An investigation of gut microbiota and butyrate producers in a hypertensive cohort of African Americans

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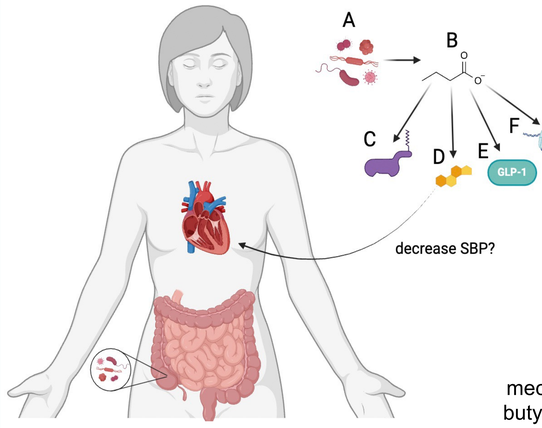
Significance & Rationale

- Hypertension (HTN) disproportionately affects African Americans (AAs) and increases risk for cardiovascular disease.[1]
- ~55% of AAs have high blood pressure and may require two or more medications to control their blood pressure.[2,3]
- Lack of scientific research outlining the relationship between the gut microbial composition and hypertension specific to AAs
- Butyrate-related mechanisms can act to decrease blood pressure; new research has demonstrated that circulating levels of butyrate are lower in hypertensive (H) than normotensive (N) subjects.[4]
- Comparing gut composition differences and butyrate producers between H and N AAs will allow for future research in butyrate supplementation and its mechanisms in reducing blood pressure



A= Microbes
B= Butyrate
C= activates G-protein coupled receptor 41/43
D= lowers circulating cholesterol
E= enhanced GLP-1 secretion
F= HDAC-1 inhibition

Figure 1. Potential mechanisms through which butyrate could decrease BP

Aims

This study aims to distinguish the gut microbiota of H and N to address the following hypotheses:

(1) Normotensive gut microbiome has a greater diversity.
(2) Normotensive subjects have more butyrate producing bacteria than hypertensive subjects.
(3) High abundance of butyrate producing microbes in the colon causes an increase in circulating butyrate levels post enema.

Methods

- BEBP Study (Figure 2)
- DNA isolated from fecal samples
- 16S rRNA gene amplified and sequenced on Illumina MiSeq Platform
- Characterize gut microbiota of each subject through gene taxonomic classification through Quantitative Insights into Microbial Ecology 2 (QIIME 2) pipeline

BEBP Study Design

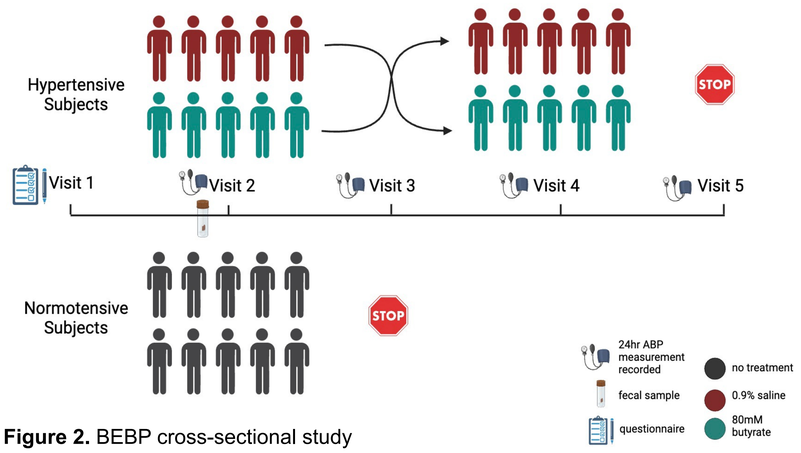


Figure 2. BEBP cross-sectional study

Results

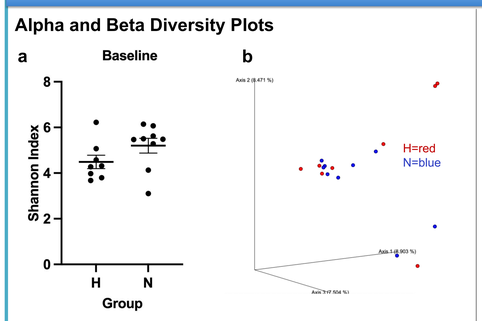


Figure 3. (a) Shannon index for H vs N demonstrating higher diversity for N group. **(b)** PCoA- Bray Curtis Dissimilarity

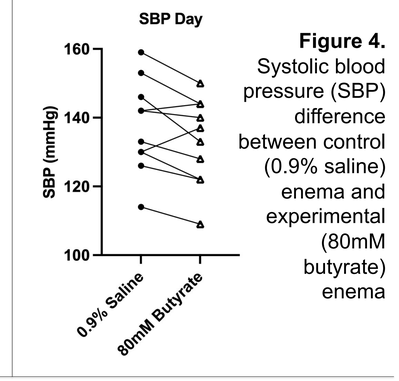


Figure 4. Systolic blood pressure (SBP) difference between control (0.9% saline) enema and experimental (80mM butyrate) enema

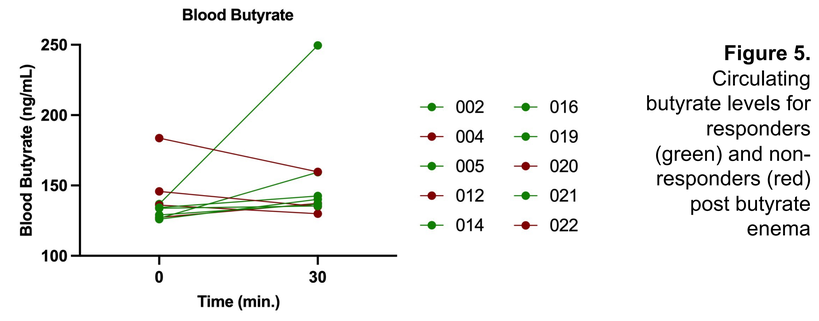


Figure 5. Circulating butyrate levels for responders (green) and non-responders (red) post butyrate enema

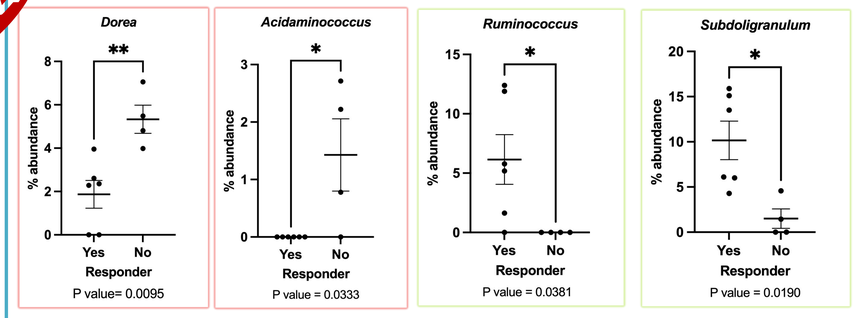


Figure 6. Statistically significant microbes for non-responders vs. responders. Mann-Whitney test was used to test for significance.**p<0.01, *p<0.05.

Conclusions and Future Directions

Conclusions:

- Higher alpha diversity (species richness) in N than H. HTN participants have a lower alpha diversity.[5,6]
- Butyrate enema decreased SBP in comparison to controls.
- N group had higher abundances of *Alistipes* and *Odoribacter* which are SCFA producers.[7]
- *Dorea* genus produces butyrate but is higher in H and non-responders; based on previous studies, *Dorea* is associated with obesity and inflammation.[8,9]
- Not all butyrate producing bacteria are associated with a decrease in BP.
- Non-responders have microbes that cause decreased permeability, leading to lower circulating butyrate levels post enema.

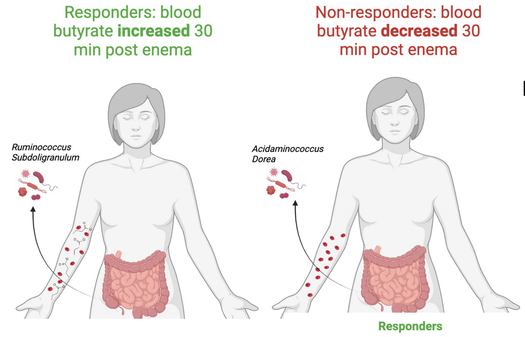


Figure 7. Differences in circulating butyrate between responders and non-responders

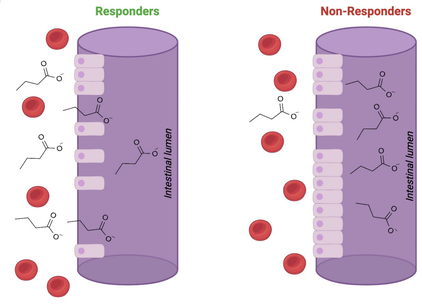


Figure 8. Possible mechanism causing higher circulating butyrate levels in responders than non-responders

Future Directions:

- Conduct a power analysis to determine statistically significant relationship for other butyrate-producing microbes (*Megasphaera*).
- Increase sample size.
- Mono-association mice model to test specific effects of *Subdoligranulum* and *Dorea* on gut permeability and compare to germ-free and normal microbiota mice.

References

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