# Detailed Study Notes: Episode 457

## Austin Robinson, PhD - Salt Sensitive vs Salt Resistant, Sodium Impacts Beyond Blood Pressure, & Group Differences in Risk

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# Introduction to this Episode

Hypertension (elevated blood pressure) is a condition that significantly increases the risk of several diseases and is a major cause of premature death worldwide. In the US, recent estimates suggest that about half of the adult population has hypertension. At a population level, high sodium intake is one of the main dietary risk factors. All population health guidelines recommend keeping sodium intake below certain levels.

While, on average, blood pressure correlates with sodium intake, there is a wide range of responses on an individual level. People who see increasing sodium intake lead to increased blood pressure are termed “salt sensitive”. Others, however, don’t see much change in blood pressure with increased dietary sodium. Such individuals are classed as “salt resistant”.

In this episode, Assistant Professor at Auburn University, Dr. Austin Robinson, is on to discuss whether people who are salt resistant need to keep their sodium intake low or not. And other individual and group differences that exist for hypertension risk and sodium physiology?

# Connection to Previous Episodes

#451: Potassium & Blood Pressure

- Findings of a 2021 study are suggestive that the association between potassium consumption and both systolic blood pressure and CVD risk is sex-specific.
- An inverse relation between potassium intake and SBP was only present in women within the highest tertile of sodium intake
- However, there were some important limitations of this study. For example, only one random spot urine sample was collected for estimation of 24-h excretion of sodium and potassium.

#375: Salt, Sodium & Health

- Potassium can moderate the effect of sodium on BP and CVD, but not abolish an effect
- Stratifying by higher/lower potassium and higher/lower sodium, it seems higher potassium has a large benefit at lower sodium intakes, but at higher sodium intakes, people are still remaining at high risk even when potassium is high

#415: Prof. Bruce Neal – Can Salt Substitutes Reduce Cardiac Events & Death?

- (29.45 - 34.25): Prof. Neal addresses the claims that the BP lowering (and CV) effect is solely down to potassium, and not sodium BP reduction in SSaSS was likely due to a combination of sodium lowering and increasing potassium intake (baseline potassium was low)
- The reductions in CV could be for a variety of mechanisms BUT it still most likely that the majority of benefit is directly due to BP lowering

#316: Michael Grandner, PhD – Societal, Social & Psychological Influences on Sleep

- As discussed towards the end of the conversation with Dr. Robinson, there are many aspects related to social, economic and racial factors that can indireclty influence risk through affecting things like sleep.
- The work of Dr. Michael Grandner was brought up as an example. Dr. Grander was on the podcast in episode 316 where he discussed research looking at how:
    - Sleep duration and quality are influenced by factors at the individual level, which is embedded within a social level, which itself is embedded within a societal level
    - How racial discrimination influences sleep
    - Significant sleep health disparities exist in the population

# Sodium & Blood Pressure

- Blood pressure correlates with sodium intake, with multiple mechanisms underlying this relationship.
- It has been estimated that almost 50% of the adult population in the United States now has hypertension (Virani et al., 2021).
- For the general population and specific patient populations (e.g., individuals with heart failure and hypertension) it is appropriate to recommend less sodium intake than what the populous consumes.
- Average daily sodium intake in the US is ~3400mg per day, which is about 7-10g of salt per day.
- For a deepdive on sodium and blood pressure, see episode 375 of the podcast.

# Importance of Measurement

- Measured as a biomarker: 24hr urinary sodium reflects sodium intake as all intake over a 24hr period is excreted (although some will be via sweat)
    - Biomarker better than food diary as its objective
    - However, sodium excretion is also highly variable from day-to-day in the same individual - This means that if only one single 24hr urine collection is taken, it will be unrepresentative of average (mean) intake in that individual.
- **J-shaped curve:** If you think of a graph plotting intake vs disease risk, as you increase intake you start to see a decrease in risk up to a certain point, after which you start to see a significant increase in risk with increasing intake. Thus giving the curve the shape of a J.
- Some studies suggested a J-shaped curve of risk
    - E.g. 2016, Mente et al. pooled analysis:
    - 2014 meta-analysis by Graudal et al.
- But this is due to the error involved in using spot measures or single measures.
- However, when multiple 24hr collections are used as the measurement method, the relationship is a linear one (i.e. lowest salt intake = lowest risk). Examples:
    - INTERSALT study
    - Engberink et al., 2017
        - See more commentary below
    - Trials of Hypertension Prevention [TOHP] I and II: See Cook et al., 2014

**Example:** Engberink et al., 2017

- Conducted an analysis comparing the associations between sodium intake and CVD risk when either:
    - Only a single baseline 24hr collection is taken
    - Multiple 24hr collections are taken over 1yr and 5yrs
- As per the figure below, when a single baseline measurement was used for sodium intake estimation, high 24-hour sodium excretion was *not* associated with an increased risk for the composite of cardiovascular events and mortality compared with low sodium intake (HR, 1.09; 95% CI, 0.61–1.95).
- But… when the researchers instead used 24-hour sodium excretion measurements (that were obtained within 1 or 5 years after baseline), high 24-hour sodium excretion was associated with a higher risk for cardiovascular events and mortality compared to the lowest tertile (1-year HR, 1.80; 95% CI, 1.03–3.13; 5-year HR, 1.73; 95% CI, 1.00–2.99).
- So if long-term estimates of sodium intake were used instead of baseline estimates, HRs for cardiovascular events and mortality were up to 85% different!
- In other words, the J-shaped curve only exists when the sub-optimal single measures are used. When 24-hour measures are used, the relationship is linear.

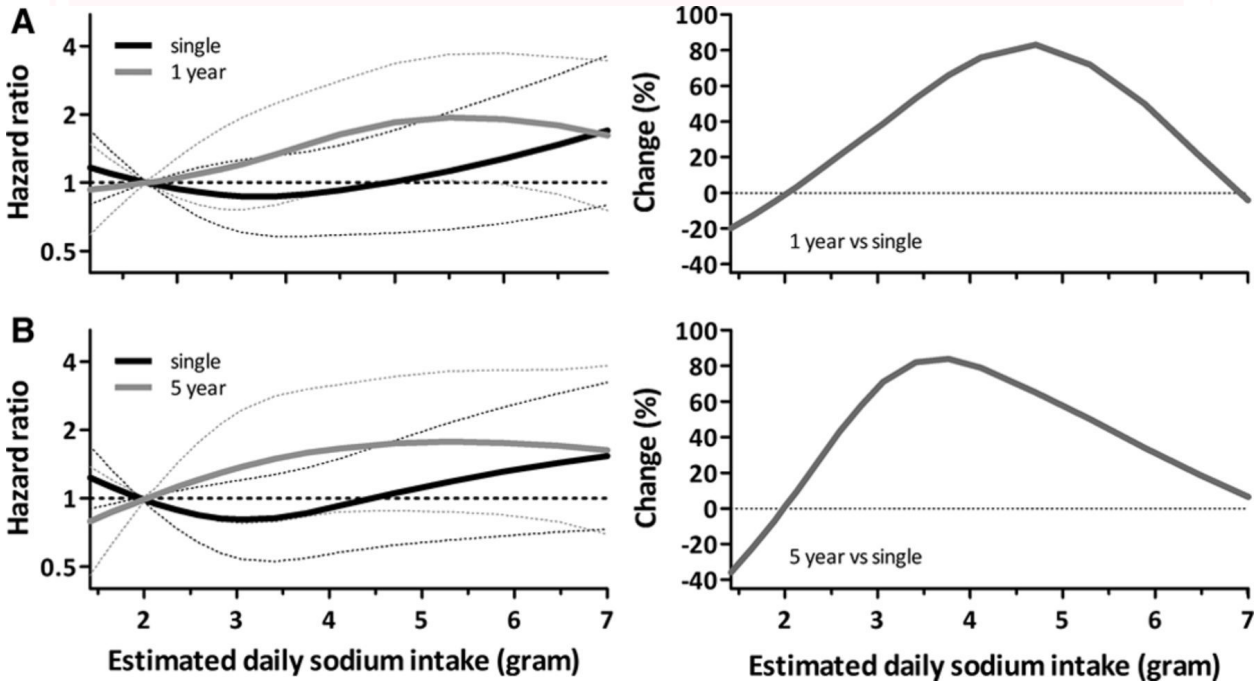


Figure from: Engberink et al., 2017

# Sodium-induced Increases in Blood Pressure

High dietary sodium can increase blood pressure through a variety of possible mechanisms. The change in blood pressure varies considerably, even within a given population (Farquhar et al., 2015):

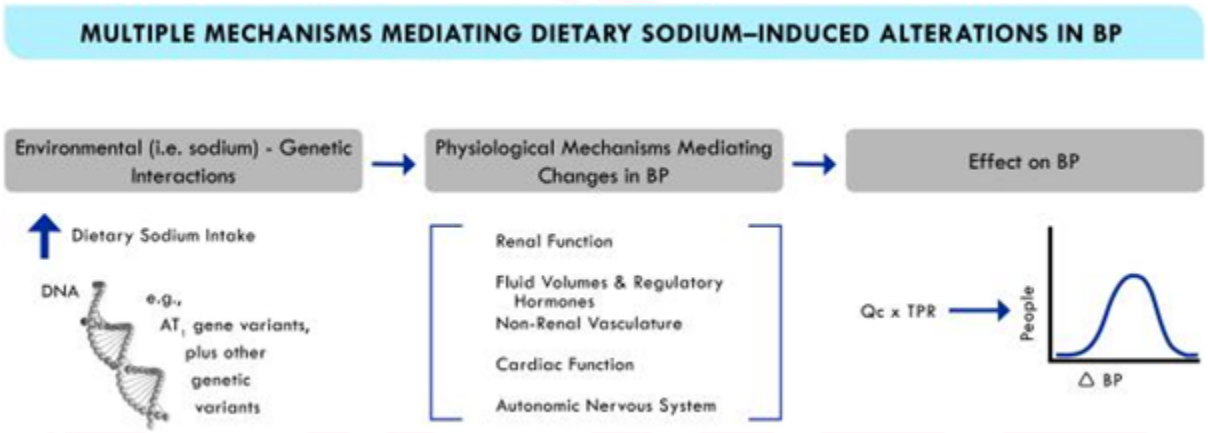


Image from: Farquhar et al., 2015

# Salt Sensitivity of Blood Pressure

***"Salt sensitivity"* describes how responsive blood pressure is to changes in dietary salt intake.**

> In other words, a person is ***salt sensitive*** if their blood pressure increases when they consume a high amount of dietary salt or decreases when they reduce the salt in their diet.
>
> If there is no change in blood pressure with increased salt intake, an individual is considered ***salt resistant***.

There could be genetic variants that influence salt sensitivity, based on data from the GenSalt Study (Gu et al., 2018).

As Dr. Robinson mentioned, among healthy adults, more people are salt resistant than salt sensitive (Elijovich et al., 2016).

***Question:*** If most people are salt resistant, does this mean public health recommendations to lower sodium intake are wrong?

- **No.** For a couple of reasons:
    a. On a population level, the evidence for the benefits of population-wide reductions is clear.
    b. On an individual level, even if your resting blood pressure doesn't change with increased sodium consumption, high sodium intake can still affect your blood vessel health, brain, or kidneys (see next section of notes).
        - Therefore, for salt-resistant people, lower salt intakes could be beneficial for health for non-BP related reasons.

Certain groups are more likely to be salt sensitive or salt-resistant:

| Salt-Resistant | Salt-Sensitive |
|---|---|
| Young | Aged |
| Middle-aged | Hypertensive |
| Normotensive | African-American |
| Caucasian | Chronic kidney disease |
| | History of pre-eclampsia |
| | Low birth weight |

Table adapted from: Farquhar et al., 2015

# Effects of Sodium Beyond Blood Pressure

High dietary sodium can cause target organ damage and may have direct effects on the brain, heart, kidneys, and vasculature. These effects can be independent of changes in BP.

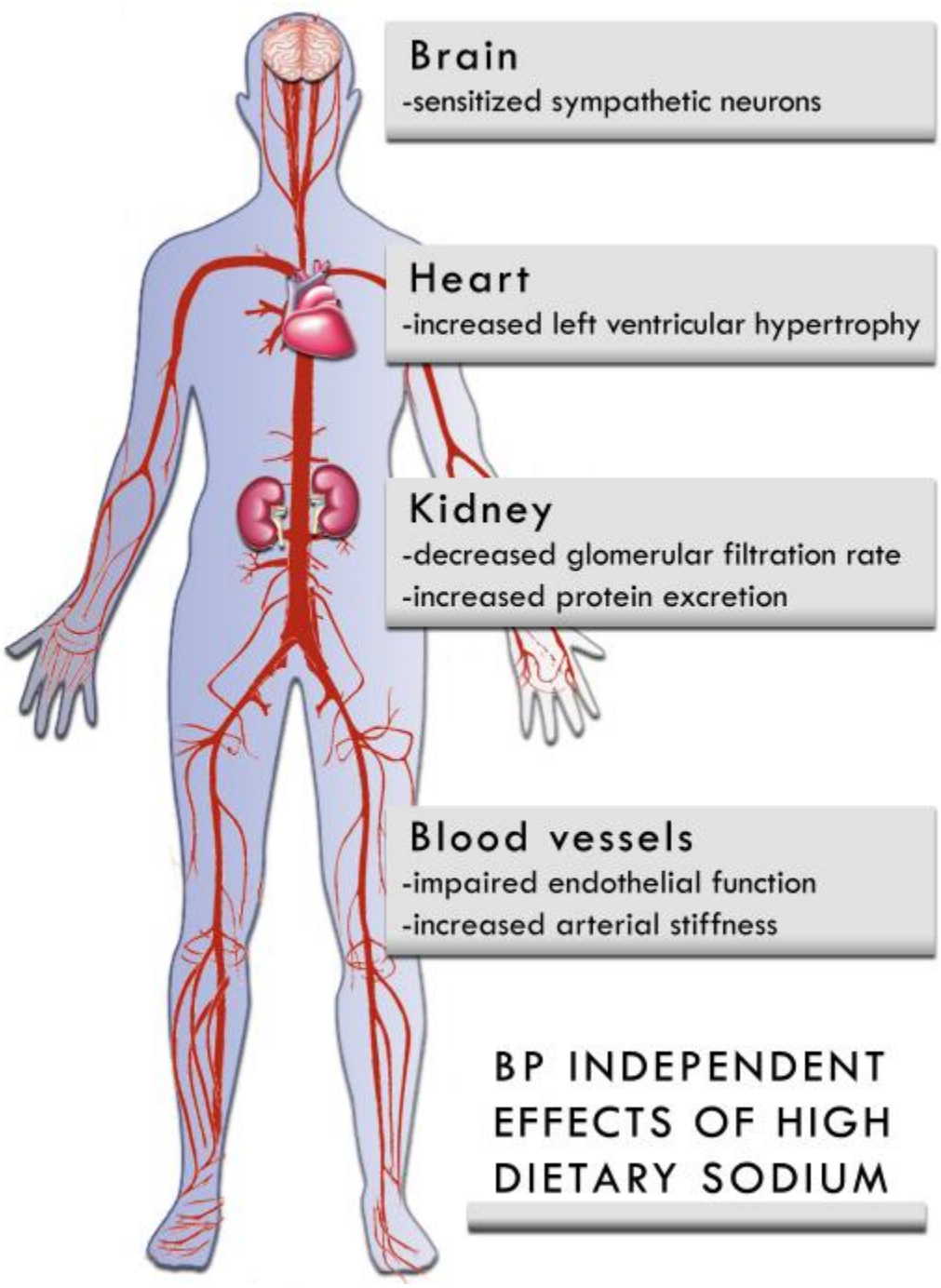


Figure from: Farquhar et al., 2015

# Orthostatic Hypotension

- **Orthostatic *intolerance*** is a condition where an upright posture leads to the development of symptoms such as:
    - Dizziness
    - Lightheadedness
    - Headache
    - Fatigue
- **Orthostatic *hypotension*** is hypotension (low blood pressure) that occurs upon the assumption of an upright posture.
    - This is sometimes, but not always, associated with orthostatic intolerance.
- For those experiencing symptoms related to orthostatic intolerance, it is common for medical doctors to recommend an *increased* salt intake.
- Loughlin et al., 2020 meta-analysis:
    - For 62% of participants, increasing salt intake led to:
        - improved time to presyncope by ~2 min
            - *[Presyncope is a state of lightheadedness, muscular weakness, blurred vision, and feeling faint.]*
        - increased systolic blood pressure during upright posture by ~12 mmHg
        - improved overall symptoms of orthostasis in 62% of study participants.
    - However, there were no clinical trials found to support the recommended level of salt and water intake.
- Increasing salt intake in such individuals seems to improve symptoms acutely. However, long-term health effects are still not fully understood.

# Impact of Race on Sodium & Blood Pressure

**Context:**

- Most of the data published on sodium and blood pressure comes from studies that were largely, or entirely, performed in non-Hispanic White men (Borell et al., 2021).
- In the US, African American individuals have a higher prevalence and severity of hypertension, and develop hypertension at an earlier age than Caucasian individuals (Fryar et al., 2017).

Some of the differences can be explained by a combination of physiological and non-physiological differences.

Some of the non-physiological reasons include that Black Americans are more likely to:

- Experience poverty (Boen et al., 2020)
- Live in socioeconomically disadvantaged neighborhoods (Mikati et al., 2018)
- Live in areas with greater adverse environmental pollution exposure (Mikati et al., 2018)
- Have fewer opportunities to obtain healthful foods (Garcia et al., 2018)

These are contributory factors to the known disparities between races in:

- Sleep (Jackson et al., 2018)
- Dietary potassium intake (Cogswell et al., 2012)

As mentioned in the episode, work highlighted by Dr. Micharl Grandner and others has shown how racial discrimination influences sleep (Grandner et al., 2012).

Looking at physiological impacts, Dr. Robinson's group published a paper (Wenner et al., 2018) demonstrating that, in response to a short-term salt load, black individuals:

1. May have an impaired ability to get rid of excess sodium
2. Are more likely to demonstrate a larger increase in blood pressure, for any given increase in levels of blood sodium

## Wenner et al. (2018) Trial

Study design:

- Thirty-nine participants with normal resting BP
    - 19 African Americans (9 males and 10 females)
    - 20 Caucasians (15 males and 5 females)

- Participants were instructed to avoid table salt and foods that are high in sodium for 24 h preceding the experimental visit, and were provided a list of common foods that are high in Na+ to avoid
- After baseline measures were taken, a 60-min HSI began at a rate of 0.15 ml/kg/min
- The HSI is a large Na+ and volume load, which has been shown to cause an increase in plasma Na+ concentration and osmolality over a short period of time

Results:

- The peak Na+ change in African American participants was greater compared to Caucasian participants
- The peak systolic BP was Δ23.2 ± 2.6 in African American participants compared to Δ16.4 ± 2.5 in Caucasian participants

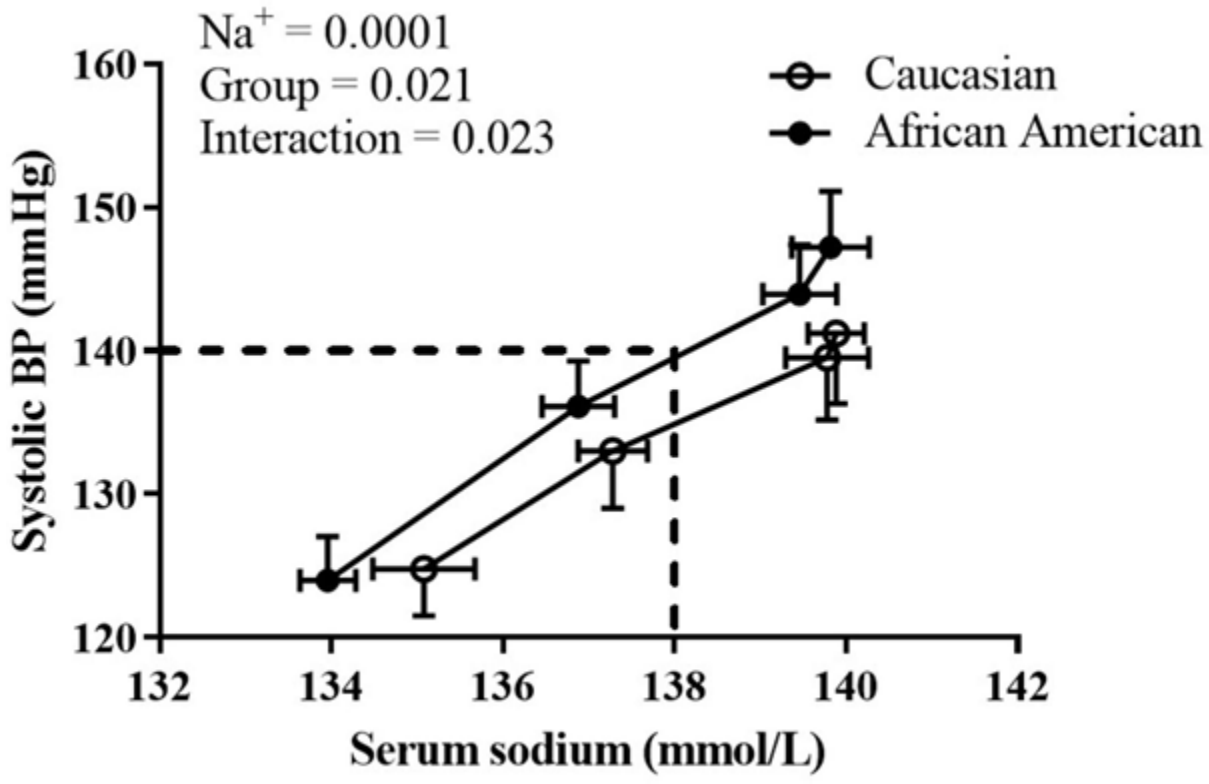


Figure from: Wenner et al., 2018

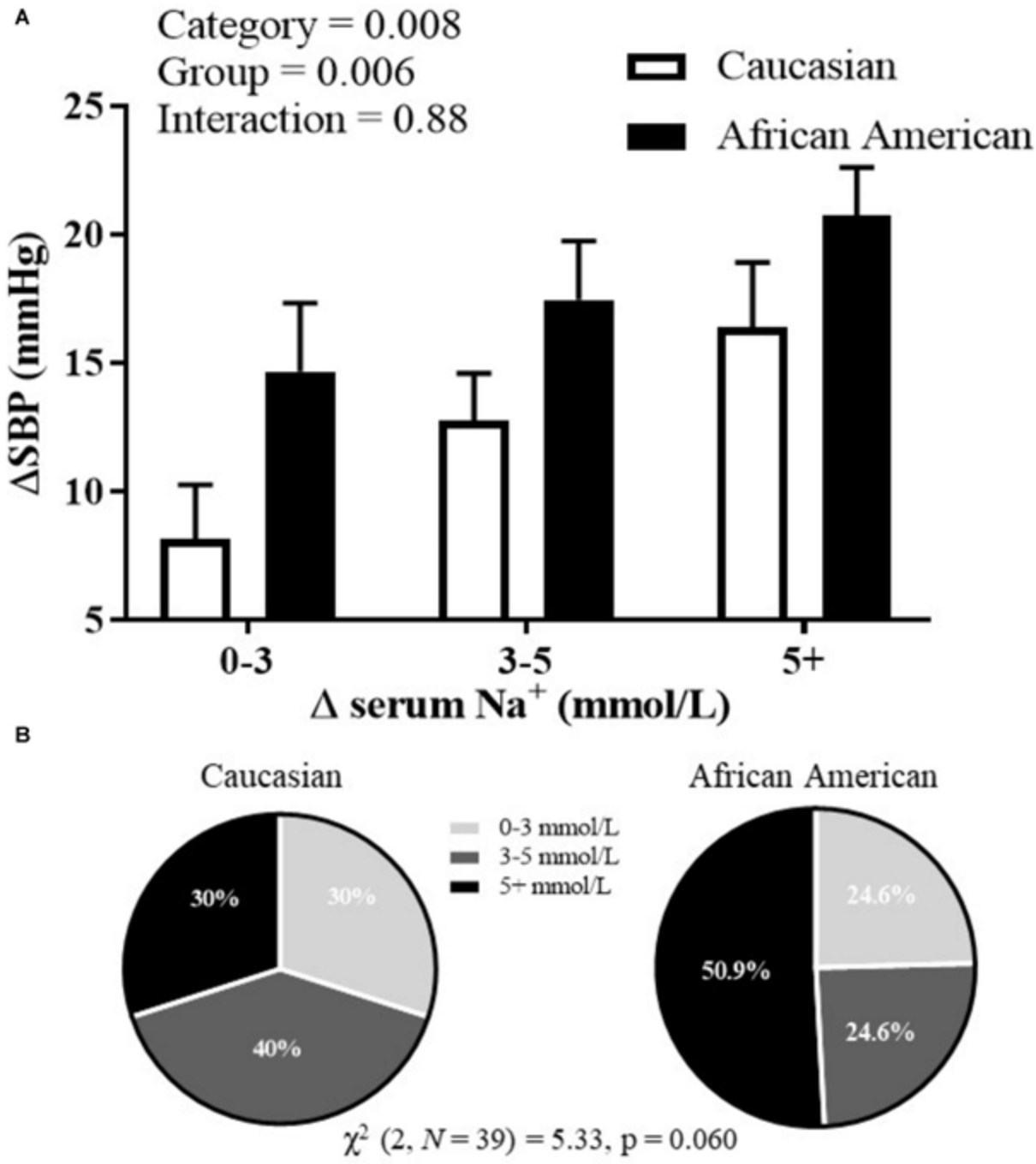


Figure from: Wenner et al., 2018

These findings seem to support large scale studies that black individuals and Asian individuals are more likely to be salt sensitive and provide some insight into why that might be.

# Key Points

1. Gold standard measurements of sodium excretion (and thus a proxy for intake) is multiple 24-hour urine collections.

2. At a population level, when best measurement methods are used, there is a linear increase in hypertension risk with increasing sodium intake.

3. There are important differences among individuals in the influences of sodium on blood pressure and CVD risk.

4. “Salt sensitivity” describes how responsive blood pressure is to changes in dietary salt intake.

5. Orthostatic hypotension: while increased salt intake in the short-term may help improve symptoms, the long-term consequences are unknown.

6. “Although there is clearly inter-individual variability within a given race or sex, there are important differences between men and women, and between Black people and non-Hispanic White people in the effects of sodium on blood pressure.” (Robinson et al., 2021)