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Palmitoylethanolamide in CNS health and disease.

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Abstract

The existence of acylethanolamides (AEs) in the mammalian brain has been known for decades. Among AEs, palmitoylethanolamide (PEA) is abundant in the central nervous system (CNS) and conspicuously produced by neurons and glial cells. Antihyperalgesic and neuroprotective properties of PEA have been mainly related to the reduction of neuronal firing and to control of inflammation. Growing evidence suggest that PEA may be neuroprotective during CNS neurodegenerative diseases. Advances in the understanding of the physiology and pharmacology of PEA have potentiated its interest as useful biological tool for disease management. Several rapid non-genomic and delayed genomic mechanisms of action have been identified for PEA as peroxisome proliferator-activated receptor (PPAR)-α dependent. First, an early molecular control, through Ca(+2)-activated intermediate- and/or big-conductance K(+) channels opening, drives to rapid neuronal hyperpolarization. This is reinforced by the increase of the inward Cl(-) currents due to the modulation of the gamma aminobutyric acid A receptor and by the desensitization of the transient receptor potential channel type V1. Moreover, the gene transcription-mediated mechanism sustains the long-term anti-inflammatory effects, by reducing pro-inflammatory enzyme expression and increasing neurosteroid synthesis. Overall, the integration of these different modes of action allows PEA to exert an immediate and prolonged efficacious control in neuron signaling either on inflammatory process or neuronal excitability, maintaining cellular homeostasis. In this review, we will discuss the effect of PEA on metabolism, behavior, inflammation and pain perception, related to the control of central functions and the emerging evidence demonstrating its therapeutic efficacy in several neurodegenerative diseases.

KEYWORDS: Acylethanolamide; Behavior; Food intake; Inflammation; Neurodegenerative disease; Pain; Peroxisome proliferator-activated receptor

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