#214 Milena Rodriguez Alvarez Advisor(s): Juan Marcos Alarcon

Activation of the inflammatory reflex by sodium bicarbonate: impact on the gut-brain-spleen axis.

Uncontrolled inflammation is key in acute severe illness in COVID19 patients, autoimmune, and tumoral processes. Low-grade systemic inflammation is also present in six of the main leading causes of death in United States. Activation of the inflammatory reflex (IR) via the splenic nerve, results in downregulation of proinflammatory cytokines and polarization of splenic immune cells towards an anti-inflammatory phenotype. Indeed, IR activators such as vagal nerve stimulation (VNS) are emerging as very promising tools to treat systemic inflammation. However, the IR circuitry remains controversial and VNS can be invasive and expensive. Recent findings point to oral sodium bicarbonate (NaHCO3) intake as a new potential IR activator in rats and humans. Critically, whether the anti-inflammatory effect of oral NaHCO3 administration is mediated by the splenic nerve is unknown. Here, we used flow cytometry to identify the number of T regulatory cells (Treg) and proinflammatory monocytes (M1) in spleen denervated (SD) or sham rats treated with water or NaHCO3. We found that shams but not SD animals showed a trend of a higher Treg count and lower M1 after receiving NaHCO3 in comparison with water. Interestingly, when comparing all the animals drinking NaHCO3, those SD showed significantly less Treg and M1 than sham animals. In the contrary, the Treg and M1 counts did not show differences between sham and SD-animals in the H2O-group. We also found increased immunolabeling of the neuronal activity marker PS6R in insular, orbital, and cingulate cortexes after NaHCO3 intake but not water. This suggests that NaHCO3 activates the IR via the splenic nerve and engages specific brain regions. Our findings shed light in our understanding of the IR circuitry and open new therapeutic avenues to treat systemic inflammatory conditions. Additionally, NaHCO3 is cost-effective, safe, and it is FDA-approved which guarantees a rapid translation into clinical practice.

Additional contributors to this project:
Christopher Roman
William Esber