Medical Cannabis : A Possible Treatment For ADD / ADHD

Patients review

Version #1. Oct 2008

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N. Robert

Table of Content

ADD/ADHD-Autistic Spectrum Disorders (ASD) : Complex Neuro-immune Disorders ...

Genetic Neurological predisposition :

- Dysfunctional dopaminergic system
- Abnormal inhibition modulation **
- Probable Abnormal neuro-transmetters levels
- Possible Endocannabinoids receptors (CB1*, CB2, …) deficiencies / possible endocannabinoids excess (2-AG)

Immune HYPER-SENSITIVITY (Metabolism & Environment):

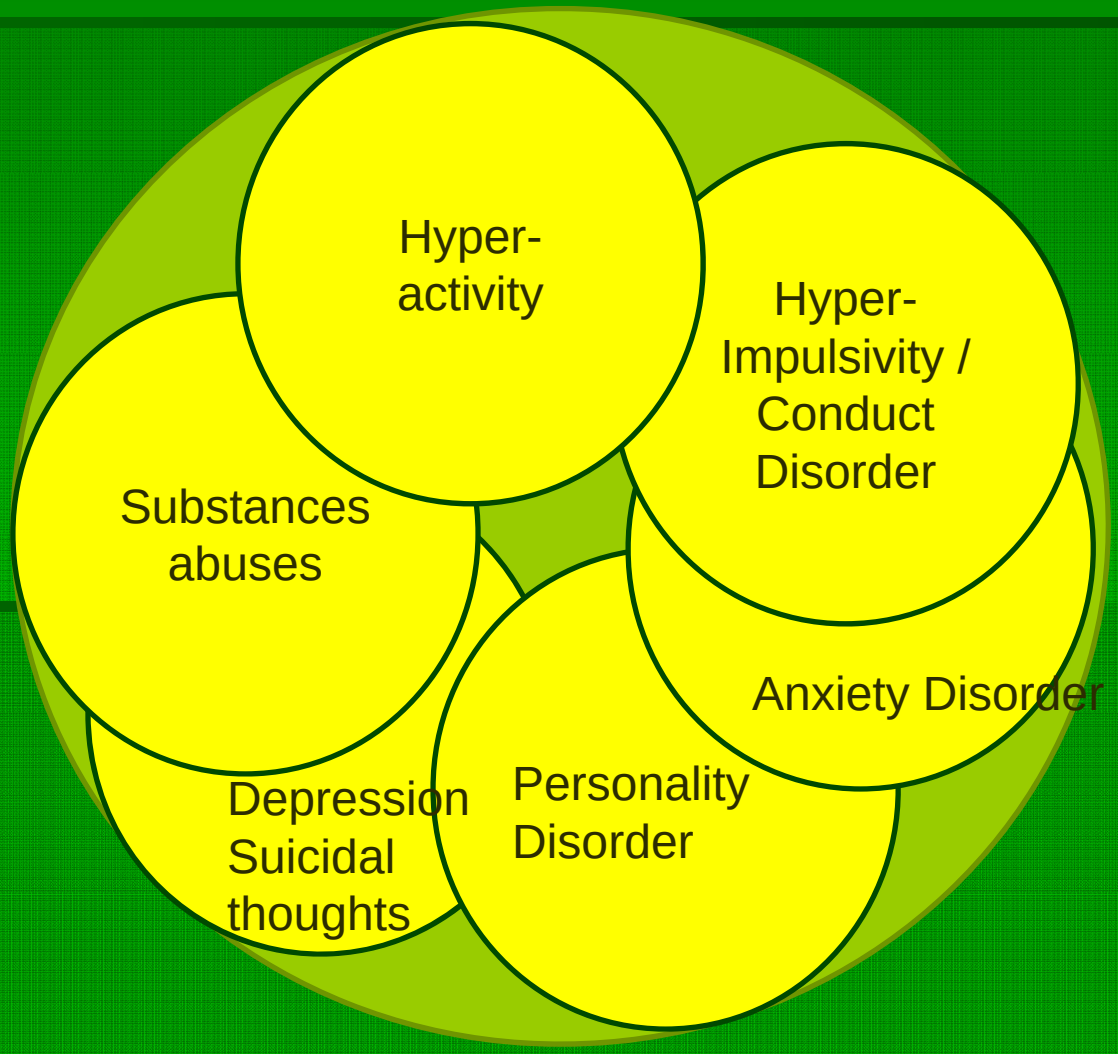
-Food intake deficiencies : Omega 3, vitamins, amino-acid (Creatine related)
-Food intoxication (gluten, casein, phosphates) due to metabolism deficiency
-Brain inflammations due to immune over-reaction (cytokinic storm / mother Hg intoxication)
-Alcoholic intoxication / brain inflammation

Emotional HYPER-SENSITIVITY :

-Low SELF-esteem
-Fears / « toxic » conditioning
-Traumatic events in childhood (divorce, death, molestations, rape…)
-Associated PTSD
- Defective emotional learning process
-Abnormal de-conditioning process

•Ref : « The spontaneous hypertensive-rat as an animal model of ADHD : evidence for impulsive and non-impulsive subpopulations », W Adriani, A Capriolo, O Granstrem, M Carli, G Laviola, Neurosc. Bio. Rev. Vol 27 (7), Nov 2003, 639-651.
* *Ref : « Abnormal latent inhibition and impulsivity in coloma mice, a model of ADHD », K J Bruno, C S Freet, R C Twining, K Egami, S Grigson, E J Hess, Neurobiol. Dis. 2007 Jan; 25(1) : 206-216

… Leading to Complex Chronic Symptoms



Chronic Symptoms

- **Hyper-Impulsivity :** vandalism in youth, 3 apartments destruction / 1 hospitalization for hand injury (windows breaking) / 1 psychiatric hospitalization (1 week) / 2 serious fight including had bone break and 5 chess bones broken. Symptom : adrenaline shoots, violence crisis (with loss of control) under white strong alcohol.
- **Hyper-Anxiety :** acute chronic onychophagia (finger nails eating) since childhood , intestinal pains due to over-anxiety and stress, fears of transportations, fears of audience.
- **Mood Disorder :** dysphoria, instinctive tendency to see everything black, light depression, suicidal ideations since childhood (12 years old). LOW SELF.
- **Chronic Alcoholism*** : many period under alcoholism (student, army, after divorce) leading to catastrophic violent events, specially under strong white alcohol (1 hospitalization in 2005 / 1 week).
- **Lack of attention** : incapacity to listen when speaking, need a lot of concentration to read, read slowly, a lot of mistakes in French writing, bad capacity.
- **Low self-esteem.**
- **PARADOXAL REACTION TO BENZODIAZEPINE.**

* Genetic predisposition in the family (mother-tree) / many alcoholism and similar behaviors.

Main Treatments

Regular treatments

- **Omega 3** daily intake : 2-3 g / day (hemp oil, colza oil & nuts oil in salad or by spoon) → reduction of impulsivity and chronic onychophagia.
- **Bedrocan®** treatment under medical prescription : approx 100/150 mg Dronabinol (THC) / day → improvement of attention / reduction of impulsivity
- **Bediol®** (6% Dronabinol 7.5% Cannabidiol CBD) → reduction of anxiety, intestinal pains, chronic prostatite.

Additional complements

- Hemp tea (industrial hemp) or caps.
- Ginger caps, tea, food → improve tonicity / attention
- Ginkgo caps → improve attention a lot.
- Amino Acid (Arginine or body-building proteins) → tonicity.

Additional supports

- 4 years FREUDIAN psycho-analysis : 2004-2008
- Regular sport activity (1-3 times / week)
- Regular sexual activity

A Tri-modal Medical Approach

Genetic Neurological predisposition

1-NEUROLOGY
- MPH / Amphetamine
- Cannabinoids

Immune HYPER-SENSITIVITY

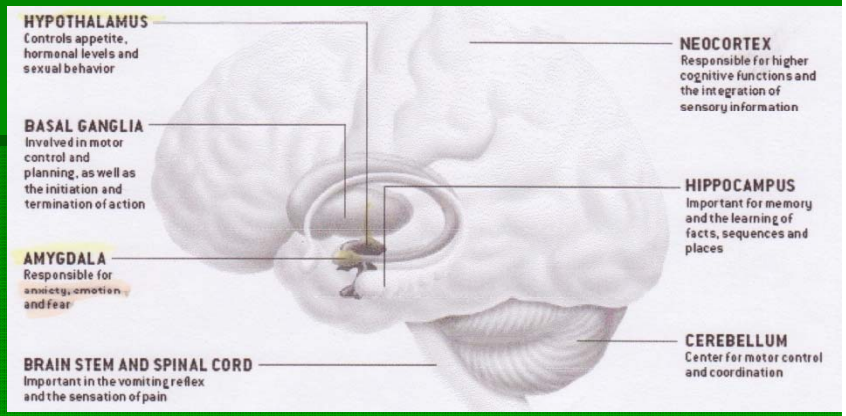
3-ENVIRONMENTAL MEDECINE
- Suppression of toxins in food intakes (caseine from milk, Gluten, food additives,…)
- Nutrition complements: vitamins, omega 3, Amino-acid, ginkgo, ginger
- Moderation of alcohol intake
- Sex / Sport / Music / ….

Emotional HYPER-SENSITIVITY

2-PSYCHIATRY

Deconditioning / Reconditioning by
- Behavioral therapy
- Psychological support
- Freudian psycho-analysis

ADD/ADHD Neurological Dysfunctioning



- Under-stimulated brain (helped by all psycho-stimulant drugs : nicotine, cafeine, amphetamine, cocaine, ….)
- Dysfunctional dopaminergic system :
  - Area : Limbic system / Amygdala-Hyppocampus (part of the mid-brain related to emotions, memory and motivation)
  - Low level of dopamine (free dopamine) ?
  - Too much or/and not enough dopamine transporters or/and neurotransmitters ?
  - Lack or deficiency of neuro-receptors / Lack of serotonin transmitters.
- <u>Under-stimulation of the retrograde inhibitory neurons / Lack of CB1 (ADHD animal model / SRH rats) :</u>

Ref : « The spontaneous hypertensive-rat as an animal model of ADHD : evidence for impulsive and non-impulsive subpopulations », W Adriani, A Capriolo, O Granstrem, M Carli, G Laviola, Neurosc. Bio. Rev. Vol 27 (7), Nov 2003, 639-651.

Science: ADHD and post-traumatic stress disorder
Californian researchers observed an association between variants of the gene that codes the cannabinoid-1 receptor with attention deficit hyperactivity disorder (ADHD) and post traumatic stress disorder. (Source: Lu AT, et al. Am J Med Genet B Neuropsychiatr Genet 2008 Jan 22 [Electronic publication ahead of print])

ADD/ADHD Neurological Dysfunctioning ... Some Paradoxes

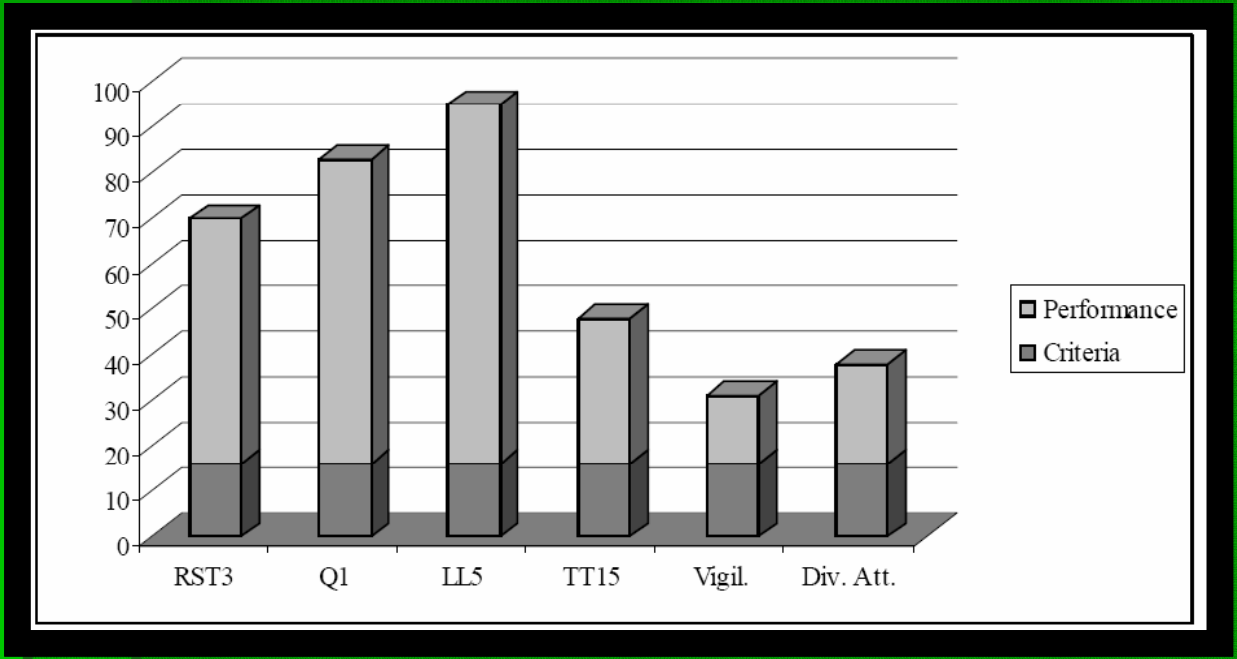
- Paradox reaction to methylphenidate.
- Possible paradox reaction to benzodiazepine (Nico and Ludo case)
- Possible catastrophic reaction to alcohol (catastrophic des-inibhition / Ludo case)
- Paradox reaction to cannabinoïds (attention and mental health) *

Ref : Cannabis Improves Symptoms of ADHD
Peter Strohbeck-Kuehner, Gisela Skopp, Rainer Mattern
2007Archiv fuer Kriminologie 220: 11-19.
(Institute of Legal- and Traffic Medicine, Heidelberg University Medical Centre, Germany).

Different psychological effects of cannabis use in adolescents at genetic high risk for schizophrenia and with Attention Deficit Disorder / Hyperactivity disorder (ADHD)
C Hollis and al.
Schizophr. Res. (2008)

Cannabinoids, Attention and Driving ... Paradox Reaction Report

- A clinical case report a paradox driving performance of a ADHD patient under cannabis :



ART2020 computerized driving skills test
RST3 : Complex reactions
Q1 : Sustained attention
LL5 : Directed attention
TT15 : Visual surveying and perception

TAP Test
Vigilance
Divided Attention

Ref : Cannabis improves symptoms of ADHD
Peter Strohbeck-Kuehner, Gisela Skopp, Rainer Mattern
2007Archiv fuer Kriminologie 220: 11-19.
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Involvement of Endocannabinoids System (ECS) in Synaptic Plasticity and Emotional Responses *

- Many studies on animals (mice, rats) in pharmacology, genetic, immunology and other fields confirm the central role of the ECS in synaptic plasticity. ECS is acting directly on the emotional short and long terms responses .
- ECS : Inhibitory modulator (attenuation) of neuron transmission (brain activity)
- ECS : inhibitory modulator of neuronal, behavioral and adrenocortical responses to stressful stimuli.
- ECS's CB1 receptor are located in large quantities in the Amygdala, Hippocampus and Cortex, which are directly involved in emotional learning and behavior.
- Proven implication of ECS in synaptic plasticity, related to anxiety, fears depression, impulsivity.
- Many neuropsychiatric disorders concerned : Autism, PTSD, depression, ADD/ADHD, anxiety disorders, personality disorders, bipolar, …

* Ref : « Endocannabinoids System and Synaptic Plasticity : Implication for Emotional Responses », MP Viveros, EM Marco, R Llorence, M Lopez-Gallardo, Neural Plast. 2007

•« Retrograde Signaling in the Regulation of Synaptic Transmission : Focus on endocannabinoids », B E Alger, Prog. in Neuro. Vol. 68 (4), 247-286, Nov. 2002.

• « The Brain's Own Marijuana », R A Nicoll, B N Alger, Scientific American Magazine, Dec 2004.

• « Circuitry foe associative plasticity in the amygdala involves endocannabinoids signaling », S C Azad, K Monory, G Marsicano, B F Cravatt, B Lutz, W Zieglglansberger, G Rammes, J. Neurosci., Nov 2004; 24(44): 9953-9961.

Involvement of ECS in Emotional Learning (Hyper-Anxiety)

- Studies on animal models :
  - CB1 KO-mutant mice exhibit pathological fears after conditioning and abnormal deconditioning process.

    Ref : « Cannabinoid CB1 Receptor Mediates Fear Extinction via Habituation-Like Processes », K Kamprath, G Marsicano, J Tang, K Monory, T Bisogno, V Di Marzo, B Tutz, C T Wotjak, The journ. Neur., June 21, 2006, 26(25):6677-6686.
  - CB1-deficient mice conditioned fears don't extinct :

    Ref : « The endogenous cannabinoid system controls extinction of aversive memories », G Marsicano, C T Wojtak, S C Azad, T Bisogno, G Rammes, M G Cascio, H Mermann, J Tang, C Hofmann, W Zleglgansberger, V Di Marzo, B Lutz, Nature, Vol 418, aug 2002.

    Ref : « Never fear, cannabinoids are here », P Sah, Nature, Vol. 418, Auf 2002.
  - Also on rats :

    Ref : « Enhancing Cannabinoid Neurotransmission Augments the Extinction of Conditioned Fear », J P Chhatwal, M Davis, K A Maguschak, K J Ressler, Neuropsychopharmacology (2005) 30, 516-524.
- ECS implication in anxiety : CB1receptors mediate neurotransmitters degradation enzyme FAAH.

  Ref : « Reduced anxiety-like behavior induced by genetic and pharmacological inhibition of the endocannabinoid-degrading enzyme fatty acid amide hydrolase (FAAH) is mediated by CB1 receptors, F A Moreira, N Kaiser, K Monory, B Lutz, Neuropharmacology 54 (2008) 141-150.

Involvement of ECS in Impulsive Behaviors.

- Studies on impulsive SRH rats (ADHD animal model proven CB1 deficient) :

Science: Cannabinoids effective in animal model of hyperactivity disorder

Attention-deficit hyperactivity disorder (ADHD) is a neuropsychiatric syndrome, affecting human infants and adolescents. The syndrome is characterised by impaired attention and by impulsive-hyperactive behaviour. Italian researchers studied ADHD in an animal model, using the spontaneously hypertensive-rat (SHR) strain, which is regarded as an animal model for ADHD.

The SHR rats were compared to normal rats. In tests it appeared that there is a subgroup within the SHR rats which reacted very impulsive. Researchers found that animals of this impulsive SHR subgroup presented a reduced density of CB1 cannabinoid receptors in the prefrontal cortex of the brain. The administration of a synthetic cannabinoid that – like THC – binds to the CB1 receptor normalized the impulsive behavioural profile in this subgroup of SHR rats, but had no effect on normal rats.

Until now there is no clinical research with cannabis or single cannabinoids in ADHD but several patients report positive effects. Additionally, a clinical study on THC in Tourette's syndrome demonstrated an improvement of obsessive compulsive behaviour.

(Source: Adriani W, et al. The spontaneously hypertensive-rat as an animal model of ADHD: evidence for impulsive and non-impulsive subpopulations. Neurosci Biobehav Rev 2003;27(7):639-51)

- Studies on Coloma mice (another ADHD animal model) : mice exhibit abnormal latent inhibition and impulsivity :

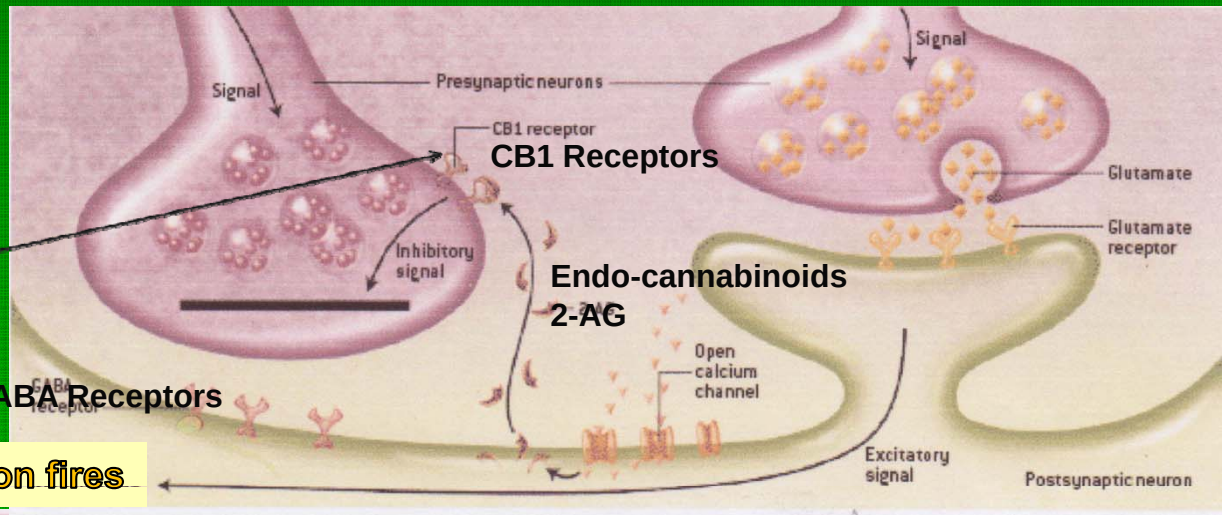
« Abnormal latent inhibition and impulsivity in coloma mice, a model of ADHD », K J Bruno, C S Freet, R C Twining, K Egami, S Grigson, E J Hess, Neurobiol. Dis. 2007 Jan; 25(1) : 206-216

ECS Implication in Neuronal Activity Regulation : Retrograde Signaling in the Inhibitory Neurons

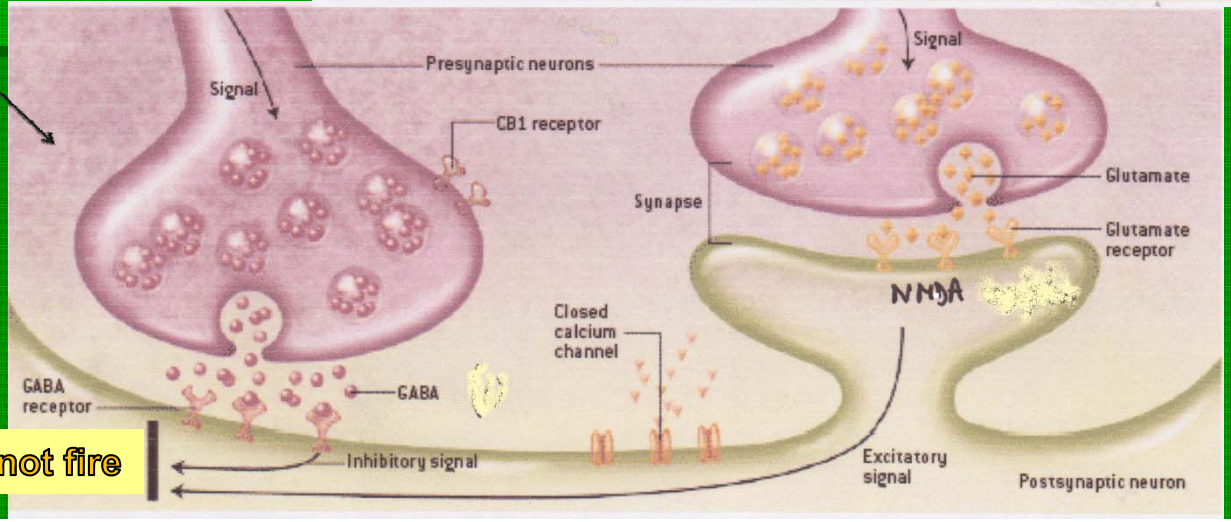
Inhibitory Neuron

Excitory Neuron

CB1 RECEPTOR
Regulate neuro-transmission.
Dronabinol / THC acts
By :
-protecting CB1 receptors from excessive 2-AG
-Stimulate inhibitory neurons (serotonin + enzyme FAAH)



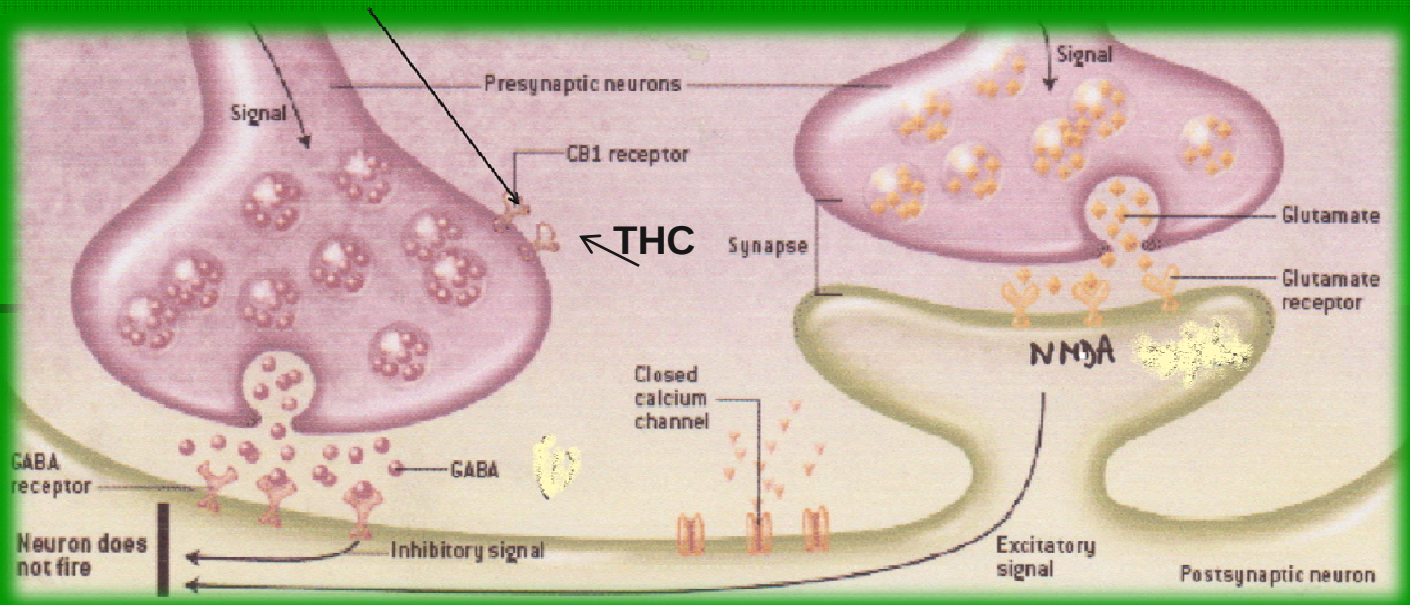
Neuron fires



Neuron does not fire

Cannabinoids Action : Inhibitory Neurons Stimulation / Protection

-Stimulation of CB1 receptors by THC (dronabinol) and/or other cannabinoids.
-Neuro-protection of CB1 from excessive 2-AG neuro-transmitters
-Stimulation of FAAH (fatty acid amine hydrolase) enzyme
-Stimulation of Serotonin release?



… Leading to less neurotransmission, less impulsivity, less hyper-activity, less uncontrolled ideas and slower brain speed.

Cannabinoids Action : Inhibitory Neurons Stimulation / Protection

Endocannabinoids cause synaptic inhibition, making neurons inhibited more difficult to fire

Phyto-cannabinoids mimic endocannabinoids effects :

- cause release of dopamine
- trigger inhibitory stimulation
- may slow neurotransmission speed
- allows persons to focus due to fewer thoughts in transmitted to cortex
- decreases emotional excitability
- decreases impulsivity

ECS and the Neuroimmune Network

- Central Nervous System (CNS) and Immune system are integrated and form an interdependent neuroimmune network
  (http://www.copewithcytokines.de/cope.cgi?key=Neuroimmune%20network)
- Brain functions as an immune organ.
  Ref : « Neurochemistry of brain neuroendocrine immune system : signal molecules », A Galoyan, Neurochemical Research 25(9-10):1343-1355 (2000).
- Emotional events / trauma may induce neuronal inflammation by pro-inflammatory cytokines in sensitive ADD/ADHD.
  (http://www.ecu.edu/physio/labakm/cytokine.htm)
- Immune system is involved in many psychiatric pathogenesis : Epilepsy, Multiple sclerosis, Alzheimer Disease, Parkinson Disease Autism, ASD Autistic Spectrum Disorder … ADD/ADHD.
  Ref : « Epilepsy and the Immune System », J A Aarli, Arch. Neurol. 2000; 57:1689-1692.
  « Role of cytokines in neurological disorders », A Aarli, Curr. Med. Chem., 2003 (10):1931-1937.
  « Connecting cytokines and brain : a review of current issues », N Quan, M Herkenham, Histol. Histopathol (2002) 17:273-288.
  « T. Hypothesis : Infection, antibiotics, vaccination-induced neuropathies : Mechanisms of pathogenesis in some cases of autism, ADHD, Tourette's, OCD, and other neurological disorders », Binstock, Bit.listserv.autism Jan 1997.

Myriads of clinical studies on the ECS suggest that it is participating directly to the Neuroimmune Network.

Involvement of ECS in Brain Inflammation / Neuro-Protection

CLINICAL STUDIES

- Receptors CB1 and CB2 are involved in the modulation of inflammatory expressions of chemokines and cytokines in brain microglia → ECS plays a role in the protection of brain inflammation and defense against excito-toxicity.

  Ref : « Cannabinoid receptors in microglia of the central nervous system : immune functional relevance »

  G. A. Cabral and F. Marciano-Cabral, Journ. Leuk. Bio., Vol. 78, Dec 2005, 1192-1197.

  « CB1 cannabinoid receptors and on-demand defense against excitotoxicity », G Marsicano, S Goodeenough, K Monory, H Hermann, M Eder, A Cannich, S C Azad, G G Cascio, S O Gutierrez, M Van Der Stelt, M M Lopez-Rodriguez, E Casanova, G Schutz, W Zieglgansberger, V Di Marzo, C Behl, B Lutz, Science, Oct. 2003, 302.

- Brain Post-mortem examination : CB2 receptor may play an important role during pathophysiological events.

  Ref : « Cannabinoid CB2 receptors are expressed by perivascular microglial cells in the human brain : an immunohistochemical study », E Nunez, C Benito, MR Pazos, A Barbachano, O Jajardo, S Gonzalez, RM Tolon, J Romero, Synapse, 2004 Sept.; 53 (4) : 208-213.

- Extreme brain inflammation case / neurotoxicity (cytokine storm): Autist / ELOI (Nico's Son)

  Ref : « Chronic Microglial Activation and Excitotoxicity Secondary to Excessive Immune Stimulation : Possible Factors in Gulf War Syndrome and Autism » Russell L. Blaylock, Journ. Amer. Phys. And Surgeons, Vol. 9 (2), Summer 2004, 46-51.

Involvement of ECS in Brain Inflammation / Neuro-Protection

CLINICAL STUDIES

- CB2 receptors are over-expressed in Alzheimer's Disease Brains → potentially directly involved in the inflammatory modulation process of the Glia.

  Ref : « Cannabinoid CB2 Receptors and Fatty Acid Amide Hydrolase Are Slectively Overespressed in Neuritic Plaque-Associated Glia in Alzheimer's Disease Brains », C Benito, E Nunez, R M Tolon, E J Carrier, A Rabano, C J Hillard, J Romero, The Journ. Of Neuroscience, Dec 2003, 23(35) : 11136-11141.

- Phytocannabinoid CBD protects neurons against Prion toxicity.

  Ref : « Nonpsychoactive Cannabidiol Prevents Prion Accumulation and Protects Neurons against Prion Toxicity », S Dirikoc, S A Priola, M Marella, N Zsurger, J Chabry, The Journ. Of Neuroscience, Sept. 2007, 27(36) : 9537-9544.

Involvement of ECS in Cells Inflammatory Responses

- Study on mice :
  - Endocannabinoids receptors CB2 and its ligand 2-AG play a crucial role in inflammatory reactions.

Ref : « Evidence of the involvement of the Cannabinoid CB2 Receptor and its endogenous Ligand 2-Arachidonoylglycerol in 12-O-Tetradecanoylphorbol-13-acetate-induced Acute Inflammation in Mouse Ear », S Oka, S Yanagimoto, S Ikeda, M Gokoh, S Kishimoto, K Waku, Y Ishima, T Sugiura, The journ. Of Biol. Chem., 2005, Vol. 280(18), 18488-18497.

« An endogenous cannabnoid tone attenuates cholera toxin-induced fluid accumulation in mice », A A Izzo, F Capasso, A Costagliola, T Bisogno, G Marsicano, A Ligresti, I Matias, R Capasso, L Pinto, F Borrelli, A Cecio, B Lutz, N Mascolo, V di Marzo, Gastroenterology, Spet. 2003, 125(3), 765-774.

  - Endocannabinoids are involved in colonic inflammations / CB1 receptors deficiency.

Ref : « The endogenous cannabinoid system protects against colonic inflammation », F Massa, G Marsicano, H Mermann, A Cannich, K Monory, B F Cravatt, GL Ferry, A Sibaev, M Storr, B Lutz, J. Clin; Invest. Apr 2004, 113 (8), 1202-1209.

- CB2 receptor deficiency is a possible cause of autoimmune reactions and environment hyper-sensitivity (metabolism disorders).

Ref : « Reduced endocannabinoid immune modulation by a common cannabinoid 2 (CB2) receptor gene polymorphism : possible risk for autoimmune disorders », JC Sipe, N Arbour, A Gerber, E Beutler, J. Leuk. Biol., 2005 jul., 78(1):231-238.

« 2-arachidonoylglycerol induces the migration of HL-60 cells differentiated into macrophage-like cells and human peripheral blood monocytes through the cannabinoid CB2 receptor-dependent mechanism », S Kishimoto, M Gokoh, M Muramatsu, T Kajiwara, K Waku, T Sugiura, J. Biol. Chem. 2003 Jul; 278 (27):24469-24475.

« Cannabidiol, extracted from cannabis Sativa, selectively inhibits inflammatory hypermotility in mice », R Capasso, F Borelli, G Aviello, B Romano, C Scalisi, F Capasso, A A Izzo, Br .J. Pharmacol. 2008 May 12.

Involvement of the ECS in Mood Disorders / Depression / Personality Disorders

- Cannabinoids improves the global emotional learning/deconditioning process, fear extinction, … leading to a stabilization of the mood in many neuropsychiatric disorder (anxiety, bipolar, schizophrenia, ….).

- Cannabidiol is proven to be an efficient antipsychotic drug (alternative treatment).

  Ref : « Cannabidiol, a Cannabis sativa constituent, as an antipsychotic drug », Braz. J. Med. Biol. Res., 2006 Apr; 39(4):421-9.

- Clinical study : endocannabinoid receptor CB1 may be involved in depression.

  Ref : « antidepressant-like behavioral effects of impaired cannabinoid receptor type 1 signaling coincide with exaggerated corticosterone secretionin mice.

  "Treating depression with cannabinoids", Kurt Blass, Cannabinoids 2008;3(2):8-10

Medical Cannabis, Freudian Psycho-Analysis And SELF Re-building ... Experience of a Patient

- ADD/ADHD are emotionally hyper-sensitive, subject to multiple micro-traumas, from childhood to adulthood.
- LOW SELF ESTEEM
- Excessive « toxic » conditioning / excitotoxicity due to excessive discharge of emotional activity.
- ECS is involved in emotional learning process (see slides 10-11)

Cannabinoids can help in the deconditioning process
(personal experience / 4 years psycho-analysis)

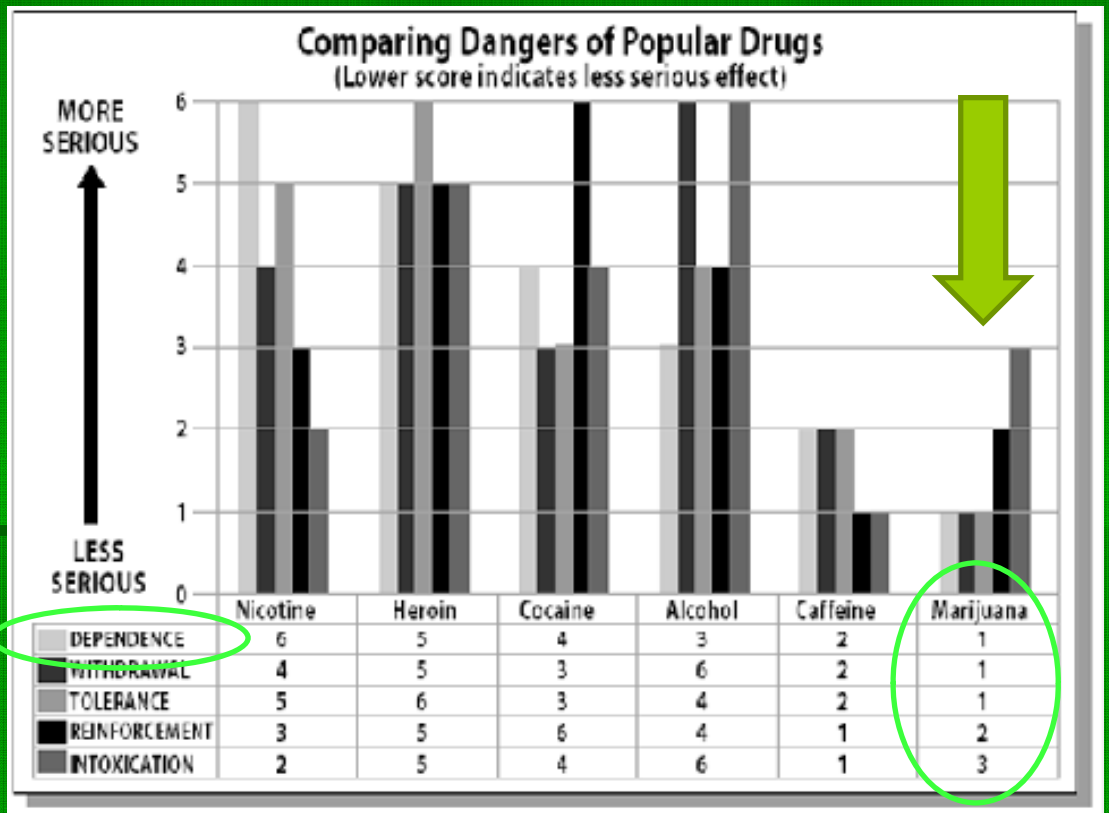
Medical Cannabis and Chronic Alcoholism

- A large number of ADD/ADHD are subject to chronic alcoholism … leading to dangerous consequences for the patient (brain intoxication, possible inflammation / increase inhibition dangerously through Calcium channel opening and endocannabinoids 2-AG generation in synaptic connections → violence/impulsivity crisis risks).
- Alcohol = brain poison.
- Risks : environment (family alcoholism, legal situation of alcohol, acceptance in Occidental cultures)
- Clinical study on mice : CB2 receptor deficiency is a risk factor for alcoholism → targeting CB2 prevents alcoholism.

Ref : « Involvement of cannabinoid CB2 receptor in alcohol preferences in mice ans alcoholism in humans », H Ishiguro, S Iwasaki, L Teasenfitz, S Higuchi, Y Horiuchi, T Saito, T Arinami, ES Onaivi, Pharmacogenomics J. 2007 Dec, 7(6):380-385.

MEDICAL CANNABIS CAN BE EFFICIENT IN PREVENTING ADD/ADHD CHRONIC ALCOHOLISM RISKS

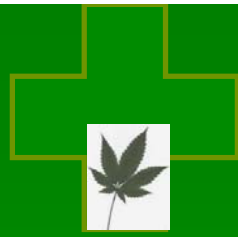
Comparing Dangers of Popular Drugs



	Nicotine	Heroin	Cocaine	Alcohol	Caffeine	Marijuana
DEPENDENCE	6	5	4	3	2	1
WITHDRAWAL	4	5	3	6	2	1
TOLERANCE	5	6	3	4	2	1
REINFORCEMENT	3	5	6	4	1	2
INTOXICATION	2	5	4	6	1	3

Source: Dr. Jack E. Henningfield, Ph.D. for NIDA. Reported by: Philip J. Hilts, New York Times, Aug. 2, 1994 "Is Nicotine Addictive? It Depends on Whose Criteria You Use."

Medical Cannabis and Dependence



- From a scientific point of view, cannabis is the less dangerous drug and less hazardous than legal products (tobacco, alcohol).
- Patients therapeutic benefits are often hidden in the name of an illegal drug dependency.

Would a patient be considered addicted to a product if this product was its only cure for pains ?

Situation in North America : Another Approach

- In 2008, Medical Cannabis is available for ADD/ADHD treatment in Canada and 13 US States (California, Oregon, ….).
- California : Medical Cannabis is available since 1996. Since that time, more that **350 000** Californians have received physician approval to use cannabis in treating a wide range of conditions, including ADD/ADHD and other neuro-psychiatric disorders.
- 2002 AAMC Poll (Ref : Jay R. Caranaugh, *Medical Cannabis and Brain Disorders,* http://www.letfreedomgrow.com/articles/poll021120.htm) :

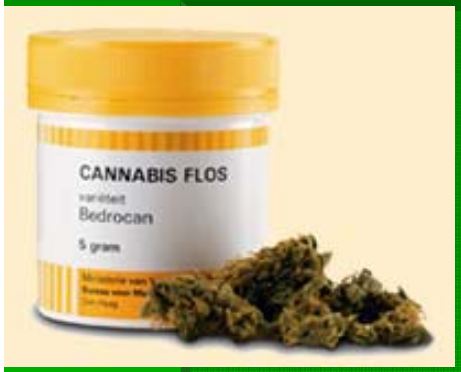
Conditions / Disorders	% of the poll
Bipolar	20 %
ADD/ADHD	13%
PTSD	7%
OCD / Tourette	6%
Autism	2%
=	48 %

Situation in North America : Another Approach

- In Canada and some US States (13) Patient access is controlled by authorized Compassion Center (medical diagnose checked under medical authority).
- A growing number of US physicians prescribe medical cannabis to treat adult ADD/ADHD.
- Arguments in favor of medical cannabis (view by US Physicians) : safe, non –toxic, well tolerated by many patients, few side effects, cheap.
- Medical Cannabis approved by medical experts :
  - Dr Lester Grinspoon, Emeritus professor of Psychiatry at Harvard Medical School. (http://www.rxmarijuana.com)
  - Dr Tom O'Connell : 1118 patient report on cannabis use on anxiety (http://www.ccrmg.org/journal/05spr/anxiety.html)
  - Dr David Bearman : http://video.google.com/videoplay?docid=-1820696077430281885

  http://davidbearmanmd.com/publications.htm#ADHD
  - * Dr Jeffrey Hergenrather: http://hempworld.com/HempPharm/articles/jeffhergenrather.html

Situation in Europe : The Netherlands Exception ...



- 3 Medical Cannabis grades available under prescription in Dutch pharmacies since 2005 :
  - Bedrocan ® : 18% Dronabinol (THC)
  - Bedrobinol ® : 11% Dronabinol
  - Bediol ® : 6% Dronabinol / 7,5% Cannabidiol (CBD)
- Growing tolerance from European judges, in various countries, concerning patients using medical cannabis for personal therapeutic purposes.
- Growing number of acquitted patients in the last years : Spain, Austria, UK, Czech. One running trial in Finland.

Conclusions and Perspectives

- Studies on animal models confirm the implication of the Endocannabinoids System ECS in the ADD/ADHD/ASD neuropsychiatric disorders and chronic symptoms associated (fears, anxiety, impulsivity).
- In 2008, 2 clinical studies on ADHD patient relate new "unexpected" experimental data.
- Positive effects of cannabis on ADD/ADHD/ASD patients behaviors and experiences (retrograde signaling in the inhibitory neurons) is scientifically understood . Cannabinoids can reduce varieties of ADHD symptoms by less Hyperactivity / Impulsivity, less « rushing » brain activity (relaxation), less Anxiety , better attention / focus, less subject to substances abuses (alcohol, tobacco, …).
- Medical Cannabis is experienced as an alternative treatment to Methylphenidate (MPH) in Canada and some US states since years.
- Dependence : cannabis is proven to be the less dangerous drug, based on scientific studies. Patients are often considered as dependent whereas they get an important therapeutic benefit from cannabinoids.
- Perspectives : advances in immunology allows to measure precisely the immune system reactions. Cytotest ® (leucocytes level s measurement,) used to identify food intolerances, opens new potential studies to evaluate efficiency of the cannabinoids.

Videos on The Web

- ECS Video Animations :
  http://www.endocannabinoid.net/VideoAnimation.aspx
- Dr Bearman / Conference :
  http://video.google.com/videoplay?docid=-1820696077430281885
- Dr Grinspoon / Harvard Medical School :
  http://www.youtube.com/watch?v=VVADnBB96Ww
- US TV :
  http://www.youtube.com/watch?v=yj72e5q61Fs
  http://www.youtube.com/watch?v=uHWaU3FYPg4

Annex

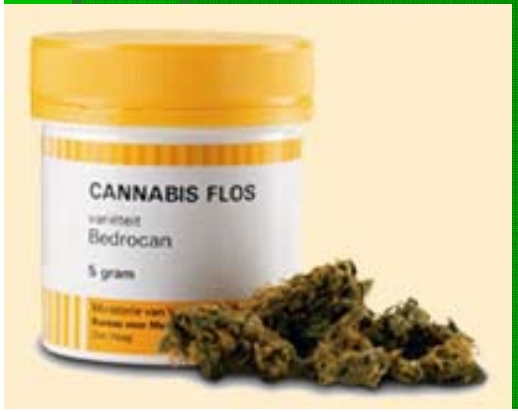
HOW TO USE MEDICAL CANNABIS?

- Vaporization : the most efficicient way (no combustion products like carbon monoxyde / temperature > 190°C)

- Incorporation in food :
  - Butter
  - Cookies / cakes / chocolate cream
  - Caps
  - Tea




- Incorporation in cigarettes (smoked) : very efficient but hazardous combustion products (CO) associated



Depending on ….

- The required chemical compounds (<u>natural phytocannabinoids need to be decarboxylated to be absorbed by the human system</u>)
- Disorders / diseases / troubles to threat
- The individual needs and reactions
- The patient history (addictions)