HABITUAL MARIJUANA USE AND THE PALEO DIET: WHAT A LONG STRANGE TRIP IT'S BEEN

Last month I had the pleasure to lecture on the Paleo Diet in Sydney, Australia at the BioCeuticals Research Symposium. After my presentation a couple who appeared to be in their late 40s to early 50s approached the podium. The man and his wife told me they had adopted the Paleo Diet a few years back and wondered if habitual marijuana smoking was aligned with Paleo. Both indicated they had been regular pot smokers for decades since their college undergraduate days. As I previously pointed out, humans have only recently (from an evolutionary perspective) acquired the technological sophistication to start fires at will. On a 24 hour clock representing the entire 2.5 million year Paleolithic era, humanity's ability to create fire first came into regular play somewhere between 48 and 36 minutes to midnight. Need I say more?

I am a child of the '60s. I came of age in southern California and northern Nevada when political, social and recreational drug standards were radically changing for many young people nationwide and for the US society as a whole. In high school and college during the '60s and early '70s, "the day," I participated on various athletic teams that required regular aerobic workouts, almost year round. Consequently, smoking anything (tobacco or dope) was completely out of the question for me. Every summer from my early 20s until I was 42, I worked as the Head Lifeguard on a major beach at Lake Tahoe, so my former aerobic workout ethic continued with me throughout my later life.

An almost universally accepted narcotic of "the day" was marijuana, dope or pot. Call it whatever you will, but this drug became emblematic of the "youth generation" who grew up during the '60s and early '70s. My generation is now approaching our retirement years, yet the legacy our age group created regarding recreational drug use lives on. So much so, that my generation and our children's generation and our grand children's generation have recently voted to legalize marijuana for recreational use in Colorado and Washington state. Additionally, if we look at national response to recreational drug use a little more than half the country's voters favor marijuana's legalization.

Nevertheless, marijuana has not been legally sanctioned for recreational use in the 48 other states, and remains the most widely used illicit drug in the US (16.7 million users during the past month).[1] The more important point of this statistic is that about 283 million Americans did not use marijuana in the past month. President Clinton claimed he never "inhaled" when smoking pot as a college student, whereas President Obama freely admitted to its use in his earlier years. Accordingly, marijuana is a drug which many if not most Americans have experimented with, particularly during their youth. Currently 43% of all high school seniors have tried pot,[2] and as many of you may have personally witnessed, marijuana is the most commonly used illicit drug on college campuses.[3]

In my blog and scientific writings, I can honestly say that I have never deliberately ventured into political or social commentary – and sorry – you won't get that perspective here either. However, I would like to remark upon the physiological ramifications of regular pot smoking or ingestion upon your health and well-being. All plant compounds (either smoked or ingested) entering our bodies on a regular basis, just like any other nutritional or dietary element, will have an effect upon our overall health. So, you be the judge, and let the data below speak for itself. In the final analysis, you (the learned reader) must decide the ultimate route that you will take for your health and well-being and that of your family.

PSYCHOLOGICAL EFFECTS

You don't have to be a scientist to understand why people smoke or ingest marijuana. For most people it produces a pleasurable "high" or euphoria. Most marijuana users know that the primary active compound in pot which elicits this narcotic drug's high is delta-9-tetrahydrocannabinol (THC). However, few pot smokers are aware that marijuana also contains over 60 related compounds called cannabinoids and more than 400 other chemicals including benzopyrene, a well-recognized carcinogen.[4]

When marijuana is smoked, THC quickly passes from the lungs to the bloodstream which then transports THC to the brain and all other organs of the body. Consumption of marijuana laced cookies, brownies or candies takes longer for the high to occur because marijuana must first be digested in the gastrointestinal tract and then absorbed before THC reaches the bloodstream. Whether pot is smoked or ingested, once THC reaches the brain it binds to specific molecular sites called cannabinoid receptors which in turn set off a series of biochemical reactions resulting in the high that users experience.[4] The greatest density of cannabinoid receptors occurs in areas of the brain that influence pleasure, memory, coordination, thinking, concentration and sensory and time perception.[5]

Predictably, acute THC intoxication is associated with impairment of cognitive function including: learning and memory, attention span, planning ability, organizational skills, problem solving, decision making, perception of facts, control of emotions and behavior[2, 4, 6, 7] and impairment of motor coordination.[2, 7, 8] Perhaps that's why even states like Colorado and Washington, which have legalized recreational marijuana use, still impose strict legal penalties for driving while high on pot, similar to the consequences of driving under the influence of alcohol. Two recent meta analyses (large, pooled, population studies) concluded that: ***"Acute cannabis consumption is associated with an increased risk of a motor vehicle crash, especially for fatal collisions,"***[9] **and** ***"The results of this meta-analysis suggest that marijuana use by drivers is associated with a significantly increased risk of being involved in motor vehicle crashes."***[10]

OK – so get stoned, but just don't drive while you are high and nobody is hurt, including yourself – but are you really? Are the effects of acute marijuana use only transitory or are there chronic, long-term effects of dope smoking which may adversely affect your health?

These potentially undesirable effects would be robustly predicted by the evolutionary medicine model: 1) introduce an evolutionarily novel agent into an organism's physiology that has been conditioned over eons of natural selection without it; 2) if the novel agent produces evolutionary discordance between the organism's genes and its environment, then 3) this discordance elicits increased morbidity (disease incidence), mortality (death) and reduced reproductive success. My mentor, Boyd Eaton coined the term, evolutionary discordance,[11] but it was Charles Darwin who first conceived of the most powerful idea in all of biology. Hence, evolution via natural selection is the organizational template for contemporary Paleo diets. This concept represents the evolutionary logic underlying the adverse health effects produced by recently introduced food staples (refined sugars, trans fats, vegetable oils, cereal grains, dairy products, salt and processed foods).

Why should recently introduced narcotic drugs affect our health in an evolutionary manner that varies fundamentally from recently introduced foods? Both items represent novel environmental factors in which our physiology and biochemical pathways have had little evolutionary experience to adapt to and both would be expected to cause evolutionary discordance, which in turn elicits increased morbidity and mortality and

hence reduced reproductive success. Natural selection then may respond to these changing environmental selective pressures by moving the organism's genome to a new set point, frequently resulting in a new species, or alternatively the species may become extinct.

Very few scientists studying narcotic drugs would argue that acute marijuana intoxication either via ingestion or smoking does not temporarily impair cognitive function in a variety of ways. The human experimental and epidemiological data outlined above is forceful, compelling and undeniable.[2, 4, 6, 7, 8] Less clear are the long-term behavioral and psychological changes which may occur from chronic marijuana use. Nevertheless a number of recent human meta-analyses support the notion that long term pot smoking fundamentally re-arranges brain structure in a manner that may in turn adversely influence cognitive function.

In a recent meta-analysis Rocchetti and colleagues reviewed 14 MRI studies examining how smoked marijuana affected the brains of healthy people without psychotic illness.[12] *"Our meta-analysis showed a consistently smaller hippocampus in users as compared to non-users. Our results suggest that in the healthy brain, chronic and long-term cannabis exposure may exert significant effects in brain areas enriched with cannabinoid receptors, such as the hippocampus, which could be related to a neurotoxic action."*

From this study, it cannot be determined if reductions in brain hippocampus size in pot smokers influences behavior or psychological factors on a long term basis.

Similar, but not as robust, results were reported in a meta-analysis by Dr. Lorenzetti and co-workers at the University of Melbourne.[13] They concluded that, *"Together, these structural imaging findings suggest that THC exposure does affect brain morphology, especially in medial-temporal regions."* Three years later in 2013 after reviewing the most recent literature,[14] Dr. Lorenzetti's research group came to a comparable conclusion: *"This review supports the notion that regular cannabis use is associated with alterations of brain morphology."* In a larger, recent meta-analysis involving both adults and adolescents, similar observations and conclusions were reached by yet another independent research group.[15]

An early study[16] by Dr. Lorenzetti and colleagues that concurrently measured brain hippocampal and amygdala volumes along with verbal learning ability and psychotic symptoms, concluded, *"These results provide new evidence of exposure-related structural abnormalities in the hippocampus and amygdala in long-term heavy cannabis users and corroborate similar findings in the animal literature. These findings indicate that heavy daily cannabis use across protracted periods exerts* ***harmful effects on brain tissue and mental health."***

One of the factors in this study which may not apply to casual pot smokers was that the subjects were "heavy" users, consuming more than five joints daily for more than 10 years. Clearly, these subjects maintained pot addictions that are not necessarily representative of recreational marijuana smokers.

Nevertheless, a just released cross sectional study in young, recreational, non-dependent, marijuana users revealed disruptions of normal anatomical brain structure in the amygdala and nucleus accumbens when compared to non-users (17). The shortcomings of this experiment and most other studies evaluating brain structural and functional changes in marijuana smokers is that they are cross sectional in nature – meaning that they view results at a single point in time. What are needed are experimental studies (randomized controlled trials [RCTs]) which randomly assign subjects to pot smoking and control groups and then compare pre-post intervention differences. RCT's on pot smoking will provide us with the definitive data we need to make informed decisions about marijuana's chronic effects upon brain function and mental health.

PSYCHOSES

When scientists do literature reviews on almost any topic, not all papers are in perfect agreement with one another and frequently yield vastly differing results and conclusions for a variety of reasons, usually involving experimental methodology. Hence to the casual reader of the scientific literature it is almost always possible to find a paper or two that conforms to your particular bias, but invariably you can also find a few which are inconsistent with your preconception. To overcome this potential prejudice, scientists have developed procedures which allow them to pool any and all individual experiments on a topic and statistically analyze the entire collective group as if it were one. This technique is called a **meta-analysis,** and represents a powerful statistical tool to make sense out of multiple studies with conflicting results. Notice that almost all studies I have cited previously regarding marijuana's adverse effects upon brain structure or function are either meta-analyses, or comprehensive reviews.

Now let's take a look at how pot smoking may adversely influence the mind, or our perceptions of reality. **"Psychoses" is a generic term referring to multiple abnormal mental conditions which frequently are characterized by "a loss of contact with reality."** You have probably heard of some of these psychoses which include: hallucinations, delusional beliefs [some may be paranoid], schizophrenia, severe depression, bipolar disorder (manic depression) and others.

The studies of marijuana use and psychoses below are all meta-analyses, and I have quoted the conclusion of each of these studies:

1. *"The results suggest that* ***the association between cannabis use and earlier onset of psychosis is robust*** *and is not the result either of tobacco smoking by cannabis using patients or the other potentially confounding factors we examined. This supports the hypothesis that,* ***in some patients, cannabis use plays a causal role in the development of schizophrenia*** *and raises the possibility of treating schizophrenia with new pharmacological treatments that have an affinity for endo-cannabinoid receptors."*[18]
2. "The results of meta-analysis provide evidence for a relationship between cannabis use and earlier onset of psychotic illness, and **they support the hypothesis that cannabis use plays a causal role in the development of psychosis in some patients. The results suggest the need for renewed warnings about the potentially harmful effects of cannabis."**[19]
3. "**Approximately every fourth schizophrenia patient in our sample of studies had a diagnosis of CUDs (cannabis use disorders).** CUDs were especially common in younger and first-episode patient samples as well as in samples with a high proportion of males."[20]
4. "The objective of this article was to examine whether cannabis use can be an independent risk factor for chronic psychotic disorders, by using established criteria of causality. **Data extracted from the selected studies showed that cannabis use may be an independent risk factor for the development of psychotic disorders.** Early screening of the vulnerability to psychotic disorder should permit improved focus on prevention and information about the specific risks related to cannabis use among this population."[21]
5. "On the basis of cohort studies that have been conducted within the last decades and recent meta-analyses **the hypothesized connection between cannabis use and psychotic disorders can be corroborated.** The risk to develop psychotic symptoms and also schizophrenic psychoses is thus explicitly elevated for young people who use cannabis."[22]

6. "**The evidence is consistent with the view that cannabis increases risk of psychotic outcomes independently of confounding and transient intoxication effects,** although evidence for affective outcomes is less strong. The uncertainty about whether cannabis causes psychosis is unlikely to be resolved by further longitudinal studies such as those reviewed here. **However, we conclude that there is now sufficient evidence to warn young people that using cannabis could increase their risk of developing a psychotic illness later in life.**"[23]
7. "**Early use of cannabis did appear to increase the risk of psychosis.** For psychotic symptoms, a dose-related effect of cannabis use was seen, with vulnerable groups including individuals who used cannabis during adolescence, those who had previously experienced psychotic symptoms, and those at high genetic risk of developing schizophrenia. **In conclusion, the available evidence supports the hypothesis that cannabis is an independent risk factor, both for psychosis and the development of psychotic symptoms.** Addressing cannabis use, particularly in vulnerable populations, is likely to have beneficial effects on psychiatric morbidity."[24]
8. "**Cannabis use, and particularly heavy cannabis use, may be associated with an increased risk for developing depressive disorders.** There is need for further longitudinal exploration of the association between cannabis use and developing depression, particularly taking into account cumulative exposure to cannabis and potentially significant confounding factors."[25]

PHYSIOLOGIC AND HEALTH EFFECTS

The mental, behavioral and psychological effects of marijuana use have received much interest in the scientific community over the past 20-30 years, however an equally important and nearly as extensive scientific literature exists regarding marijuana's effects upon other body organs, systems and tissues.

LUNG AND RESPIRATORY FUNCTION

For the past 40 years of my life, I have had the luxury of spending part of my summers on Lake Tahoe's pristine east shore. The high, alpine air here at 6,300 ft above sea level is nothing short of exhilarating and filled with therapeutic negative ions naturally generated near waterfalls and crashing waves. Each summer when I first arrive, I take in a deep breath of this magical elixir and contemplate Mark Twain's famous quote, *"Three months of camp life on Lake Tahoe would restore an Egyptian mummy to his pristine vigor."*

One unfortunate summer a number of years ago, northern California and Nevada had one of the worst wildfire seasons on record. The entire Tahoe basin was filled with smoke – our eyes reddened and watered, we coughed incessantly, our heads hurt and the alpine magic that once was, no longer existed. To my way of thinking I can't imagine how anyone would ever intentionally put their lungs and respiratory system into a smoky forest fire environment on a regular basis – yet that is exactly what pot smokers do.

Incinerated and inhaled marijuana, like tobacco contains a toxic combination of gases and other chemicals that can be injurious to the lungs and respiratory system.[26] The most recent reviews of habitual incinerated marijuana inhalation have concluded that it increases cough, sputum production, upper lung emphysematous changes, chronic bronchitis, and large airway inflammation.[27-29] Whether or not pot smoking initiates or promotes lung cancer has remained controversial[4, 27, 28] partially because few adequately powered (statistically), prospective epidemiological studies have ever been conducted. Recently, just such a study has been published in which "heavy" marijuana smokers (lifetime use of more than 50 joints) were followed for a 40 year period.[30] The results of the study showed a more than twofold risk of developing lung cancer even after statistical adjustment for tobacco and alcohol use.

CARDIOVASCULAR FUNCTION

In healthy, young adults the risk for fatal or serious health threatening events from cardiovascular disease (CVD) is low to non-existent, yet the medical literature reveals case study after case study of young marijuana smokers showing increased morbidity (disease incidence) from CVD and even fatal CVD events attributable to marijuana use.[31-38] Older pot smokers are also at an increased risk for CVD events including myocardial infarctions (heart attacks), sudden cardiac death, cardiomyopathy, stroke, transient ischemic attack, atrial fibrillation and arteritis.[4, 39-41]

SPORTS AND ATHLETIC FUNCTION

If you aspire to be a national or international caliber athlete, smoking pot is definitely something you don't want to do. Whether you are an Olympic, professional or college level athlete, you can be randomly tested for illicit drug use including marijuana. Testing positive can potentially ruin your athletic career from the sport's regulatory bodies and/or legal fallout. Marijuana has been on the International Olympic Committee's list of prohibited drugs since 1989.

More importantly, acute marijuana use reduces maximal exercise test duration and increases sub-maximal exercise heart rates.[4, 42] Both of these changes will impair acute aerobic exercise performance. The available evidence[43] suggests that habitual dope smoking will impair exercise training, which in turn will impair performance on race day.

IMMUNE FUNCTION

A recent paper[44] which compiled the results of 122 studies and 446 references concluded that, "*endocannabinoids* (the body's naturally produced cannabinoids) *enhanced immune response, whereas* ***exogenous cannabinoids (marijuana) had immune-suppressant effects***." It has been previously suggested that immune system impairment by marijuana use may increase infectious disease susceptibility.[45] Taken together**, this information suggests that habitual pot smoking likely increases the incidence of the common cold and its severity in a manner similar to smoking tobacco**.[46] For athletes, the greater the incidence and severity of the common cold, the greater your training intensity will be reduced, which in turn will reduce your performance on race day.[47]

DENTAL AND ORAL HEALTH

Habitual dope smokers are apt to have an increased prevalence of dental caries, oral infections, periodontal disease, mouth dryness, leukodemia (blue, grey or white appearance on the mouth's inside cheeks) and an increased prevalence of the fungus Candida albicans than non-smokers.[4, 48, 49] To say nothing of their foul breath.

PREGNANCY

If you are pregnant or nursing and regularly smoke pot, whether you know it or not, your unborn fetus or dependent nursing infant is also getting high with you, even if you are not high when you nurse. As a regular marijuana smoker, the primary psychoactive ingredient in pot (THC) does not simply exit your body like alcohol after a few hours or a few days, but remains in your system for 10-30 days because it is stored in your body fat.[4] This fact allows potential employers to screen your urine for past marijuana use, and furnishes your baby/fetus with THC whether or not you are acutely smoking pot or not. OK – no big deal, you are

unemployed and your urine will not be screened. What about your baby? Do you want this beautiful boy or girl to also participate in your marijuana addiction?

A recent and comprehensive review of marijuana, the pregnant woman and her child has this to say, "***Current evidence indicates that cannabis use both during pregnancy and lactation, may adversely affect neurodevelopment, especially during periods of critical brain growth both in the developing fetal brain and during adolescent maturation, with impacts on neuropsychiatric, behavioural and executive functioning. These reported effects may influence future adult productivity and lifetime outcomes.***[50]

Perhaps just as important as neurodevelopment is the risk pot smoking places upon a healthy pregnancy and delivery. Marijuana use, even for a short period during pregnancy, increases the risk of adverse birth outcomes including low birth weight, pre-term labor, small gestational age, stillbirth and admission to the neonatal intensive care unit.[51-54]

FERTILITY

As a couple, whether you realize it or not, your chances of achieving successful fertilization, a normal pregnancy and a healthy infant are dependent not just upon the mother's health but also upon the father's. If Mom is a chronic marijuana smoker her chances of a healthy conception are reduced because THC disrupts the normal menstrual cycle, suppresses oogenesis (egg development) and impairs embryo implantation and development.[55, 56] But remember the woman is only one half of the fertility equation, and regular pot smoking by the father is just as risky for conception. THC reduces sperm count and motility, increases ejaculation problems, produces a loss of libido and thereby increasing the risk for impotence.[55-57]

EDUCATIONAL ACHIEVEMENT

It's bad enough to know that your dope smoking as young parents may have prevented successful conceptions, normal pregnancies and healthy infants, but it adds insult to injury (if you live long enough) to think that your pot addiction during your child's formative and adolescent years may contribute to their own marijuana/drug addictions. **An increasing body of scientific literature indicates that chronic marijuana exposure during the youth and adolescent formative years are related to a range of adverse outcomes in later life, including poorer educational achievement, lower income, unemployment, greater welfare dependence, and reduced life satisfaction (59-63).**

CANNABINOID HYPEREMESIS

Unless you have a medical background, most of you have never heard of the word, hyperemesis, much less cannabinoid hyperemesis. This isn't surprising as the condition was first described in the medical literature in 2004.[64] This illness is characterized by cyclical vomiting without other identifiable causes in chronic marijuana users.[65-68] Patients with cannabinoid hyperemesis are unresponsive to conventional anti-vomiting drugs and report that compulsive hot baths and showers represent the only reliable treatment to improve symptoms.[66-68] Nevertheless, an obvious cure exists – abstinence. When marijuana use resumes, the condition may recur.[4]

SUMMARY

I will repeat myself from a passage earlier in this essay. “So, you be the judge, and let the data speak for itself. In the final analysis, you (the learned reader) must decide the ultimate route that you will take for your health and well being and that of your family.”

Cordially,

Loren Cordain, Ph.D., Professor Emeritus

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