

## Medicinal Cannabis: How Cannabinoids Can Help Treating ADHD?

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This work is a review of the **Endocannabinoid System** (ECS) implication in ADHD. It reports two European cases, sample of the growing number of Medicinal Cannabis (MC) recommended/prescribed for the treatment of ADHD cases.

Scientific studies have demonstrated a relation between cannabinoid receptors (CB1, CB2), endocannabinoids (Anandamide, 2-Arachidonylglycerol), the **Central Nervous System** and the **Neuro-immune System**<sup>12</sup>. CB1 receptors, abundant in the brain, interact with the **Dopaminergic System**<sup>34567</sup>. Genetic studies found a correlation between Cannabinoids Receptors Gene and ADHD<sup>8</sup>. Regarding behaviour, CB1 are possible targets to reduce hyper-impulsivity<sup>910</sup>, Tourette Syndrome tics<sup>11</sup>, fears<sup>1213</sup>, anxiety<sup>1415</sup> and improve emotional learning (synaptic plasticity<sup>16</sup>) and distractibility<sup>1718</sup>. The neuro-chemical mechanism of action is **Retrograde Signaling Inhibition**<sup>19</sup>. This is dopamine mediated. An increase in unbound cannabinoid levels leads to cannabinoids replacing dopamine bound to dopamine transporters binding sites. With more dopamine available to slow down the speed of neurotransmission there are fewer, slower moving neural inputs and the cerebral cortex has a better opportunity to focus and attend to the neural stimulation.

Cannabinoids are accepted by many cannabinoid medicine specialists for treating ADHD. Two patients, from **Luxembourg** (52, retired policeman) and **France** (35, engineer), had the opportunity to experiment MC therapy with Dutch products<sup>20</sup>, available in pharmacies since 2005. Both report an improvement of their condition and chronic symptoms (distractibility, agitation, alcoholism, depression, anxiety, obsessive/suicide thoughts), without unacceptable side effects. CBD, no-psychoactive cannabidiol, was found necessary to reduce anxiety and adverse dronabinol effects<sup>21</sup> (**dronabinol/CBD ratio: 1/1-3/1**). MC therapy was considered complementary to psychotherapy. Both clinical experience, particularly in California, and scientific data suggest that targeting ECS with exocannabinoids is an exciting new alternative to treat ADHD. Many doctors, who have experience with patients, recommend cannabinoids for ADHD<sup>22</sup>. **Further clinical studies** are required to investigate this new field.

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<sup>3</sup> *Cannabinoid CB1 Receptor-mediated Modulation of Evoked Dopamine Release and of Adenylyl Cyclase Activity in the Human Neocortex*, Steffens et. al., British Journal of Pharmacology (2004) 141, 1193-1203

<sup>4</sup> *Cannabinoids and Schizophrenia : Where Is The Link ?*, K. Müller-Vahl, Cannabinoids 2008;3(4):11-15

<sup>5</sup> *D2, but not D1, Dopamine Receptor Agonists Potentiate Cannabinoid-Induced Sedation in Non Human Primates*, P. Meschler et. al., The Journal of Pharmacology and Experimental Therapeutics, Vol. 292 (2000), N°3 952-959

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<sup>9</sup> *The Neuropharmacology of Impulsive Behaviour*, T. Pattij et. al., Trends in Pharmacological Sciences Vol.29 N°4 (Special issue : Pharmacology in The Netherlands) 192-199

<sup>10</sup> *The Spontaneous Hypertensive Rat (SRH) as an Animal Model of ADHD: Evidence for Impulsive and non-Impulsive Subpopulation*, Adriani et. Al., Neuroscience and Behavioral Reviews, Vol 27, Issue 7, Nov 2003, 639-651

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<sup>12</sup> *Cannabinoid CB1 Receptor Mediates Fear Extinction via Habituation Like Processes*, Kamprath et. al., The Journal of Neuroscience, June 21, 2006, 26(25):6677-6686

<sup>13</sup> *Enhancing Cannabinoid Neurotransmission Augments the Extinction of Conditioned Fear*, Chhatwal et. al., Neuropsychopharmacology (2005) 30, 516-524

<sup>14</sup> *Modulation of Anxiety-like Behavior Induced by Genetic and Pharmacological Inhibition of the Endocannabinoid-degrading Enzyme Fatty Acid Amide Hydrolase (FAAH) is Mediated by CB1 Receptors*, Moreira et. al., neuropharmacology 54 (2008) 141-150

<sup>15</sup> *Modulation of Anxiety Through Blockage of Anandamide Hydrolysis*, D. Piomelli et. al., Nat Med. 2003 Jan;9(1):76-81

<sup>16</sup> *Endocannabinoid System and Synaptic Plasticity: Implication for the Emotional Response*, Viveros et. al., Neural Plasticity Volume 2007 (2007)

<sup>17</sup> *Cannabis Improves Symptoms of ADHD*, Strohbeck-Kuehner et. al., Cannabinoids 2008;3(1):1-3

<sup>18</sup> *Different Psychological Effects of Cannabis Use in Adolescence at Genetic Risk for Schizophrenia and with ADHD*, Hollis et. al., Schizophrenia Research, Vol. 105, Issue 1, 216-223

<sup>19</sup> *Endogenous Cannabinoids Mediate Retrograde Signalling at Hippocampal Synapses*, Nicoll et. al., Nature 2001, vol. 410, n°6828, pp. 588-592

<sup>20</sup> *BedrocanBV Medicinal Cannabis products* : Bedrocan® (18% dronabinol / THC), Bedrobinol® (11% dronabinol), Bediol® (6% dronabinol, 7,5% cannabidiol CBD) – <http://www.bedrocan.nl>

<sup>21</sup> *A Tale of Two Cannabinoids: The Therapeutic Rationale for Combining Tétrahydrocannabinol (THC) and Cannabidiol (CBD)*, Russo et. al., Medical Hypotheses (2006) 66, 234-246

<sup>22</sup> *Dr Jensen testimony at the US Representative Mark Souder Holds Hearing on Medical Marijuana – Committee Hearing – 1 april 2004 /*

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