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Potential antinociceptive effects of cannabinoid compounds on migraine-associated responses in an experimental model in female rats

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Introduction
Migraine is a painful and debilitating neurological disorder characterized by attacks of throbbing headache, frequently associated with photo and phonofobia, as well as nausea and vomiting. Despite advances in the pharmacological treatment of migraine, it is estimated that half of the patients do not achieve satisfactory pain control, highlighting the need for novel therapeutic options. In this context, cannabinoid compounds, including cannabidiol (CBD), cannabigerol (CBG), and tetrahydrocannabinol (THC), have demonstrated a potential for migraine treatment.
Objective
To assess the efficacy of different combinations of cannabinoid compounds in an animal migraine model.
Methods
Adult female Wistar rats were used, and protocols were approved by CEUA-BIO/UFPR #1589. The CBD "plus minor cannabinoid traces" (CBC, CBN, and CBG), CBD/CBG 2:1 ratio, CBD/THC, and CBD/CBG 2:1 Ratio/THC (CBD 30 mg/kg; THC 0.3%) or vehicle were administered systemically via intraperitoneal injection. Thirty minutes later, the animals received an intraganglionar injection (i.g.) of saline or calcitonin gene-related peptide (CGRP, 0.1 nmol/10 µL) into the trigeminal ganglion to induce cutaneous allodynia, which was evaluated by application of von Frey filaments (0.04 – 8g) to the periorbital area, from 0.5 to 6 hours after CGRP injection. The same animals were tested in the open field 1 hour after saline or CGRP injection to assess locomotion and anxiety-like behavior. In addition, 24 hours after i.g injections, the same animals were exposed to bright light for 1 hour to reactivate cutaneous allodynia, which was assessed from 0.5 to 4 hours.
Results
In female rats, treatment with CBD "plus minors traces," CBD/THC and CBD/CBG 2:1 prevented the development of cutaneous allodynia induced by CGRP, but CBD/THC showed long-lasting effects (up to 3 hours). CBD/CBG 2:1/THC did not change significantly the mechanical threshold compared to the control group. CBD plus minors and CBD/THC, but not CBD/CBG 2:1 and CBD/CBG 2:1/THC, prevented the development of photosensitivity. Data from the open field test are being analyzed, and ongoing experiments in male rats will be included in the final presentation.
Conclusion
CBD plus minor cannabinoids and CBD/THC exhibited promising antinociceptive and anti-hyperalgesia effects in a pre-clinical model of migraine, which remains to be validated in the clinical setting.