrong (1988) the threat of dehydration is potentially more serious than the acute loss of any electrolyte, including sodium: "Clearly, the acute need of an exercising adult is water, not salt; water depletion may result in heat exhaustion in a matter of hours" (1988, p 321). Sodium depletion heat exhaustion requires at least 3–5 days to develop (Leithead and Lind, 1964; McCance, 1936). Water depletion is more likely to lead to increased core temperature and heatstroke than sodium depletion (Anderson et al., 1983). Vasopressin (anti-diuretic hormone) can be stimulated by both increased plasma osmolality and decreased plasma volume which will result in thirst and reduced urinary water loss. Several studies have reported that vasopressin levels are higher in blacks than in whites (Bakris et al., 1997; Bursztyn et al., 1990; Crofton et al., 1986), although nothing is known about different ethnic thresholds in thirst. Bankir et al. (2007, p 309) suggest the following hypothesis: "Associated changes in the thresholds for thirst and vasopressin secretion, as a result of a different set point of the hypothalamic 'osmostat', could have provided a survival advantage with respect to the ability to conserve water in African populations". These authors conclude that their hypothesis is consistent with the work of Young (2007) cited earlier. Therefore, it appears reasonable to include issues of water retention with any further studies about sodium and blood pressure.

Psychological stress in relation to sodium homeostasis

A small body of literature suggests that psychological stress may be involved with sodium homeostasis and ethnic differences have been reported. Thus, in a laboratory experiment where subjects underwent competitive mental, competitive reaction time, and mental arithmetic tests, Light and Turner (1992) found that African Americans showed significantly lesser increases in sodium excretion rates than whites. Another type of stress manifestation is associated with high end-tidal CO_2 ($PetCO_2$). High measures of this trait were found to be associated with slow breathing frequencies at rest and an increased tendency to worry and experience feelings of vulnerability (Dhokalia et al., 1998; Schaefer, 1979), as well as a marker for sodium sensitivity of blood pressure in whites (Anderson et al., 2001). $PetCO_2$ and marinobufagenin (MBG), a sodium pump inhibitor which increases when plasma volume is expanded, were examined in a sample of African Americans and whites. Results indicated that African Americans had higher resting $PetCO_2$ which the authors suggest plays a role in slower urinary excretion of sodium and greater blood pressure sensitivity to high sodium intake (Anderson et al., 2001). Finally, higher levels of anxiety, a lower level of control of anger, and an increased level of irritation has been observed in white normotensive salt-sensitive individuals when compared with those who are salt-resistant (Deter et al., 1997). To my knowledge, no comparative ethnic studies have been carried out with respect to these emotional states and sodium homeostasis.

Culture, social stress, and skin color: new approaches

It has been traditional for epidemiologists, geneticists and clinical research physicians to rely on three classical measures of environmental stress—socioeconomic status, education, and income—as covariates in models examining ethnic differences in the relationship of sodium homeostasis to essential hypertension. However, Cooper cautions us that

> Using the empirical measures of SES that are available, such as education, fails to eliminate the difference in exposure to the myriad factors that constitute the social influences on health for U.S. blacks and

whites. These weak proxies cannot summarize the influence of lifestyle exposures (2004, p 280).

In recent years, anthropologists, most reasonably owing to their orientation and sensitivity to issues of culture and society, have been in the forefront of developing models that capture the psychological experience of one's race/ethnicity, social environment and skin color in innovative ways.

For example, Dressler, building on the concepts of Thorstein Veblen (1918) and Max Weber (1946), developed a measure of lifestyle incongruity. Lifestyle incongruity measures the "extent to which a high status style of life (based on possession of material goods and exposure to mass media) exceeds an individual's occupational class" (Dressler, 1990, p 182). In an African American community in the American south higher lifestyle incongruity was associated with higher blood pressure, particularly so among person aged 40–55 (Dressler, 1990). A second study in the same community (Dressler, 1991) tested the hypothesis that the effects of high lifestyle incongruity on blood pressure would be attenuated by kin support in older individuals and by non-kin (e.g. co-workers) support in younger individuals. Results of this study supported the hypothesis.

Later, building on the cultural consensus model of Romney et al. (1986), Dressler introduced the concept of "cultural consonance in lifestyle" (Dressler et al., 1998), which assesses the extent to which an individual's behavior accords with a shared cultural model of lifestyle and social support in a given local community. Again, research results from the same southern African American community (Dressler and Bindon, 2000), indicated that high cultural consonance is linearly associated with lower systolic blood pressure where kin support is also high; where reported kin support is low, the lowest systolic blood pressure is found where cultural consonance was at intermediate levels. The authors explain this outcome as follows: "In this community, to be a success in life is not to be the conspicuous consumer but rather to achieve a basic domestic comfort, . . ." and participate in the community of the church (Dressler and Bindon, 2000, p 256).

Finally, studies of the relationship of within-race variations in skin color and its relationship to blood pressure have yielded inconsistent results (Gravlee et al., 2005). By examining skin color both by reflectometry and then matching survey respondents to standardized portraits of various skin tones in Puerto Rico, the ascribed skin color of *negro* interacted with socioeconomic status such that those individuals who were designated *negro* and who had high SES had the highest blood pressures. Skin pigmentation as a continuous variable was not significantly associated with blood pressure (Gravlee et al., 2005). Sweet et al. (2007) presented similar findings in a study of African Americans from the CARDIA study. When skin color was dichotomized into light and dark, among those with darker skin, systolic blood pressure increased with increasing income, although not significantly; among those with lighter skin, systolic blood pressure decreased as income increased. According to Gravlee et al. (2005) results from studies using the innovative approach of socially ascribed skin color provide the strongest evidence of an association between skin color and blood pressure. As Sweet et al. suggest: "Future research should explore . . . more subtle and insidious forms of racism and yet unmeasured or unidentified factors that may prevent African Americans with darker skin from realizing the health benefits of economic success" (2007, p 2257–2258).

CONCLUSIONS

An enormous amount of research concerned with sodium homeostasis has been carried out during the past half century and has yielded significant knowledge about ethnic differences in sodium's impact on blood pressure regulation. Many of the consistent findings such as greater sodium-sensitivity, lower potassium excretion and higher serum sodium levels in African Americans need further exploration in order to define more precise physiological mechanisms. The genetic alleles associated with the complex disease of hypertension has accounted for only a small proportion of its variance. However, the fact that several genes related to sodium homeostasis have variants which differ in frequency among ethnic groups and genetic variants associated with climate and latitude have been discovered support the importance of understanding sodium's role as a genetic risk factor for hypertension. These gene variants may also suggest pathways for pharmaceutical researchers involved with developing medications to target sodium retention.

The interaction of environmental factors and genotypes are of course essential to furthering our understanding in this area. Environmental factors such as diet, psychological stress, coping with anger and anxiety, alcohol use and obesity reasonably interact with genetic variants in all populations. The stress experienced by African Americans from interactions initiated by race and skin color perceptions—unique to each individual—has begun to be explored but remains to be explained in terms of precise physiological impacts. Innovative models developed by anthropologists should be incorporated into research designs by investigators from other disciplines such as clinical epidemiology and medicine.

With respect to anti-hypertensive medications prescribed, although two categories of medications effectively impact the RAAS system, neither angiotensin-converting-enzyme inhibitors (ACEIs) nor angiotensin receptor blockers (ARBs) have been shown to be more effective in African Americans than other agents acting on different pathways. However, for African American patients with diabetes, both ACEI and ARB medications are recommended inasmuch as they have been found to slow progression of kidney disease (Appel et al., 2008).

It has been found that sodium-sensitivity has an increased risk not only for essential hypertension, but for having blunted nighttime dipping of blood pressure as well as for the development of left ventricular hypertrophy and proteinuria (Weinberger et al., 2001) The importance of discovering a simple procedure to categorize salt-sensitive individuals is indicated by the important finding that salt-sensitive hypertensives and normotensives as well as hypertensive salt-resistant subjects have a significantly greater risk of mortality than salt-resistant normotensives, independent of elevated blood pressure (Weinberger et al., 2001).

Although the sodium/blood pressure story is incomplete, this past half century of research has shown that sodium intake must be addressed in trying to control the high blood pressure observed in both whites and African

Americans, and in all ethnic groups and nations. Reasonably, future research about the role of water in relation to sodium during thermoregulation will help complete the story of sodium. Public health efforts which encourage food producers to reduce the sodium content of its products would be a step forward. Patients should also be encouraged to consume fresh fruits and vegetables advocated by the DASH diet; a shift to following this regimen would reduce sodium intake (Sacks et al., 2001). Preventive care which would encourage patients to modify their dependence on packaged foods and fast foods—although not easy to accomplish—should be practiced by physicians.

Cooper (2004) reasonably informs us that genomics has neither described pathophysiology nor improved treatment for common chronic illnesses. However, biomedical genetic research focused on ethnic health disparities has developed a momentum and is likely to continue. As social scientists continue to develop measures which more accurately capture the effects of environmental stressors such as "status incongruity" and "cultural consonance" we may be able to partition more accurately the variance in blood pressure accounted for by genetic and environmental factors across ethnic groups.

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