PPAR-α AGONISTS CAUSE ANALGESIA THROUGH IKca AND BKca POTASSIUM CHANNELS ACTIVATION

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Palmitoylethanolamide (PEA), the naturally occurring amide of palmitic acid and ethanolamine, modulates pain and inflammation (1). We identify PPAR-α (peroxisome proliferator-activated receptor-α) as the target of PEA responsible for these actions. PEA activated PPAR-α in vitro and attenuated acute pain in wild-type mice, but not in mice lacking PPAR-α (PPAR-α⁻/⁻)(2). The synthetic PPAR-α agonists GW7647 and Wy-14643 also exerted potent analgesic effects, which were contingent on PPAR-α expression and independent on PPAR-α-induced anti-inflammation. PPAR-α induced analgesia occurred within minutes from agonist administration and was regulated by calcium-operated BKca and IKca potassium channel antagonist (3). Our finding show that PPAR-α mediates the acute analgesic actions of PEA trough the control of potassium channels, suggesting a role for this nuclear receptor in the control of pain initiation.

References