P.6.d.024 Reviewing "apinaca", an emergent synthetic cannabinoid receptor agonist

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Introduction: Since 1990 there is an explosive increase in the creation of new molecules that act on the cannabinoid system. The velocity of proliferation of New Psychoactive Substances (NPS) makes almost impossible to control consumption and trade. Moreover, there is almost no research available and, despite its widespread use, the pharmacology of these molecules is not characterized [1].

Material and Methods: A review of the publications of the molecule is done by searching for keywords "AKB-48" "AKB48" "APINACA" "Synthetic cannabinoids". The history and current state of knowledge about the drug is exposed. There are too little publications about this topic, specially clinical ones, so all the indexed articles of interest are included and also data of the World Health Organization (WHO) review of the topic.

Results: The AKB-48, or APINACA, was firstly report in Japanese herbal smoking blends in 2012 [2], nevertheless the origin of the nomination is thought to be in Thailand. One of the differences with earlier JHW-type synthetic cannabinoids, is that the molecule has an indazol ring connected to an adamantyl group through a carboxamide linkage [1]. It also has high affinity for the CB2 receptor and somewhat less for the CB1 [3]. APINACA is clandestinely manufactured. In its pure form is a white powder, soluble in methanol and ethanol, so it can be orally ingested or smoked. The dose needed to produce the desired effect is actually unknown and also have not been described any clinical utility (APINACA review, Expert Committee on Drug Dependence WHO, 2014). Adarsh S. and colleagues conducted the first characterization of their metabolism in vitro, in a sample of human hepatocytes, describing 17 new metabolites of phases I and II, including glucuronidated metabolites, permitting the identification of the substance in urine analysis for forensic and clinical use [1]. The consequences, of using these compounds are unknown, it is presumed that psychosis and dependence are possible, given the similarities with marijuana. Synthetic cannabinoids intoxication, like the overuse of THC, can cause tachycardia, hypertension, nausea, vomiting, drowsiness, hallucinations and acute psychotic reactions [4]. Specifically regarding this molecule, it has been described the potential genotoxic properties of alkylindazoles and aminoalkyl indoles. VJ Koller et al. describes the inhibition of cell division and the induction of a significant number of micronucleus that reflects structural or numerical chromosomal aberrations, so the use of these cannabinoids may produce adverse effects on health, damaging genetic material [5].

Conclusions: The european Early Warning System (EWS) informs specially an increase in the detection of new cannabinoids that are sold like a "legal alternatives" of marijuana. APINACA is currently not under international control, we don't even know the real consumption prevalence. Further characterization of pharmacodynamics, pharmacokinetics and epidemiology of the compound is needed, due to its potential harm and lack of evidence.

References

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P.6.e. Addiction – Other (basic)

P.6.e.001 When motivation becomes maladaptive – similarities between drug addiction and obesity

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Purpose of the study: Motivation directs our behavior toward rewards to maximize hedonic feeling and survival chances. However, motivation can be destructive when out of control, resulting in addictive behavior. As motivated behavior can be directed at both natural rewards, such as palatable food, and drugs of abuse, could there be similar mechanisms underlying drug addiction and obesity? In this study we evaluate whether obese rats show high motivation to obtain palatable food similar to the motivation to obtain cocaine exhibited by rats that underwent cocaine self-administration and extinction. We then examine also whether similar synaptic changes occur in both groups.

Methods: In one study, rats performed cocaine self-administration for two weeks (2 hours/day) followed by 2–3 weeks of extinction. Reinstatement of drug-seeking behavior was then induced by drug-associated cues. In a second study, rats were put on a high-fat-high-sugar (HFHS) diet for 8 weeks, followed by normal chow diet for the rest of the experiment. During the chow diet period motivation to obtain pellets of the HFHS food was assessed using the progressive ratio task (i.e. an increasing amount of lever presses was required for obtaining consecutive food pellets) and the fixed ratio 5 (FR5) test (every 5 presses resulted in one food pellet). Both groups of rats (cocaine and food) were then used for electrophysiology experiments, in which the strength of glutamatergic synapses in the nucleus accumbens core (NAcore) was examined by measuring the ratio between the current mediated by AMPA and NMDA receptors (A/N).

Results: While 8 weeks of HFHS diet induced obesity (average weight gain of 390±7 g) in some rats it did not in others (average weight gain of 285±6 g). Comparing these obesity prone (OP) and obesity resistant (OR) rats, respectively, we found that the OP rats consumed more calories and performed more lever presses on the behavioral tests examining the motivation to obtain HFHS pellets. We then examined the A/N in the NAcore of OP and OR rats and