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CANNABINOID CHRONICLES

Medical Cannabis News and Information

Parkinson's Disease and Medical Cannabis

Parkinson's disease (PD) is a progressive degenerative nerve disease that is caused by the death of dopaminergic neurons (central nervous system cells that produce the neurotransmitter dopamine) within a small region of the brain called the substantia nigra. The substantia nigra plays an important role in regulating physical movement such that early PD symptoms include tremors, rigidity, slowness of movement and difficulty with walking and gait. Later, thinking and behavioral problems may arise, with dementia commonly occurring in the advanced stages of the disease; depression is the most common psychiatric symptom. Other symptoms include sensory, sleep and emotional problems.

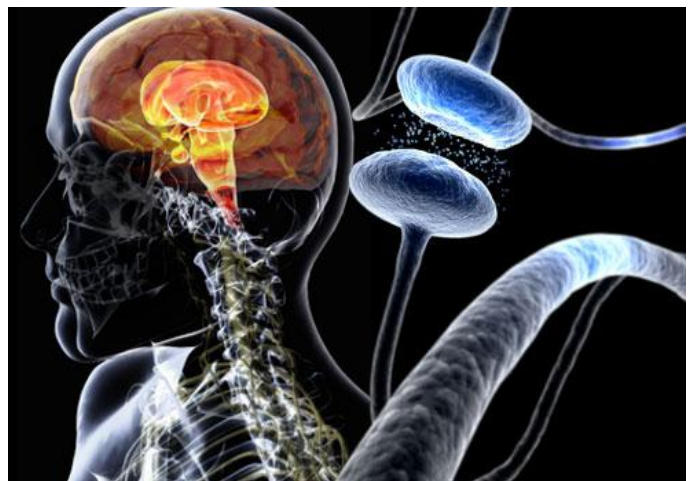
Parkinson's disease is more common in older people, with most cases occurring after the age of 50. The cause of dopaminergic neuron death is presently unknown although there is speculation of several mechanisms that may be responsible. A small proportion of cases, however, can be attributed to known genetic factors. Other factors have been associated with the risk of developing PD, but no causal relationships have been proven.

There are no known cures - current treatments are primarily pharmacological, using the drugs levodopa (or other dopamine agonists) and carbidopa. The former is converted to dopamine in the brain and the latter prevents levodopa from being broken down before reaching the brain. Levodopa can cause a variety of side effects, one of which is quite serious called dyskinesia (difficulty in performing voluntary movements). Because PD can result in a myriad of symptoms, various drugs are used in tandem to try to counter these issues.

The effectiveness of cannabis on PD is inconclusive at the moment but several surveys and observational studies

show promise. According to a study (Mar/Apr 2014) in *Clinical Neuropharmacology* (<http://www.ncbi.nlm.nih.gov/pubmed/24614667>) participants using smoked medical cannabis had significant improvements in motor disability and impairment. These results were found in addition to reported decreases in tremor, rigidity, and dyskinesia, and improvements in pain and sleep disturbance. This study was flawed in that it included only 22 participants, there was no blinding to treatment (i.e. both the participants and researchers knew that they were using cannabis, which means that the results were potentially a result of "expectancy effects"), and they used a "within-subjects" design, which has well-documented weaknesses.

Another study from Sept. 2014 published in the *Journal of Psychopharmacology* (<http://www.ncbi.nlm.nih.gov/pubmed/25237116>) found that treatment with 300 mg/day of the cannabinoid cannabidiol (CBD) in patients with PD, without dementia or comorbid psychiatric conditions (i.e. those occurring at the same time as the primary disease), increased well-being and quality of life compared to patients who had received the placebo. However, there was no improvement in measures of motor (i.e. movement) andsee page 4



International Association for Cannabinoid Medicines (IACM) Bulletin

Daily cannabis use by adolescents and adults is not associated with reduced brain mass

Daily cannabis use is not associated with brain shrinkage when controlling for the effects of alcohol consumption on those who both drink and smoke cannabis, a new study led by neuroscientists at the University of Colorado at Boulder. Dr Kent Hutchison, the senior author of the study, said his team reviewed a number of scientific papers that showed cannabis causes different parts of the brain to shrink, and his team found the studies were not consistent.

“So far, there's not a lot of evidence to suggest that you have these gross volume changes” in the brain, Hutchison said in an interview. In particular, his study examined a publication released last year by researchers at Northwestern University that identified changes to the nucleus accumbens and the nucleus amygdale (regions of the brain that are key to regulating emotion and motivation) in cannabis users who smoke one to seven cannabis cigarettes a week. Hutchison's team tried to replicate those results by recruiting dozens of adults and adolescents and conducting brain imaging on them, and comparing daily cannabis users to non-users. But he said they took a different approach to rule out the effects of alcohol. “We found no evidence of differences in volumes of the accumbens, amygdala, hippocampus or cerebellum between daily versus non-users, in adults or adolescents,” Hutchison's paper said.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25632127>

Association between psychosis and cannabis may in part be based on alcohol use

In a prospective study with 341 subjects with a high risk for the development of psychosis researchers found that cannabis use was associated with a higher risk of psychosis, but this effect was partly mediated by the concurrent use of alcohol. Researchers wrote that “results highlight the need to control for other substance use, so as to not overstate the cannabis/psychosis connection.”

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25572323>

Cannabis use was associated with a decreased risk of bladder cancer

In a study with 84,170 men aged 45-69 years the use of cannabis was associated with a 45% reduction in bladder cancer incidence, while tobacco use was associated with a 52% increase of cancer risk. Authors concluded that “cannabis use may be inversely associated with bladder cancer risk in this population.”

Kaiser Permanente Los Angeles Medical Center, USA.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25623697>

CBD in combination with another substance improved anti-cancer effects of CBD in glioblastoma

A sub-population of glioblastoma cells (an aggressive brain tumour), glioma stem cells, is specifically endowed to resist or adapt to the standard therapies, leading to therapeutic resistance. Researchers investigated mechanisms underlying glioma stem cell resistance to cannabidiol (CBD). Combining CBD treatment with the inhibition of the so-called system Xc resulted in robust anti-tumour effects, that is, decreased glioma stem cell survival.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25590811>

CBD reduced inflammation in an animal model of multiple sclerosis

Treatment with either CBD (cannabidiol) or PEA (palmitoylethanolamide, an endogenous fatty acid amide) in a mouse model of multiple sclerosis reduced the severity of the disease, accompanied by diminished inflammation. However, the combination of CBD and PEA was less effective than either drug alone.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25637488>

Endocannabinoids relax smooth muscle cells of blood vessels

Research with parts of the aorta of mice and rats demonstrates that the constrictions of blood vessels caused by certain receptors (GPCRs) is attenuated by the formation of the endocannabinoid 2-arachidonoylglycerol (2-AG). Authors concluded that “endocannabinoid release has a therapeutic potential in case of increased vascular tone and hypertension.”

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25595485>

Endocannabinoids kill prostate cancer cells

The endocannabinoids 2-AG (2-arachidonoyl glycerol) and a synthetic analogue of anandamide, methanandamide, induced programmed cell death in prostate cancer cells.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25545857>

Peripheral activation of the CB1 receptor reduces bowel motility

A synthetic cannabinoid (AM841), which activates CB1 receptors, but does not penetrate into the brain, reduces bowel motility through an action on CB1 receptors in the small and large intestine. Authors concluded that this cannabinoid “represents a new class of potential therapeutic agents for the treatment of functional GI [gastrointestinal] disorders.” Cumming School of Medicine, University of Calgary.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25572435>

For more info visit: www.cannabis-med.org/

Colorado Children's Hospital to Conduct 3-Year Study on Cannabis for Epilepsy

Starting in spring 2015, Dr. Kelly Knupp, a pediatric epilepsy specialist, will be heading a 3-year, \$500,000 observational study at Children's Hospital in Aurora, Colorado. With a growing number of families claiming that cannabinoid-based medicines have reduced epileptic seizures in children, families are moving to cannabis-friendly states in order to access cannabis legally.

Currently, there are around 250 children with medical cannabis cards who have Dravet's Syndrome in the state of Colorado. Out of these 250 children, over 100 of them are patients at Children's Hospital, even though the hospital is not legally permitted to administer cannabis as a form of treatment.

Knupp and her colleagues will be using the \$500,000 state-funded grant in order to conduct the observational study. The study is going to consist of analyzing the results from 150 medical marijuana patients who consume cannabis products regularly to reduce or relieve their most serious side effects.

Source: <http://www.medicaljane.com/2015/01/23/childrens-hospital-in-colorado-to-conduct-3-year-study-on-cannabis-for-epilepsy/>

Significant Link Between Cannabis Use and Onset of Mania Symptoms

In a paper published in the *Journal of Affective Disorders*, mental health researchers from Warwick Medical School carried out a review of scientific literature examining the effect of cannabis use. The literature sampled 2,391 individuals who had experienced mania symptoms.

Lead author Dr. Steven Marwaha said the review suggested that cannabis use significantly worsened mania symptoms in people who had previously been diagnosed with bipolar disorder.

Source: www.sciencedaily.com/releases/2015/02/150210160101.htm

US Academy of Pediatrics: Cannabis Has Medical Value for Some Children

The American Academy of Pediatrics is requesting that the US Drug Enforcement Administration (DEA) reclassify cannabis as a less harmful substance, from Schedule I to II or III, in order to facilitate research of the substance for medical use. It recommends decriminalizing cannabis and says it recognizes that children with some diseases could benefit from cannabis. Cannabis has been in Schedule I since 1970, classified as having no medicinal value and a high potential for abuse. Researchers have suggested that this classification has set cannabis research back years.

Source: http://www.huffingtonpost.com/2015/01/26/pediatricians-call-on-dea_n_6550486.html

Moderate Lifetime Cannabis Smoking Linked to Airway Irritation But Not Lung Function

A 2014 research study based on analysis of publicly available data has found that recent cannabis use was associated with symptoms of airway inflammation, but that moderate lifetime use was not associated with clinically significant changes in measures of lung function. The study is the largest cross-sectional analysis of the relationship between cannabis use and measures of lung health to date.

Researchers at Emory University analyzed data from the 2007-2010 National Health and Nutrition Examination Survey (NHANES). The NHANES conducts high quality, standardized spirometry to measure lung function through recording the volume of air a person can force out of his or her lungs (forced vital capacity, or FVC) and the volume of air forced out in the first second of the maneuver (forced expiratory volume, or FEV1).

In the nearly 3,000 adult participants with data regarding patterns of lifetime cannabis use, cumulative exposure of less than 20 joint-years (one joint year = smoking an average of one joint per day for a year) was not associated with deleterious changes in lung function, as measured by the FVC and FEV1. Greater than 20 joint-years of exposure, however, was associated with measurable and clinically significant changes in lung function, but the changes displayed a different pattern than those observed in obstructive lung disease from tobacco use and are of uncertain clinical significance to overall lung health, according to the researchers.


"While over 20 joint-years is significantly associated with a change in lung function, it is inconclusive whether or not this represents early lung function impairment similar to long-term tobacco use," says lead author Jordan A. Kempker, MD, MSc. These results may also be due to a relatively low amount of smoke exposure in cannabis smokers compared to tobacco smokers, Kempker explains.

"Furthermore, smoking marijuana seems to increase symptoms of respiratory irritation, such as bronchitis, and our study was inconclusive about whether those effects are permanent. We also did not study the association of marijuana smoking with the development of cancer," says Kempker. The authors conclude: "With current marijuana smokers reporting a mean joint-year exposure of 15.8 joint-years, these data represent important public health implications. With the shifting political climate in the U.S. these are important public health concerns that necessitate further inquiry into this growing field."

Source: www.sciencedaily.com/releases/2015/01/150128170201.htm AND <http://www.atsjournals.org/doi/abs/10.1513/AnnalsATS.201407-333OC>



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general symptoms, and no evidence for possible neuroprotective effects, and the sample size was small with only 21 participants.

According to a study published in *Journal of Neurology, Neurosurgery and Psychiatry* (<http://jnnp.bmj.com/content/84/11/e2.58.abstract>) in 2013, the cannabinoid THC also may prove useful in the treatment of PD by assisting in the prevention of damage caused by free radicals, and activating PPAR γ , a receptor whose stimulation leads to the formation of new mitochondria (the part of cells that produces energy).

To date, no large, placebo-controlled, randomized, double-blind clinical trials have been conducted on whole-plant cannabis and PD so there is no evidence to demonstrate that cannabis use improves symptoms or slows disease progression. However, there is a lot of evidence to support cannabis use for sleep disturbances or pain, and mounting evidence that cannabinoids can act as neuroprotective agents.

Dr. Okun (www.parkinson.org) states, "...though most available large studies have not shown a benefit, that does not mean that there will not be a benefit. Much more research will be needed to understand which patients, which symptoms, and how best to safely administer medical marijuana in Parkinson's disease, especially over the long-term."

Sources:

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Image courtesy:

http://img.webmd.com/dtmcms/live/webmd/consumer_assets/site_images/articles/health_tools/parkinsons_disease_overview_slideshow/3d4medical_rm_photo_of_parkinsons_disease_composite.jpg

**** April is Parkinson's Awareness Month ****

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"Peace we want because there is another war to fight against poverty, disease and ignorance."

-- Indira Gandhi (Indian politician, 1917-1984)