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Palmitoylethanolamide, a naturally occurring disease-modifying agent in neuropathic pain.

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Abstract

Persistent pain affects nearly half of all people seeking medical care in the US alone, and accounts for at least $80 billion worth of lost productivity each year. Among all types of chronic pain, neuropathic pain stands out: this is pain resulting from damage or disease of the somatosensory nervous system, and remains largely untreatable. With few available treatment options, neuropathic pain represents an area of significant and growing unmet medical need. Current treatment of peripheral neuropathic pain involves several drug classes, including opioids, gabapentinoids, antidepressants, antiepileptic drugs, local anesthetics and capsaicin. Even so, less than half of patients achieve partial relief. This review discusses a novel approach to neuropathic pain management, based on knowledge of: the role of glia and mast cells in pain and neuroinflammation; the body's innate mechanisms to maintain cellular homeostasis when faced with external stressors provoking, for example, inflammation. The discovery that palmitoylethanolamide, a member of the N-acylethanolamine family which is produced from the lipid bilayer on-demand, is capable of exerting anti-allodynic and anti-hyperalgesic effects by down-modulating both microglial and mast cell activity has led to the application of this fatty acid amide in several clinical studies of neuropathic pain, with beneficial outcome and no indication of adverse effects at pharmacological doses. Collectively, the findings presented here propose that palmitoylethanolamide merits further consideration as a disease-modifying agent for controlling inflammatory responses and related chronic and neuropathic pain.

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