Clinical Endocannabinoid Deficiency (CECD)

Migraines
Fibromyalgia
IBS
http://europepmc.org/abstract/MED/15159679/

An emerging literature documents the "eCB deficiency syndrome" as an etiology in migraine, fibromyalgia, irritable bowel syndrome, psychological disorders, and other conditions. … Evidence indicates that several classes of pharmaceuticals upregulate the eCB system, including analgesics (acetaminophen, non-steroidal anti-inflammatory drugs, opioids, glucocorticoids), antidepressants, antipsychotics, anxiolytics, and anticonvulsants. Clinical interventions characterized as "complementary and alternative medicine" also upregulate the eCB system: massage and manipulation, acupuncture, dietary supplements, and herbal medicines. Lifestyle modification (diet, weight control, exercise, and the use of psychoactive substances--alcohol, tobacco, coffee, cannabis) also modulate the eCB system. http://www.ncbi.nlm.nih.gov/pubmed/24622769

..."Disorders of opioid and endocannabinoid systems can also be found in suicide victims."...

The cannabinoid 1 (CB 1) receptor as the primary mediator of the endocannabinoid (EC) system was found to play a role in eating disorders (EDs), depression, anxiety, and suicidal behavior.

Altogether, these observations suggest that alterations of the endocannabinoid tone might be associated with the development of stress-related diseases, including anxiety, depression and obesity.

Expression of cannabinoid receptor 1 is increased in human Achilles tendinosis suggesting that the cannabinoid system may be dysregulated in this disorder.

ECS, eCB, ECs all stand for Endocannabinoid System, AEA stands for Anandamide.
Treatment of **immune dysregulation** using cannabinoid derivatives
Additionally, **stroke severity** was found to be increased in CB1 receptor knock-out mice
Defective CB1 receptor function is also implicated in **Huntington's Disease**
[https://www.google.com/patents/US20140066497](https://www.google.com/patents/US20140066497)

**Endocannabinoid Dysregulation in the Pancreas and Adipose Tissue of Mice Fed With a High-fat Diet**

The present invention relates to a method for the diagnosis of **miscarriage** in female human beings based on the detection of the presence of the enzyme anandamide hydrolase (FAAH) active in blood cells and in particular in lymphocytes

**Chronic Traumatic Encephalopathy (CTE)** causes an **endocannabinoid deficiency**, which causes a significant decrease in circulating cannabinoids and damages CB1 receptors and CB2 receptors that bind to the endocannabinoids. Cannabidiol has been shown to provide anti-inflammatory, neuroprotective, and anti-convulsive effects.

Pharmacological modulation of cannabinoid system within the gastrointestinal tract might be therapeutically useful in conditions on which **intestinal inflammation** and barrier dysfunction takes place after exposure to stress.

Seminal plasma AEA levels were lower in men with **asthenozoospermia** and **oligoasthenoteratozoospermia** compared with normozoospermic men.

**IBS** subtypes and their symptoms show distinct alterations of endocannabinoid and endocannabinoid-like fatty acid levels.

These findings suggest that **chronic inflammation** might develop also because of endocannabinoid and palmitoylethanolamide tissue concentration impairment, the correction of which might be exploited to develop new anti-inflammatory drugs.

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Deficiency of CB2 receptor led to an increased disease score.

The endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) are bioactive lipids derived from the n-6 family of polyunsaturated fatty acids that are essential fatty acids. Symptoms of essential fatty acid deficiency in rats - growth retardation, scaly skin, and increased transepidermal water loss.

Basal serum concentrations of AEA and 2-AG, but not PEA or OEA, were significantly reduced in women with major depression relative to matched controls, indicating a deficit in peripheral endocannabinoid activity.

These findings suggest that chronic inflammation might develop also because of endocannabinoid and palmitoylethanolamide tissue concentration impairment, the correction of which might be exploited to develop new anti-inflammatory drugs.

These results suggest that abnormal CB1 receptor-mediated anandamide signaling is implicated in the etiology of PTSD.

The discovery that mammal tissues express cannabinoid receptors was accompanied by the discovery of endogenous ligands to these receptors called endocannabinoids, which along with CB1 and CB2 constitute the endocannabinoid system. It was discovered that certain disorders cause the levels of endocannabinoids, the density of the cannabinoid receptors and the efficiency of the coupling of the cannabinoid receptors to increase. It has been noted that this upregulation of the endocannabinoid system often suppresses undesirable symptoms and signals, suggesting that the endocannabinoid system is autoregulatory.

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On the first scan, CB1 receptor binding was 20-30% lower in patients with alcohol dependence than in control subjects in all brain regions and was negatively correlated with years of alcohol abuse.


These results show a different modulation and functioning of the endocannabinoid system in ischemics compared with nonischemics.


The changes in the endocannabinoid system in ischemics may contribute to cardiac dysfunction and therefore represents a potential therapeutic target.


Low CB1 receptor expression was more frequently identified in stage IV than in stage I/II or III cancer


Among the various candidates, endocannabinoids (eCBs), and in particular anandamide (AEA), represent potential biomarkers of human fertility disturbances. Any perturbation of the balance between synthesis and degradation of eCBs will result in local changes of their tone in human female and male reproductive tracts


After abstinence, reduced CB1R [cannabinoid receptor 1] availability extended also to other areas such as the ventral striatum and mesotemporal lobe. In conclusion, whereas the acute alcohol effect is an increase in CB1R availability, chronic heavy drinking leads to reduced CB1R availability that is not reversible after 1 month of abstinence.


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Striatal cannabinoid CB1 receptor mRNA expression is decreased in the reserpine-treated rat model of Parkinson's disease.  

Changes in endocannabinoid transmission in the basal ganglia in a rat model of Huntington's disease.  

The inventive method relates to a method for the determination of susceptibility or diagnosis of autism or autism spectrum disorders. Diagnosis or determination of susceptibility determinations are predicated on quantitative analysis of endocannabinoid levels or endocannabinoid receptor expression.  
https://www.google.com/patents/US20120225015

One way of supplementing [endocannabinoids] EC to infants is via an infant formula which contains increased levels of endocannabinoids or endocannabinoid-promoting compounds. Such a formula may be useful to promote appetite and weight gain in infants.….  
….These results may indicate a direct effect of the CBl receptor antagonist on sucking-related nerves, and/or an effect on a digestive system-related mechanism. These tissues/organs were found to express CBl receptors. These findings imply that infants with failure-to-thrive as a result of a deficient endocannabinoid system, may be treated with peripherally acting food additives or medications...  
https://www.google.com/patents/WO2009044402A1

the invention relates to a method for determining the optimal time for implantation of an embryo in a mammalian endometrium comprising detecting the levels of an endocannabinoid in the early, mid and late stage of the menstrual cycle in a subject.  
https://www.google.com/patents/CA2707682A1

In particular, the invention relates to a method for diagnosing a threatened miscarriage, comprising detecting the level of an endocannabinoid in a body fluid sample from a subject mammal.  
https://www.google.com/patents/WO2009071950A1

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This study provides evidence that a tightly regulated endocannabinoid signaling is critical to **normal preimplantation embryo development and migration of trophoblast stem cells.**

[Re: Exercise] We show that eCB signaling is indeed intensity dependent, with significant changes in **circulating eCBs observed following moderate intensities**

**The changes of** anandamide [cannabinoid] and 2-AG [cannabinoid] contents in different stages of gliomas may qualify them as the potential endogenous biomarkers for **glial tumor malignancy.**

It is concluded that the prognostic value of endoglin as a marker of neovascularization in **prostate cancer** can be influenced by the expression level of markers of the endocannabinoid system.

Cannabinoid-receptor 1 null mice are susceptible to **neurofilament damage** and **caspase 3** activation

[Loss of CB1 receptors leads to decreased cathepsin D levels and accelerated lipofuscin accumulation in the hippocampus.] Early onset of age-related changes in the brain of cannabinoid 1 receptor knockout (Cnr1(-/-)) mice suggests that cannabinoid 1 (CB1) receptor activity significantly influences the progression of brain aging.

recent evidence suggests that changes in endocannabinoid system could be involved in some **actions of antidepressants**

**krill oil** (KO), more efficiently than fish oil, was able to downregulate the endocannabinoid system

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Expression of spontaneous nicotine withdrawal was accompanied by fluctuation in levels of the endocannabinoid anandamide (AEA).

The dysbalance between [Endocannabinoid System] ECs and adipocytokines appears to be an important determinant of coronary circulatory function in obesity.

Altered endocannabinoid signalling after a high-fat diet in Apoe(-/-) mice: relevance to adipose tissue inflammation, hepatic steatosis and insulin resistance.

AEA-mediated activation of CB₁ receptors is crucial for social interaction, and that PCP-induced social withdrawal results from deficient endocannabinoid transmission.

Acute alcohol exposure in rats (8% ethanol in the liquid diet for a period of 24 h) is associated with a decrease in the levels of endocannabinoids in different brain regions.

AEA levels were significantly lower when compared to controls in both perigenual anterior cingulate (p=0.017) and frontal cortices (p=0.018) of type 1 alcoholics.

Significant alterations of a balance in the cannabinoid system between the levels of endogenous ligands and their receptors occur during malignant transformation in various types of cancer, including gliomas.

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..whereas lack of [Cannabinoid receptor 2] CB2 in HSCs promotes fibrosis...

Blocking the postpartum mouse dam's [Cannabinoid receptor 1] CB1 receptors impairs maternal behavior as well as offspring development and their adult social-emotional behavior.

...suggesting that the decline in cognitive functions is accelerated in the absence of CB1 receptors. This rapid decline in CB1-deficient animals is accompanied by a loss of neurons in the CA1 and CA3 regions of the hippocampus.

Alterations of the endocannabinoid system may constitute an important factor in the aetiology of certain neuropsychiatric disorders, and, in turn, enhancers of endocannabinoid signaling could represent a potential therapeutical tool in the treatment of both anxiety and depressive symptoms.

The results revealed that the lack of cannabinoid CB1 receptors increased the severity of motor impairment and DA lesion, and reduced L-DOPA-induced dyskinesias.

The reduced expression of CB1 in the older obese may be an attempt to reduce lipogenesis to avoid greater insulin resistance.

Dysregulation of the endocannabinoid system (ECS) is a universal and, perhaps, causative feature of obesity.

Finally, clinical studies support and confirm the obtained findings in animal models and lead us to propose that mice lacking CB1 cannabinoid receptor could represent a
validate and appropriate model to evaluate depressive-like disorders in animals. 

These data show a tightly regulated influence of the ECS on impulsive behaviors and suggest the involvement of endocannabinoid signaling in the pathophysiological modulation of ADHD and related disorders. 

Multiple sleep alterations in mice lacking cannabinoid type 1 receptors. 

[neurodegenerative disease] Our data therefore represent an example of an inherited disorder related to endocannabinoid metabolism. 

Changes in the endocannabinoid system may give insight into new and effective treatments for cancer. 

Accumulating evidence indicate that the endocannabinoid system is dysregulated in prostate cancer, suggesting that it has a role in prostate homeostasis. 

… “our findings indicate that [Cannabinoid Receptor 1] CB1 deficiency enhances the circadian HPA axis activity peak and leads to central impairment of glucocorticoid feedback, thus further outlining the essential role of the endocannabinoid system in the modulation of neuroendocrine functions." 

[Endocannabinoid System]….disruption of this fine regulation might cause different skin diseases, such as acne, seborrhoea, allergic dermatitis, itch, psoriasis and hair follicle regression (catagen) 

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Altered expression of the CB1 cannabinoid receptor in the triple transgenic mouse model of *Alzheimer's disease*.

Deficiency of cannabinoid receptor of type 2 *worsens renal functional* and structural abnormalities in streptozotocin-induced diabetic mice.

Endocannabinoid receptor deficiency *affects maternal care* and alters the dam's hippocampal oxytocin receptor and brain-derived neurotrophic factor expression.

“...highly stressed individuals with severe motion sickness had an absent [Endocannabinoid] EC response”

Reductions in circulating endocannabinoid levels in individuals with post-traumatic stress disorder following exposure to the World Trade Center attacks.

The dual effect of cannabinoid receptor-1 deficiency on the murine postoperative ileus.

Cannabinoid receptor 1 deficiency in a mouse model of *Alzheimer's disease* leads to enhanced cognitive impairment despite of a reduction in amyloid deposition.

CB1 cannabinoid receptor-mediated aggressive behavior.

Genetic background modifies the effects of type 2 cannabinoid receptor deficiency on bone mass and bone turnover.

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Modulation of strain-specific differences in gene expression by cannabinoid type 2 receptor deficiency.

Deficiency of CB1 receptor signaling is associated with anhedonia, anxiety, and persistence of negative memories.

Cannabinoid (CB2) receptor deficiency reduces the susceptibility of macrophages to oxidized LDL/oxysterol-induced apoptosis (regulates plaque build-up)
http://www.jlr.org/content/49/11/2338.short

Cardiorespiratory regulation and protect from some adverse cardiovascular consequences

CB2-deficient mice have a markedly accelerated age-related trabecular bone loss and cortical expansion

Chronic Heart Failure:

Age-Dependent Cognitive decline

CB1 Receptor Deficiency inhibits new blood vessel growth

Deficiency of CB2 cannabinoid receptor in mice improves insulin sensitivity but increases food intake and obesity with age.

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Deficiency in endocannabinoid signaling in the nucleus accumbens induced by **chronic unpredictable stress**.

Mice Lacking CB1-CB2 receptors both show **inflammatory responses in colon**

CB1 deficiency altering normal progesterone and estrogen levels induces **preterm birth in mice**.

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**Please note**: there are many synthetic (man-made) cannabinoids out there.. the definitions will help you get through some of the research easier.

**Definitions**: [http://goo.gl/TG7qqX](http://goo.gl/TG7qqX)

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**Numerous interviews and more research can be found here**: researchECS.com

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Questions, corrections, or additions please email backblastareaclear@gmail.com

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