The science of cultivating happiness: role of (endo) cannabinoids

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**Abstract:** The role of the endocannabinoid system (ECS) in human physiology is well documented and scientifically supported. There is a large body of evidence that the endocannabinoids regulate mood, emotion, motivation, memory, pleasure perception, appetite, metabolism and more. The connection between cannabinoids and emotional states has long been empirically and scientifically established. Even the first discovered active constituent of the hemp plant *Cannabis sativa*, delta9-tetrahydrocannabinol (delta9-THC) has been known to produce euphoria and enhancement of sensory perception, among other effects.

Since the discovery and characterization of cannabinoid receptors, the abundance of these receptors in the brain has puzzled scientists. It seemed unusual that our cells would be so fine tuned to these relatively rare molecules found primarily in one genus of the plant kingdom. The discovery of arachidonylethanolamide (AEA), a THC analog, later named anandamide, gave insight into a new class of signaling molecules, the endocannabinoids. Until this discovery serotonin and endorphins were thought to be the “happy molecules”, known for their implicit role in regulating and manipulating emotional states, but the discovery of endocannabinoids has pointed to novel biochemical pathways to happiness. The name anandamide itself (ananda - the Sanskrit word for “joy, bliss, happiness”) suggests its involvement in mood. Recent research also suggests a strong link between serotonergic and endocannabinoid systems, implicating a connection between the release of endocannabinoids and serotonin (Best and Regehr, 2008). Indeed, cannabinoid receptors appear as heteromer receptors with serotonin, dopamine, adenosine, and opioid receptors throughout the brain, indicating significant communication between these different chemical signaling systems (Ferre et al, 2009; Vinals et al, 2015).

Current findings demonstrate an important role of endocannabinoid signaling in stress responses, where endocannabinoids have been found to modulate different components of the adrenocortical response to stressor exposure. Is has been shown that chronic stress downregulates ECS and induces depression like symptoms, presumably through a combination of reduced endocannabinoid expression and reduced CB1 receptor expression. Endocannabinoids as well as exogenous cannabinoids modulate activation of various neuronal circuits involved in neuroendocrine stress processing including the major neuroendocrine stress response system in mammals, the hypothalamic-pituitary-adrenocortical (HPA) axis. The effects of stress are different in different regions of the brain but chronic unpredictable stress has been shown to significantly downregulate the ECS of hedonic brain hotspots (Wang et al, 2015).

New evidence suggests that mood disorders, such as chronic depression and schizophrenia, may be linked to immune system dysregulation and inappropriate inflammatory cytokine release (Fernandez-Egea et al, 2016; Anisman et al, 2008). The ECS modulates cytokine release primarily via CB2 receptors located on a variety of immune system cell types as well as numerous other cell and tissue types throughout the body (Pacher and Mechoulam, 2011). Through immune system manipulation and cytoprotective free radical scavenging, both endogenous and exogenous cannabinoids may modulate emotional states in a less obvious manner deserving our attention (Panikashvili et al, 2006; Hampson et al, 1998).

Since we are currently facing ever increasing incidences of depression, anxiety and other mood disorders, research focusing on the connection of the endoconnabinoid system and emotional states is of utter importance. There are two aspects of positive emotional states, one temporary (hedonia) and one static (eudaimonia) (Berridge at al, 2011). While hedonia is largely influenced by circumstances and acute environmental cues, eudaimonia is a measurement of the level of one’s satisfaction with life as a subjective assessment of life lived well. The ECS has been shown to be involved in both aspects, by positively modulating the sensitivity to positive stimuli and acting like a buffer system that dampens negative emotions (Matsunaga et al, 2014).

Research has provided us with overwhelming amount of data regarding our ECS. Data show that different pharmaceutical drugs affect the endocannabinoid system, with acute and chronic exposure having very different effects in the ECS. Even paracetamol, fever and pain medication we give to our children, blocks the breakdown of anandamide, thereby affecting our ECS (Dania et al, 2007). ECS signaling disruption via chronic acetaminophen administration may even cause autism spectrum disorder symptoms in children (Schultz, 2010). Recent research even suggests that genes coding for cannabinoid receptors have a strong role in the level of happiness we experience and the magnitude of our response to positive stimuli (Matsunaga et al, 2014).

The very foods we choose to eat, the supplements (probiotics, omega 3 fatty acids) we take, and the variety of meals and drinks consumed over time have an effect on the level endocannabinoids and cannabinoid receptors that the human body can produce. Even the ambiance of meals makes a difference (Schrieks et al, 2015). The foods and pharmaceuticals that we consume affect anabolic and catabolic enzymes responsible for building and degrading both endogenous and exogenous cannabinoid compounds (McPartland et al, 2014). Some foods such as extra virgin olive oil contain phenolic compounds which may encourage enhanced expression of cannabinoid receptors (Di Francesco et al, 2015). Massage and aerobic exercise have been shown to increase the levels of endocannabinoids. Even acupuncture and fasting modulate the ECS (McPartland et al, 2014).

The means of pursuing happiness are as individual as our ECS. Our perception and emotional evaluation of our environment determine to a large degree our physiological reactions. The same circumstances that may be calming to some may be stressful for others. But the underlying biochemistry of happiness remains the same, with endocannabinoids and the ECS playing a pivotal role in long term well-being of all individuals. In this case, ignorance is no longer bliss.

In light of thousands of citizens worldwide still being arrested every year just for the simple act of using an herb containing cannabinoids to feel better or happier, we should ask ourselves if ignoring the potential of these molecules is not a greater crime. With the pressures of modern society growing, our ECS being exposed to more challenges than ever (stress, environmental toxins, endocrine disruptors, microbial threats, etc…), our basic human right to be healthy is in serious danger. With the overwhelming worldwide evidence where prohibition has brought us we come to the conclusion that: **Bliss is not the problem ~ ignorance is.**

**Key words:** endocannabinoid system, anandamide, 2-arachidonoyl glycerol, 2-AG, cannabinoid receptors, phytocannabinoids, happiness, CB1, CB2, stress, hedonia, eudaimonia, Cannabis sativa, delta-9-tetrahydrocannabinol, THC, Cannabidiol, CBD

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