

# Impact of Ozone Exposure on Metabolic Health

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## Description

Exposure to ozone has been associated with metabolic disorders in humans, yet the precise underlying mechanisms remain obscure. This study sought to delve into the involvement of the gut-liver axis and elucidate the potential mechanisms driving metabolic disorder using a combination of histological examination, microbiome analysis, and metabolomics in mice subjected to ozone exposure over varying durations and concentrations. The research subjected mice to ozone at concentrations of 0.5 ppm and 2.5 ppm for both subacute (4-week) and subchronic (12-week) periods. The findings revealed that ozone exposure led to a dose-dependent slowdown in weight gain and a reduction in hepatic lipid content. Additionally, there were notable alterations observed in the histological features of the intestinal epithelium. Specifically, the number of intestinal goblet cells decreased, while the number of tuft cells increased following ozone exposure. Furthermore, the study identified significant downregulation of the tight junction protein Zonula Occludens-1 (ZO-1) and an increase in epithelial cell apoptosis coupled with compensatory proliferation, indicating a compromised chemical and physical integrity of the intestinal barrier. This impairment in the intestinal barrier was proposed as a pivotal mechanism contributing to the observed metabolic disorder.

## Barrier function

Metabolomic analysis revealed substantial alterations in hepatic and cecal metabolic profiles, primarily associated with lipid metabolism and oxidative stress pathways. Notably, there was a dose-dependent increase in the abundance of Muribaculaceae in both the colon and cecum, which correlated with a reduction in metabolites such as bile acids, betaine, and L-carnitine. This disruption in the balance of gut microbiota and associated metabolites further exacerbated the perturbation of intestinal barrier function and lipid metabolism. Overall, the study's findings underscored the detrimental impact of subacute and subchronic ozone exposure on metabolic homeostasis through the disturbance of the gut-liver axis, particularly via

impairment of the intestinal barrier function. These insights provide valuable mechanistic understanding regarding the health risks associated with environmental ozone exposure and other oxidative stressors. In summary, the study highlights the importance of considering the intricate interplay between environmental factors, gut microbiota, and host metabolism in the development of metabolic disorders. Such insights not only contribute to our understanding of the pathophysiology of metabolic diseases but also have implications for the development of targeted therapeutic interventions aimed at mitigating the adverse effects of environmental pollutants on human health. Moreover, the study's findings shed light on the potential role of oxidative stress in mediating the detrimental effects of ozone exposure on metabolic health. Oxidative stress, characterized by an imbalance between the production of Reactive Oxygen species (ROS) and the body's antioxidant defenses, has been implicated in the pathogenesis of various metabolic disorders, including obesity, diabetes, and non-alcoholic fatty liver disease.

## Intestinal barrier

Ozone exposure is known to induce oxidative stress in various tissues, including the liver and intestine, which could contribute to the observed metabolic disturbances. Furthermore, the study underscores the importance of maintaining the integrity of the intestinal barrier for overall metabolic health. The intestinal barrier serves as a critical defense mechanism, preventing the translocation of harmful substances, such as bacteria and endotoxins, from the gut lumen into systemic circulation. Disruption of the intestinal barrier can lead to increased intestinal permeability, systemic inflammation, and metabolic dysfunction. Overall, the study provides novel insights into the complex interplay between environmental exposures, gut microbiota, and host metabolism in the development of metabolic disorders. By elucidating the underlying mechanisms, these findings have the potential to inform the development of targeted interventions aimed at mitigating the adverse effects of environmental pollutants on metabolic health and reducing the burden of metabolic diseases in the population.