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Dynamic Transcriptomic Response Over Time in Immune Cells Reveals Diverse Biological Effects Following Acute THC Administration

Evidence has demonstrated that cannabis modulates immune function. However, the underlying mechanisms of its immunological effects are not fully studied. To understand how cannabis alters the transcriptome in vivo, we intravenously administered the principal component of cannabis, 0.03mg/kg Delta-9-tetrahydrocannabinol (THC), to 20 healthy participants. Blood was drawn prior to, at 70 minutes-post, and 300 minutes-post THC administration. Whole transcriptome sequencing of peripheral blood mononuclear cells (PBMCs) was performed at these three timepoints. We performed a linear mixed model to identify dynamically changed genes by THC exposure across three timepoints. We characterized the patterns of gene expression changes as “growth” (increased with time), “peak” (increased at 70 minutes, then decreased at 300 minutes), “recession” (decreased with time); and “trough” (decreased at 70 minutes, then increased at 300 minutes). A total of 5,626 genes reached a false discovery rate (FDR) < 0.05, comprising 5,436 growth, 33 peak, 59 recession, and 88 trough patterns. These dynamically changed genes are involved in multiple functional domains. For example, one of the top ranked “growth” genes, CXCR1 (IL-8RA), encodes the pro-inflammatory chemokine interleukin-8, playing a critical role in activating immune cells and mediating inflammation. TNFRSF21 (Tumor Necrosis Factor Receptor Superfamily Member 21), which is involved in cell apoptosis, exhibited a recession pattern. Overall, Gene Ontology (GO) enrichment analysis revealed that “growth” genes were predominantly associated with immune response pathways, while “peak” genes were enriched in protein processing pathways. Notably, “recession” and “trough” genes were enriched in neurobiological GO terms. Our results, for the first time, demonstrate the temporal complexity of the transcriptional response to acute THC exposure, suggesting that cannabis modulates diverse biological pathways and providing new insights into the molecular mechanisms underlying its immunological effects.

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