THE THERAPEUTIC USE OF CANNABIS

CLINICAL ENDOCANNABINOID DEFICIENCY SYNDROMES

A deficiency in the Endocannabinoid system with dynamic changes signaling from acute and chronic stress, aside from other causes, genetic, age, or drug induced has been postulated in numerous common subjective pain syndromes that lack objective signs, are treatment resistant and whose sufferers have all endured the stigma of a psychosomatic label. The common denominator of all these syndromes is hyperlagesia and central sensitization.

All humans posses an underlying endocannabinoid tone that is the reflection of the two main endocannbinoids Araquidonylethanolamide or Anandamide AEA, and 2 Araquidonylglycerol 2AG.

The greatest evidence for a clinical deficiency in the ECs is for the triad syndrome of: Irritable Colon Syndrome, Migraine and Fibromyalgia

Irritable Colon Syndrome

Gastrointestinal propulsion, secretion and inflammation in the gut are all modulated by the ECs, and cannabis was one of the fist effective clinical treatments in the cholera attacks in the 19th century. Anandamide inhibits the

contractile force of the circular and longitudinal muscles through a non CB1-CB2 mechanism. There are also increased TRVP1 nerve fibers that contribute to the visceral hypersensitivity and pain. These two findings alone justify the use of CBD for this syndrome; since CBD can increase the anadamide tone and desensitize the TRPVP1. It has also been shown interplay between the benefits caused by the use of probiotics and cannabis through the ECs

Migraine

Cannabis was a mainstay of treatment for migraine in Europe and USA for a century between 1843 -1943, and today we have enough evidence to justify its use based on the findings of:

- Low AEA levels in the Cerebro spinal fluid of patients with chronic migraine

-Low 2AG and AEA levels in platelets of patients with episodic migraine without aura

-AEA modulates activity in the trigeminovascular system

-AEA diminishes blood pressure dilatation in the dura mater

-AEA prevents release of NO in the dural artery smooth muscle

-AEA and 2AG produce analgesia in the periaqueductal gray matter

And several other data. There is enough evidence to support the use of CB1 agonists like THC in migraines, but preferably at low doses and, as the agonist that it is, with regular doses of CBD to desensitize the TRPV1 receptor that causes vasodilatation

Fibromyalgia

The most common diagnosis in USA rheumatology clinics, is, like migraine, more prevalent in women and always disrupts sleep. It is a central sensitization consistent with neuropathic pain at the root of the syndrome, with secondary hyperlagesia in association with ECs hypofunction in the spinal cord. There is also depression and anxiety associated.

The ECs is a proposed target through the use of cannabis and this has proved to reduce pain and stiffness, increase relaxation and somnolence and general well being. Cannabis has been much more valued as effective by patients than the current treatments of serotonin and adrenergic uptake inhibitors, and the anticonvulsant pregabaline.

Additional conditions suggesting CED

Motion sickness

AEA levels and CB1 expression has been demonstrated to be low

Multiple sclerosis

Significant deficits in AEA and 2Ag in the CSF of patients, especially with secondary progressive cases

Diabetic neuropathy

Decreased levels of several TRPV1 Endogenous ligands, AEA among others.

Huntington´s disease

Significant decrease in CB1 receptor availability, with underactivity of the ECs that correlates inversely with disease activity

Parkinson's disease

Elevations of AEA might be a compensatory reaction to the loss of dopamine in the striatal circuits that causes a low encocananbinoid tone

Fear extinction memory

Inhibition of ECs transmission inhibits fear extinction, while activation though the CB1 receptors potentiate memory extinction by increasing hippocampal 2Ag, and amygdalar AEA levels mediated by the glucocorticoids.

Stress induced anxiety

Stress or aversive experiences produce anxiety through a rapid reduction in AEA signaling, while elevating AEA signaling stops anxiety induced by both acute and chronic stress through the CB1 receptor. Stress also increases 2AG release to reduce the anxiety through both receptors CB1 and CB2

Posttraumatic stress disorder PTSD

A compensatory upregulation of CB1 receptors happens as a reaction to reduced EC levels, both hippocampal 2 AG and amygdalar AEA, along with a reduced Cortisol levels too. Women show a higher availability of CB1 receptors rending them more susceptible to developing PTSD.

Major depression

People with depression have relatively lower EC levels.

Schizophrenia

AEA levels are negatively correlated with psychotic symptoms, and Cananbidiol alleviates them.

Anorexia Nervosa and Bulimia

Chronic upregulation of CB1 receptors is presumed to be due to a an ECs hypoactivity

Autistic Spectrum disorders ASD

Ananadamide mediates the action of oxytocin, a neuropeptide crucial for social behavior to control social reward, and increasing anandamide activity at CB_1 receptors improves ASD-related social impairment and identifies FAAH as a novel therapeutic target for ASD. Also, autism associated mutations commonly disrupt tonic endocannabinoid signaling.

Anhedonia

Exposure to chronic stress can produce anhedonia, or impairment to reward sensitivity, secondary to a deficiency in AEA signaling.