

Endocannabinoids: From Drosophila Physiology and Autophagy Regulation to Therapeutic Insights

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The endocannabinoid system (ECS) and autophagy are both essential physiological mechanisms within cells. However, limited research explores the relationship between endocannabinoids, specifically 2-AG, and autophagy. We have chosen to study *Drosophila* as our research subject to examine the impact of endocannabinoids from an organism perspective. We believe that *Drosophila* can serve as an initial research platform, providing a more convenient method for studying both exogenous and endogenous cannabinoids. In this study, we manipulated the levels of 2-AG in *Drosophila* by modulating the expression of synthetic and degrading enzymes, MAGL and DAGL. When MAGL was inhibited, the lifespan, anti-starvation ability, and autophagy of *Drosophila* increased, while DAGL was inhibited or overexpressed, such functions suppressed. By adding autophagy inhibitors, we confirmed the relationship between autophagy and physiological functions. These findings could be beneficial to the efficiency of cannabinoid drug applications and mitigate side effects on the nervous system and liver function.