Session title: ePoster Area – open 24/7
Session type: ePoster Session
Presentation number: P.291

Abstract title:

Antidepressant-like effect and molecular mechanism of action of cannabidiol in the lipopolysaccharide model of depression in mice

Biography

Graduated in Biomedical Sciences in the University of Lleida (UdL) in 2015, Masters degree in Mental Health Research in the Autonomous University of Barcelona (UAB) in 2016, and currently finishing a PhD in Molecular Biology and Biomedicine in the University of Cantabria (UC).

E. Florensa-Zanuy[12,3], A. Architravo[3], A. Adell[23], E. Garro-Martinez[12,3], E. Castro[12,3], A. Diaz[12,3], A. Pazos[12,3], F. Pilar-Cuellar[12,3].
[1]Universidad de Cantabria UC, Pharmachology, Santander, Spain.
[2]Centro de Investigación Biomedica en Red de Salud Mental CIBERSAM, Instituto de Salud Carlos III, Santander, Spain.
[3]Instituto de Biomedicina y Biotecnologia de Cantabria IBBTEC- Universidad de Cantabria-CSIC-SODERCAN, Cellular and molecular signalling, Santander, Spain.

Major Depression is an incapacitating disease spread worldwide. As its etiology is still unknown, some hypotheses have been postulated, being the neuro-inflammatory one of the most recent. The current treatment for depression is far from optimal and there is an urgent need to find fast-acting drugs with fewer side effects. In this regard, cannabidiol (CBD), the major non-psychotropic component of *Cannabis sativa*, appears as a promising antidepressant drug. We have evaluated CBD's behavioural and molecular effects in a neuro-inflammatory model of depression induced by lipopolysaccharide (LPS).

Male NMRI mice were injected LPS (0.83 mg/Kg i.p.). CBD (30 mg/Kg, i.p.) was administered 30 min before. Behavioural tests were performed 12h after LPS to assess anhedonic- (sucrose preference test, SPT), anxious- (open field test, OFT) and depressive-like behaviour (tail suspension test, TST). ELISA and qPCR were used to study IL-6 and TNF in plasma and prefrontal cortex (PFC), respectively. Kynurenine (KYN), tryptophan (TRP) and serotonin (5-HT) were quantified by HPLC in hippocampus (Hp) and cortex (Cx). NF-κB levels were determined by Western Blot in the nuclear fraction of Cx samples. A two-way ANOVA analysis followed by Newman-Keuls post-hoc test was used for statistical analysis (significance was set at $p<0.05$).

LPS increased the immobility time in the TST ($p<0.01$ *vs* vehicle), and this was prevented by CBD ($p<0.01$ *vs* LPS). In the SPT, LPS mice had a decreased preference ($p<0.001$ *vs* vehicle), which was prevented by CBD ($p<0.01$ *vs* LPS). However, CBD could not prevent the decrease in the time spent in the centre induced by LPS in the OFT ($p<0.001$ *vs* vehicle).

The study of IL-6 and TNFα plasma levels showed that CBD partially prevented the increase in IL-6 induced by LPS ($p<0.001$ in LPS *vs* vehicle; $p<0.001$ in CBD+LPS *vs* LPS) but not the increase in TNFα ($p<0.05$ LPS *vs* vehicle). Similarly, in PFC CBD prevented LPS-induced IL-6 increase ($p<0.001$ LPS *vs* vehicle; $p<0.05$ CBD+LPS *vs* LPS) but not the increase in TNF ($p<0.001$ LPS and CBD+LPS *vs* vehicle).

The KYN/TRP ratio was increased by LPS in Hp ($p<0.01$) and Cx ($p<0.001$), and this was prevented by CBD

(p<0.01 *vs* LPS in Hp; p<0.05 *vs* LPS in Cx). Likewise, the KYN/5-HT ratio increased with LPS (p<0.001 in Hp and Cx) and was decreased by CBD when compared to the LPS group (p<0.001 in Hp and Cx). Furthermore, NF-κB levels were increased in the nuclear fraction of Cx by LPS (p<0.001) and this was prevented by CBD (p<0.01 *vs* LPS).

This study showed that CBD exerts antidepressant and anti-anhedonic effects in the LPS model of depression in mice, preventing the increase in IL-6 levels in plasma and PFC, in the KYN/TRP and KYN/5-HT ratios, and in the nuclear NF-κB levels in different brain areas. Altogether, our data suggest that the modulation of inflammatory pathways is involved in CBD's antidepressant effect.

Conflict of interest:
Disclosure statement:\rThis research was supported by the Ministerio de Economía y Competitividad (SAF2015-67457-R MINECO/FEDER), the Ministerio de Ciencia Innovación y Universidades (RTI2018-097534-B-I00), and Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM CB/07/09/0029).

Topics:
Mood disorders
Neuro-inflammatory/ auto-immune
Pharmacology