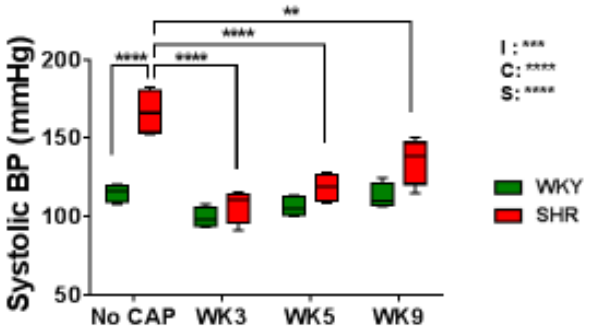
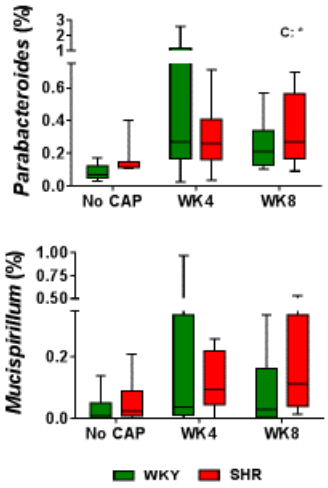
SUPPLEMENTAL MATERIAL

Figure S1. CAP persistently decreased systolic BP in the SHR. Systolic BP was obtained by tail-cuff across the duration of experiment.



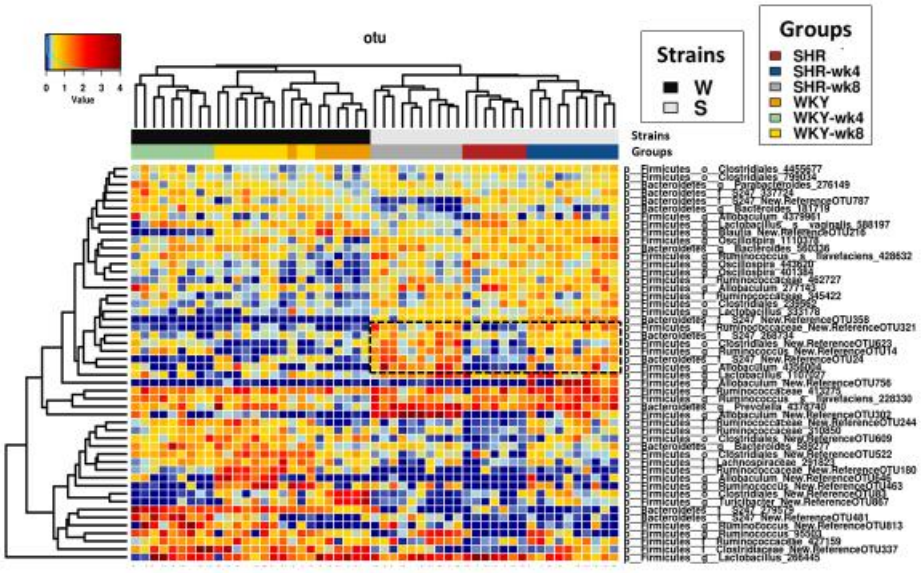
Significant reduction in systolic BP by CAP treatment (WK3) was maintained after withdrawal of CAP (WK5 and WK9). The two factors and their interaction in two way ANOVA are indicated as: I for interaction; C for CAP; S for rat strains. ** indicates P<0.01, *** P<0.001, **** P<0.0001 in two-way ANOVA and its followed Tukey's multiple comparisons. CAP, captopril. BP, blood pressure. WKY, Wistar Kyoto (rat). SHR, spontaneously hypertensive rat. ANOVA, analaysis of variance.

Figure S2. **Relative abundances of *Parabacteroides* and *Mucispirillum*.**



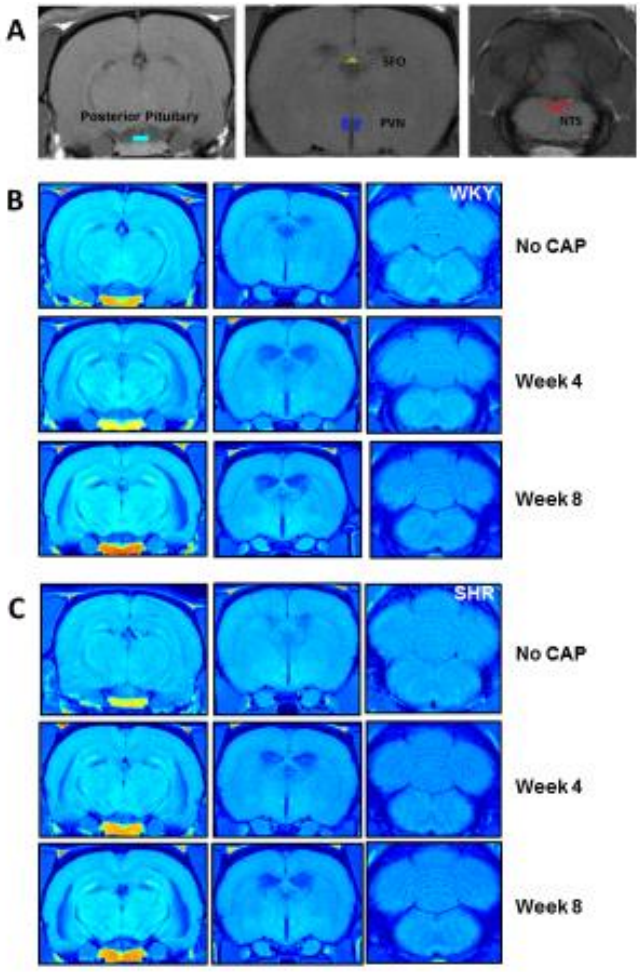
The factor C is for CAP. * indicates P<0.05 in two-way ANOVA. CAP, captopril. ANOVA, analaysis of variance.

Figure S3. Hierarchical clustering heatmap was generated based on the correlation between top 50 gut microbiota OTUs and environmental factors (no CAP, CAP on and off).



The hierarchical clustering is a multivariate analysis classifying groups of samples based on “most-like” pairing, followed by subsequent linking of “2nd most-like” samples until all samples are linked according to their similarities. Dashed line marks the bacterial OTUs that persistently responded to CAP. CAP, captopril. OTU, operational taxonomic unit.

Figure S4. (A) Map of investigated brain regions as per Paxinos-Watson. (B) Representative photographs of neuronal activity changes, determined by manganese-enhanced signal in multiple cardiovascular regulatory regions in the WKY and SHR at week 0 (No CAP), week 4 (CAP on) and week 8 (CAP off).



CAP, captopril. WKY, Wistar Kyoto (rat). SHR, spontaneously hypertensive rat.