ABSTRACT

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The increasing use of cannabinoids among pregnant women, including tetrahydrocannabinol, hexahydrocannabinol, cannabidiol, cannabigerol, and cannabinol, has become a major cause for concern due to the potential adverse effects on fetal health. Prenatal cannabis exposure has been linked to cognitive, attention, and memory deficits in the developing fetus, although the mechanisms underlying these effects are not fully understood. The placenta, a vital organ for fetal development, immune protection, and regulating inflammatory cytokines, may play a role in the relationship between cannabis use during pregnancy and fetal neurodevelopmental disorders. Inflammation during pregnancy, whether from infections or other sources, can impair placental function and further increase the risk of the above-mentioned disorders in the child. Despite the growing evidence of placental dysfunction and abnormal fetal neurodevelopment due to prenatal cannabis exposure, little is known about the relationship between them. This study aimed to assess the pharmacological effects of exocannabinoids on specific inflammation-related molecules using an *ex vivo* model of healthy human placental explants. Placental explants were exposed to exocannabinoids for 48 hours, followed by treatment with lipopolysaccharide (LPS), a principal component of Gram-negative bacteria cell walls that elicits an acute inflammatory response. The study analyzed the gene expression, as well as the pro-inflammatory cytokine levels of IL-1β, IL-6, IL-18, and TNF-α following treatment. Our results suggest that both psychoactive and non-psychoactive cannabinoids prevented the increase in LPS-stimulated inflammatory response, indicating a potential immunomodulatory effect. These findings are expected to inspire further research and raise questions about the safety of cannabis use during pregnancy.