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## Abstracts of

## 40° CONGRESSO NAZIONALE DELLA SOCIETÀ ITALIANA DI FARMACOLOGIA – PROCEEDINGS

## THE SCIENTIFIC VALUE AND APPROPRIATE USE OF DRUGS

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EDRA SpA

Via G. Spadolini, 7
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Tel. 0039 (0)2-88184.1
Fax 0039 (0)2-88184.301
www.edraspa.it

astrocyte activation and other adverse effects as sedation, motor incoordination, anhedonia. Consistently, CL39 determine a significant, aversion-free antinociception in animal model of acute and chronic pain; thus emerging as a promising candidate to be further investigated as innovative analgesic and anti-addiction therapeutic.

# KYNURENINE NEGATIVELY EXACERBATES THE THC EFFECTS ON TETRAD AND SENSORIMOTOR RESPONSES IN ADULT MICE

**(1) Sarah Beggiato, (2) Sabrin Bilel, (1,3) Mariachiara Zuccarini, (4) Luca Ferraro, (2,5) Marti Matteo**

(1) Department of Medical, Oral and Biotechnological Sciences, University of Chieti-Pescara, Chieti, Italy
(2) Department of Morphology, Experimental Medicine and Surgery, Section of Legal Medicine and LTTA Centre, University of Ferrara, Ferrara, Italy
(3) Aging Research Center and Translational Medicine (CeSI-MeT) Chieti, Italy
(4) Department of Life Sciences and Biotechnologies, University of Ferrara, Ferrara, Italy; Laboratory for the Technology of Advanced Therapies (LTTA Centre), University of Ferrara, Ferrara, Italy
(5) Collaborative Center for the Italian National Early Warning System, Department of Anti-Drug Policies, Presidency of the Council of Ministers, Italy

**BACKGROUND:** The main psychoactive component of marijuana (Δ-9-tetrahydrocannabinol, THC) and synthetic cannabinoids intake, is correlated with untoward physiological effects in vulnerable individuals (D'Souza et al., 2016). Thus, cannabinoids misuse could be considered as a relevant factor in precipitating and/or perpetuating psychosis in these subjects. It has been reported, in rats and monkey, that the reinforcing effects of THC can be reduced by increasing endogenous kynurenic acid (KYNA) levels (Justinova et al., 2013). KYNA, a neuroactive metabolite deriving from tryptophan degradation (Schwarcz et al., 2012). Several studies suggest a pathophysiologically relevant association between increased brain KYNA levels and cognitive dysfunctions in individuals with schizophrenia (Wonodi and Schwarcz, 2010; Sathyasaikumar et al., 2011).
**METHODS:** Male ICR (CD-1®) mice (25-30 g body weight) were treated with THC (30 mg/kg; i.p.) and kynurenine (20 mg/kg, i.p.), alone or in combination. Following the drug administration, body temperature, acute mechanical and thermal analgesia, motor activity sensorimotor responses (to visual, acoustic and tactile stimulation) were evaluated. Furthermore, brain levels of KYNA were measured 1 and 4 hours after kynurenine injection.
**RESULTS:** Brain KYNA levels were significantly increased 1 hour, but not 4 hours, after kynurenine administration. The administration of kynurenine, amplified the THC-induced impairment of sensorimotor responses. In particular, kynurenine increased the THC-induced reduction in the visual placing response, acoustic response and tactile response (vibrissae, corneal and pinna reflexes). Furthermore, by using the "tetrad paradigm for screening cannabinoid-like effects" it has been observed that kynurenine significantly increased THC-induced motor activity reduction (as evaluated by the bar test, drag test and rotarod test) and hypothermia (core and surface body temperature), but not THC-induced analgesia.
**CONCLUSIONS:** Overall, the present data indicate that increased brain KYNA levels exacerbate "tetrad" and sensorimotor responses induced by the acute administration of THC. This confirm the existence of a cross-talk between the KP and endocannabinoid system which could be involved either in the psychotropic properties of THC or in the ethiopatogenesis of schizophrenia.