Effects of Cannabis on cognitive functioning, personality and educational performance.

An extract from 'Cannabis: A General Survey of its harmful Effects' Update January 2019

In 1986 two wide-ranging review studies were carried out of all the papers into cognitive functioning and cannabis up to that time. The results were inconclusive. However it was suggested that the differential impairment observed in subjects - some users suffered damage while others did not under identical conditions, may be because of a differential vulnerability of the subjects: for example, some may be more susceptible to cerebral impairment (Wert and Raulin 1986). This suggestion has now been accepted in general for many illnesses. It should be pointed out that, the American market was at that time still dominated by weaker preparations of cannabis.

Since then, testing methods have become more sensitive and cannabis damage has been found to be subtler than expected and of a different type from that caused by alcohol.

Renewed testing of some of the older studies, with more sophisticated techniques, found definite differences between users and non-users especially in the fields of sustained attention and short-term memory (Page et al 1988).

The following experiments were normally carried out at least 24 hours after abstention from cannabis to get rid of the intoxicating effects.

Block and others (1990) found that intense prolonged use of cannabis impairs the ability to express oneself verbally and to solve maths problems.

Schwartz et al (1989) in a study of teenagers using 7% THC long-term (It was already in the USA in the late eighties), showed significant impairment of short-term memory, persisting for at least 6 weeks after stopping. Unfortunately the money then ran out.

Prolonged use of marijuana lessens the ability to focus attention and screen out irrelevant information (Solowij 1991,1995a, 1995b) In 1999 she reported that this held true even after abstention for 2 years. She also found a direct relationship between the degree of impairment and length of time of abuse.

Sixty-five heavy users of cannabis (smoking every day) male and female, were compared with sixty-four "light" users (median of one/day in the last 30 days). After abstention for a minimum of 19 hours, the heavy users had significantly greater impairment than the light ones on attention and executive functions (decreasing mental flexibility and reduced learning ability) after adjustment for confounding factors (Pope et al 1996).

Hall and others (1994), Lundqvist (1995), Leavitt et al and various other researchers all reported that long-term cannabis use produces the following effects:

"impaired ability to carry out complex thought operations and impaired ability to screen out distracting impressions;
reduced ability to process information;
no effect on long-term memory but impaired short-term memory, particularly with regard to information which is of a kind unfamiliar to the individual or which is complex in nature;
difficulty in carrying out tasks which require intellectual flexibility, long-term strategic planning and the ability to learn from experience;
no effect on the ability to deal with the routine, familiar demands of everyday life, but problems when faced with the task of expressing oneself verbally in a new, unfamiliar situation or in a situation where old ways of thinking and old knowledge are inadequate" (in Ramstrom 2003).

Dr Thomas Lundqvist of Lund University Hospital, Sweden, is one of the researchers who has contributed most to this aspect of cannabis use. In his PhD thesis in 1995 he studied the cognitive damage acquired by some 400 of the long-term cannabis abusers who had sought treatment at his

outpatient clinic. His clinical observations provide a wealth of information about the various effects of cannabis. He divided the cognitive functions impaired into 7 different categories.
A summary of his findings can be found in *"Adverse Health Consequences of Cannabis Use: A Survey of Scientific Studies Published up to and including the Autumn of 2003"* by Jan Ramstrom as follows:

Verbal Ability

Having a vocabulary that corresponds to one's age, finding the words for what one wants to say, understanding others and having the ability for abstract thought.

Logical-analytical ability

Ability to analyse and draw logical conclusions. Ability to understand causal connections and ability to judge oneself in a critical/logical manner.

Psychomotility

Ability to maintain attention and to vary the degree and focus of attention. Ability to understand other points of view and to change one's own point of view. Some degree of general flexibility with regard to different ways of looking at and interpreting societal phenomena.

Memory

Short-term memory/working memory: Ability to remember what has just happened or been communicated, which is a prerequisite not only for the integration of what has just been communicated but also for the integration and organisation of a whole range of cognitive processes, as well as a precondition for a reasonably adequate temporal perception
Long-term memory: This consists of both "episodic memory", which makes it possible to remember events and their temporal context. And "semantic memory", which has more to do with what we call ”knowledge", e. g. different facts and the inter-relationships between different phenomena.

Analytical and synthetic ability

Based on the ability to combine the other functions. Makes it possible to synthesise, sort out and organise mental material.

Psychospatial ability

Makes it possible to orientate oneself, other people and various phenomena in time and space, which is a precondition for temporal organisation as well as one of the prerequisites for social orientation.

Gestalt memory (holistic memory)

Enables us to understand and form patterns – not only to understand that there is a connection, but also to understand its nature and structure. For example, enables us to make and maintain the connection between a person, a name and a social role.

Thomas Lundqvist (1995 thesis):He found more or less pronounced weaknesses in all categories for all 400 subjects. Lundqvist also described a personality profile which he said was typical of cannabis users:

'Have difficulty in finding the words to express what they really mean.
Have a limited ability to be amused by or enjoy literature, film, theatre or the like.
Have a feeling of boredom and emptiness in everyday life, along with feelings of loneliness and of not being understood.
Externalise problems and are unable to take criticism.
Are convinced that they are functioning adequately.
Are unable to examine their own behaviour self-critically.
Feel that they have low capacity and are unsuccessful.
Are unable to carry on a dialogue.
Experience difficulty in concentrating and paying attention.
Have rigid (fixed) opinions and answers to questions.
Make statements such as "I'm different, other people don't understand me, I don't belong to society".
Do not plan their day.
Think they are active because they have many on-going projects - which they seldom see through to completion.
Have no daily or weekly routines'.

Ten former cannabis abusers were interviewed between 2 and 10 months after they had stopped concerning any changes they had experienced. All said their way of thinking and their perception of the world had changed. Most importantly they said their verbal ability, logical analytical ability and psychomotility had got better.

Nearly 10 years before, Hendin and others (1987) had asked 150 white long-term (6 days/week for at least 2 years) cannabis users subjective questions regarding their habit and its effects on them. No alcohol or other drugs were used by them, nor were they socially disadvantaged or marginalised in any way. Two thirds felt their main problem was one of memory impairment. Just under half said their ability to concentrate on a complex task had worsened and the same number couldn't finish jobs. Just over 40% considered their ability to think was less clear and 36% were less ambitious.

Cannabis users often claim that the drug gives them insight, increases self-awareness and gives them a deeper understanding of life. Many of the researchers were struck by the consistency of exactly the opposite results. Introspection was inhibited, thoughts and feelings were separated and individuals were less able to distinguish what is reality.

Obviously a reduction in memory capability will impact on learning ability and should be cause for concern especially with regard to our children. Exposure to drugs and vulnerability from them is at its highest in the teenage years. A paper on the development of the brain by Giedd (1999) points out that the brain is still maturing into the mid-twenties and Chambers and others (2003) say that the motivation/risk taking areas of the brain develop faster than the parts responsible for inhibition. Charles Nelson, a child psychologist from The University of Minnesota said, "Adolescents are capable of very strong emotions and very strong passions but their pre-frontal cortex hasn't caught up with them yet. It's as though they don't have the brakes that allow them to slow these emotions down". Another study into the effects of marijuana on morphological changes in the brain in 2000 (Wilson et al), found that the age at which marijuana exposure begins is important. Subjects who started to use marijuana before the age of 17 were compared with those who began later. The younger starters had smaller whole brain and percent cortical grey matter and larger percent white matter volumes, the males had significantly higher CBF (Cerebral Blood Flow) than other males. Both sexes who started younger were physically smaller in height and weight.

Adolescents are minors and their decisions to use or not use drugs are not conventionally regarded as being as free and informed as in the case of choice for adults (Kleiman1989).
If a child uses cannabis regularly during the transition period from childhood to adulthood, then educational achievement, becoming independent from parents, relationships including marriage and career choice, all these processes may be expected to be affected (Baumrind and Moselle 1985, Polich, Ellickson, Reuter and Kahan, 1984). The possible excalating use of cannabis and progression to the use of other drugs, not to mention the risk of accidents especially while driving should all be causes for concern (Kleiman 1989, Polich, Ellickson, Reuter and Kahan, 1984).

A clinic in Sweden, The Maria Ungdomsmottagning in Stockholm, finds it often easier to give help to young people dependent on heroin than to firmly addicted cannabis users (Ramstrom 2003). Parents' associations in Sweden and the USA, campaigning against drugs, take a very strong anti-cannabis position as they have witnessed numerous cases of the development of teenagers come to an abrupt stop because of its use (Ramstrom 2003).

Baumrind and Moselle (1985) said the forging of a personal identity is central to the maturing of children and Ramstrom in 1991 emphasised the importance of social integration to develop identity in the later teenage years. The ability for abstract thought is also crucial for forging an identity (Baumrind and Moselle 1985, Ramstrom 1991 and Steingart 1969).

The ability to perform formal thought operations is the basis of the ability for abstract thought – the vision of a world differing from reality. This skill also provides the foundation for long-term planning of the development of one's own personality. For example a child may say, "When I grow up I'll be a doctor". This should be replaced by a statement reflecting an increasingly maturing adolescent, "If I work hard, choose the right subjects and get good grades, I will be able to apply to medical school"(Lundqvist 1995).

Ramstrom (2003) said, "If the development of identity does not progress, the teenager remains at a childish level of development characterised by both a lack of independence and a deficient integration in the adult world". He also said, " Deterioration of short-term memory obviously makes learning more difficult, but it also has a negative effect on the individual's ability to make plans, to establish new relationships and to make realistic assessments of the world around him or her".

Kerstin Tunving wrote in an article in 1987, "To sum up, the impression is, based on clinical observations, that teenagers who abuse cannabis "sleep away" their teens. They often do not develop at the same pace as youth of the same age, but stay childish and dependent".

In recent years, researchers have found associations between cannabis use and mental and social problems in the late teens and early adulthood, psychosis (Arsenault 2002) depression and suicidal thoughts (Bovassa 2001 and Patton et al 2002), crime and unemployment (Fergusson and Horwood 1997, Fergusson et al 2000, 2002).

Detailed descriptions of the long-term effects of cannabis use on teenagers is present in textbooks, Heinemann 1984, Ranstrom 1987, Lunqvist report 1995, and in a paper by Kolansky and Moore 1971.

Holmberg (1981) studied over 1000 Swedish 15 to 16 year olds, with a follow up 11 years later. The following results were found:
Mortality rates were 5 to 8 times higher among the original abusers. They also had experienced more medical and social problems, 10% had had a psychotic episode during the time and the 2.4% who were heavy users were more likely to have become properly addicted.

A very extensive longitudinal in-depth study of young cannabis users was carried out by Newcombe and Bentler in 1988. It focused on the transition to adulthood. Not surprisingly the risk of impairment to mental functions increased, they were less able to make careful plans, had negative psychosocial factors in the teenage years and were more likely to drop out of school or training courses. They found it harder to hold down a job, experienced more divorces and had worse social networks.

Confirmation of these findings came from Fergusson and his co-workers in 1997, 2000 and 2002 (Christchurch Study). They said, "Cannabis use, and particularly regular or heavy use, was associated with increased rates of a range of adjustment problems in adolescence/young adulthood – other illicit drug use, crime, depression, and suicidal behaviours – with these adverse effects being most evident for school aged regular users".

It has already been mentioned that cannabis use can impair memory, attention and therefore learning (Baumrind and Moselle 1985), thus potentially increasing the risk of high school failure and possible drop-out. These findings were supported in cross-sectional studies by Kandel (1984), Robins and others 1970, and Hawkins and others in 1992. They all found a positive relationship with cannabis use as an adult and the risk of dropout from school.
Longitudinal studies by Kandel in 1986 and Newcombe and Bentler 1988, however, gave mixed support for the idea. Kandel looked at her cross-sectional study again and reported that the connection all but disappeared as the dropout students using cannabis had lower aspirations than the controls. Newcombe and Bentler found only a negative effect of *hard drugs* in adolescence and completion of high school.

More recently, Lynskey and Hall conducted a review of papers on educational attainment in 2000. They concluded that cannabis use significantly increases the risk of poor school performance and early school leaving.

To quote, "Cross-sectional studies have revealed significant associations between cannabis use and a range of measures of educational performance including lower grade point average, less satisfaction with school, negative attitudes towards school, increased rates of absenteeism and poor school performance……… A number of prospective longitudinal studies have indicated that early cannabis use may signify increased risks of subsequent poor performance and in particular, early school leaving. This association has remained after control for a wide range of prospectively assessed co-variables…….In particular , early cannabis use appears to be associated with the adoption of an anti-conventional lifestyle characterised by affiliations with delinquents and substance-using peers, and the precocious adoption of adult roles including early school leaving, leaving the parental home and early parenthood".

The survey proposed that the link between early cannabis use and educational attainment arises because of the social context within which cannabis is used and not because cannabis use causes impairment. However Solowij (1998) concluded there is evidence that long-term cannabis use (daily or near-daily for 10 years or more), was associated with the impairment of selective attention. Few adolescents will have used cannabis intensively or for long enough to produce the effects seen in adults.

Hall added that this does not mean that acute cognitive impairment is irrelevant in adolescents, only that cognitive impairment found in those who use cannabis is more likely to be the results of acute intoxication than the effects of long-term use. If adolescents used regularly then school performance would suffer especially if they were poor or average to start with.

Solowij also said (1998) in her book "Cannabis and Cognitive Functioning", "Use more often than twice per week for even a short period of time, or use for 5 years or more at the level of even once per month, may each lead to a compromised ability to function to their full mental capacity, and could possibly result in lasting impairments (this does not imply that use below theses levels may be considered safe)".

I can certainly concur with these findings. I have seen the performance of a few of my students, bright grammar school boys, slowly deteriorate. They fail to achieve the grades they deserve and some miss out on the university of their choice. They will never admit to using cannabis, the information often comes from their peers, and some parents simply do not want to know.

In another paper in 2001 Hall said that it is clear that heavy cannabis use may compromise educational attainment and thus future achievement.

Two papers in 2002 added to the evidence. One by Solowij et al examined the effects of the duration of cannabis use on specified areas of cognitive functioning among users seeking treatment for cannabis dependence. Their results confirmed that long-term heavy cannabis users show impairments in memory and attention that endure beyond the period of intoxication and worsen with increasing years of regular cannabis use. And Bolla and colleagues also found heavy cannabis use to be associated with persistent decrements in neurocognitive performance even after 28 days of abstention. They said it was unclear if these decrements would resolve with continued abstinence or grow progressively worse with continued heavy marijuana use.

The preliminary results of a longitudinal study into the effects of marijuana use on IQ in The Canadian Medical Association Journal (2002), reported that current use of the drug had a negative effect on global IQ scores only in subjects who smoked 5 or more joints a week. It was not found in previously heavy users who had now given up so did not have a long-term impact. IQs were tested in 9 to 12 year olds and again when they reached 17 to 20. The drop was around 4 points.

In 2003 Pope and others found early-onset cannabis users exhibiting poorer cognitive performance than late-onset users or control subjects especially in verbal IQ, but they could not determine the cause of this difference from their data.

Fergusson, Horwood and Beautrais in 2003 found an increased cannabis use to be associated with an increase in school leaving, qualifications, failure to enter university and failure to obtain a university degree. This connection persisted after control for confounding factors. There was no evidence to suggest the presence of reverse causal pathways, i.e. that lower educational achievement lead to increased cannabis use. The findings support the view that cannabis use may act to decrease educational achievements in young people. It is likely that this reflects the effects of the social context within which cannabis is used rather than any direct effect of cannabis use on cognitive ability or motivation.

Lynskey and others in 2003 published the results of another study of high school completion. They concluded: "Early regular cannabis use (weekly use at age 15), is associated with an increased risk of leaving school early". And Bray and others in 2000 said a teenage marijuana user's odds of dropping out are more than twice that of a non-user.

The National Household Survey on Drug Abuse in America in 2002 reported that marijuana use is linked to poorer grades. A teenager with an average "D" grade is 4 times more likely to have used marijuana than a teenager with an average "A" grade.

Professor Robin Murray, Director of The Institute of Psychiatry in London, was quoted in The Times on Saturday 12th February 2005, " One of the reasons why some young people who smoke cannabis start performing badly at school or university is that they are cognitively impaired by the cannabis lingering in their brain. A young person who smokes cannabis every day, or even 3 times a week, can be in a state of low-grade intoxication most of the time. However, if you stop, these adverse cognitive effects also stop".

The most recent evidence on cannabis and cognitive functioning comes from Greece and a study by Messinis and some of his colleagues (March 2006). They concluded that long-term marijuana use is linked to "subtle deficits in specific neuropsychological domains". Those who smoked at least 4 joints a week for several years performed significantly worse than non-users. In particular, verbal learning (the ability to remember previously learned words) and executive functioning (organising and coordinating simple tasks), were among the worst affected.

Wadsworth and others in January 2006 aimed to examine whether an association existed between cannabis use, cognitive performance, mood, and human error at work. There was a positive relation between cannabis use and impairment of cognitive functioning and mood. No more errors were reported in the workplace than in the controls. There was also a positive correlation with lower alertness and a slower response in organising things. Memory problems were evident at the start of the week and psychomotor slowing and poorer recall of episodes at the end of the week.

Ranganathan and D'Souza in 2006 reviewed the literature on the acute effects of cannabinoids on memory tasks in humans. Their conclusion suggested that cannabinoids impair all stages of memory including encoding, consolidation and retrieval.

In contrast to other research findings, Dr Igor Grant, editor of the Journal of The International Neuropsychological Society which he founded, wrote in the July 2003 edition that marijuana smoking has only a marginally harmful long-term effect on learning and memory. No effect at all was seen on other functions including reaction times, attention, language, reasoning ability and perceptual and motor skills. Dr Grant said he found the findings to be of particular significance since several states are considering whether to make it available as a medicinal drug. The paper was sponsored by a state-supported programme to oversee research into the use of cannabis to treat certain diseases. (Dr Grant is Director of The University of California Center for Medicinal Cannabis Research).

Dr Thomas Lundqvist in a review of the cognitive consequences of cannabis use in 2005 documented studies into the subject using brain-imaging techniques to try to reveal any neurotoxic effects of cannabis.
Neuro-imaging data has been extracted from studies on acute and chronic abusers of marijuana in resting and in challenging cognitive situations.

Several studies at rest, using different techniques CBF, PET, SPECT, fMRI showed sub-normal cerebral blood flow or lower cerebellar metabolism in long-term users assessed within one week of abstention. Marijuana users showed 9% lower values of average whole brain activity compared with controls. Also at rest, acute exposure to marijuana gave rise to increases in dose-related CBF (Cerebral Blood Flow) in experienced users in some areas of the brain but not others e.g. those that are memory related.

When given a cognitive challenge, the controls showed significant activation in the pre-frontal cortex. Heavy smokers 24 hour to 28 days after washout, dislplayed diminished activity in this region but increased activity in another (the cingulate) which was not seen in the controls. There is thus a differential of cortical activity in subjects with a history of heavy cannabis use. CBF was decreased in areas associated with attention and attentional moderation of sensory processing.

In one study using PET scans, following a 25 day abstention, heavy users had no deficit in their executive functioning, at the same time as showing hypo-activity in some of the areas responsible for executive functioning and hyperactivity in others. This suggests there may be an alternative neural network employed as compensation i.e. they "work harder" to meet the demands of the task.

Lundqvist concluded that neuropsychological and brain-imaging techniques point to deficits in attention, memory and executive functioning.

He also suggested that studies failing to detect cognitive decline associated with cannabis use may reflect insufficient heavy or chronic use of cannabis in the sample or use of insensitive assessment instruments.

Herning and others (2005) also proposed a “blood flow theory” to account for the deficits in cognitive functioning among users of cannabis. Using Transcranial Doppler Sonography they recorded blood flow velocity in the cerebral arteries of heavy, moderate and light users, 3 days after admission to an in-patient research unit and after 28 to 30 days of monitored abstention. The conclusion was that “Chronic marijuana use is associated with increased cerebrovascular resistance through changes mediated in part, in blood vessels or in the brain parenchyma. These findings might provide a partial explanation for the cognitive deficits observed in a similar group of marijuana users”.

Marijuana’s well-known effects on memory (short-term) according to neuroscientists, may be the result of misfiring brain cells. A paper published on 19th November 2006 by Robbe and others found that rats given THC experienced disruptions in the synchronous brain-cell firing that causes the formation of memories. There was a slowing of brain wave activity, principally theta and fast-ripple waves (believed to be involved in short-term memory formation) but also gamma waves (thought to help in moving memories into long-term storage). At very high doses the drug appeared to prevent learning altogether.

Chronic abuse of different drugs cause similar brain changes. Whether long-term users favour cocaine, cannabis or PCP, autopsies of their brains show a number of common gene changes consistent with diminished brain plasticity (ability to learn from new experiences and adapt to new situations). A paper by Lehrmann and others found that the anterior pre-frontal cortex (decision-making region) was dysfunctional in the brains of drug users. The brains of 42 deceased abusers were studied. Nearly 80% of them had similar alterations in genetic output compared to the controls. Genes involved in calcium signalling were turned down and those in lipid and cholesterol-related pathways were turned up. The abuser’s ability to make sound decisions could be threatened.

An Australian study by George Patton et al 2007, on nearly 2000 Victorian high school 14 to 15 year olds since 1992 has found that, “while both alcohol and cannabis carried health risks, the overwhelming evidence was that cannabis was “the drug for life’s future losers”. Almost two thirds had tried cannabis before they were 18. They are more likely to suffer poor long-term mental health than drinkers, more likely to graduate to amphetamines, ecstasy and cocaine, and be less likely to be working, be qualified or in a relationship. They concluded, “Heavier teenage cannabis users tend to continue selectively with cannabis use. Considering their poor young adult outcomes, regular adolescent cannabis users appear to be on a problematic trajectory”.

Jan Van Ours and Jenny Williams wrote a discussion paper in September 2007 about cannabis and educational attainment. People between 25 and 50 were interviewed. Those initiated into cannabis use earliest suffer the greatest adverse effects. Future earnings and prospects are both damaged. They concluded that, “1. Preventing cannabis uptake will improve the educational outcomes of youths, and 2. even if cannabis use cannot be prevented, delaying the age at which uptake occur will deliver educational benefits”.

A paper in 2008 by Quinn et al found that adolescent rats were less averse to repeated doses of THC than adult rats but had greater residual cognitive deficits andd changes in hippocampal protein expression. The dose mimicked that of heavy cannabis use in humans. The adults after 2 weeks avoided the region of the cage associated with injections but the youngsters didn’t. Many more protein changes were found in the adolescents and they had trouble with short-term memory. It was pointed out that the brains of the young rats were not yet fully developed so they were more vulnerable.

In 2008 Fegusson updated his findings from the Christchurch Study. He found, “ …increasing cannabis use in late adolescence and early adulthood is associated with a range of adverse outcomes later in life. High levels of cannabis use are related to poor educational outcomes, lower income, greater welfare dependence and unemployment and lower relationship and life satisfaction”.

2008 Perkonigg et al found that youth cannabis use commonly extends into adulthood. Over 3000 (14 to 24 years old) German young people were followed. Of those who had repeated use of cannabis at baseline, 56% were still using it 4 years later and 46% 10 years later.

2008 Jager and Ramsey looked at long-trm consequences of adolescent marijuana use on the development of cognition, brain structure and function in an overview. They concluded: Over the last decade there has been a steady increase in the prevalence of frequent cannabis use among teenagers, accompanied by a decrease in age of first use. Evidence from both animal and human studies suggests that the severity of the effects of cannabis use on cognitive development is dependent on the age when cannabis use begins. One possible explanation is that those who begin cannabis use early in adolescence are more likely to become heavily dependent. It is plausible that chronic cannabis abuse will then interfere with educational and vocational training. From a more biological perspective, however, use of cannabis during critical developmental periods in the still maturing brain may induce persistent alterations in brain structure and brain function. Therefore, the effects of frequent cannabis use during adolescence could be different from and more serious than during adulthood, an issue increasingly recognized in the field of cannabis research. In this paper we review the relevant animal and human literature on long-term effects of frequent exposure to cannabis during adolescence on the development of cognition, brain structure and function, and discuss implications, methodological and conceptual issues, and future prospects.

2008 Caldeira et al found that first year college students show high rate of cannabis use disorders. In a group of students who had used cannabis more than 5 times in the past year, 1 in 10 met the criteria for dependence and 14.5% met the criteria for cannabis abuse. 474 participants had used cannabis more than 5 times and of those: 24.3% regularly put themselves in physical danger when under the influence; 10.6% continued to use despite problems with family or friends; 40.1% reported concentration problems and 13.9% said they missed classes.

Yucei, Solowij et al 2008, performed high-resolution structural magnetic resonance imaging on 15 men (average age 39.8 years) who smoked more than 5 joints/day for 10 years, and compared them with images from 16 individuals (Average age 36.4 years) who were not cannabis users. The hippocampus (memory and emotion) and the amygdala (fear and aggression) tended to be lower in cannabis users, by 12% and 7.1% respectively. They concluded, " Although modest use may not lead to significant neurotoxic effects, these results suggest that heavy use might indeed be toxic to human brain tissue".

Ashtari and others in 2009 discovered that the developing brains of teens may be disrupted by heavy marijuana use. They used DTI (Diffusion Tensor Imaging) in 14 heavy smokers (Averaging nearly 6 joints/day in the final year of their smoking (they had smoked from 13 to 18/19 years of age). Abnormalities were seen in areas connecting memory, decision-making, attention, language and executive functioning skills – exactly the critical areas which develop in late adolescence. The images suggested damage or an arrest in developmentof the myelin sheath (insulation) that surrounds brain fibres. This abnormal white matter development could slow down information transfer and affect cognitive functioning. Five of the subjects also had a history of alcohol abuse.

Gobbi et al 2009, discovered that daily consumption of cannabis in teens can cause depression and anxiety and have irreversible long-term effects on the brain. 'Teenagers who are exposed to cannabis have decreased serotonin transmission which leads to mood disorders as well as increased norepinephrine transmission which leads to greater long-term susceptibility to stress', she said. Damage caused is more serious during adolescence than adulthood.

Rubino et al 2009 looking at changes in adolescent morphology induced by adolescent THC treatment. THC pretreated rats had a significantly lower total dendritic length and number than vehicles, as well as reduced spine density. Our data suggest that THC pretreated rats may establish less synaptic contacts and/or less efficient synaptic connections throughout the hippocampus and this could represent the molecular underpinning of the cognitive deficit induced by adolescent THC treatment.

2009 Hester et al in 2009, using brain-imaging technology showed that during a decision game, chronic marijuana users showed less activity in an error-processing part of the brain than peers who do not use. They did not make more mistakes than the controls but were significantly less likely to realise it they had done 91% compared with 77%. This deficit in awareness may contribute to their continued use of the drug.

2010 A study from Australia by Degenhardt et al found that occasional cannabis use in adolescence predicts later drug use and educational problems. Nearly 2000 secondary school pupils were followed from 14.9 to 24 years of age. Those who continued cannabis use into early adulthood had higher risks of later adult alcohol and tobacco dependency and illicit drug use., as well as being less likely to complete a post secondary qualification.

2010 Dumontheil and others found that lack of concentration in adolescents is to do with brain structure, their mental capacities are not the same as adults. They found an unexpected level of activity in the prefrontal cortex which is involved in multi-tasking and decision-making. This means it continues to do a lot of needless work when making decisions. This "chaos" continues till the late 20s. These chaotic thought patterns are a result of too much grey matter. As we age the amount of grey matter decreases.

2010 Demirakca T et al discovered diminished gray matter in the hippocampus of cannabis users. Chronic cannabis use has been associated with memory deficits and e reduction in volume of the hippocampus, but no study yet has accounted for the different effects of THC and CBD. Cannabis users showed lower GM (gray matter) volumes located in a cluster of the right anterior hippocampus. An inverse correlation of the ratio YHC/CBD with the volume of the right hippocampus was observed. Conclusion: Lower volume in the right hippocampus in chronic cannabis users was corroborated. Higher THC and lower CBD were associated with this volume reduction indicating neurotoxic effects of THC and neuroprotective effects of CBD, confirming previous preclinical and clinical results.

2010 Hanson et al found that marijuana users demonstrated poorer verbal learning, verbal working memory and attention memory compared to controls. Improvements were seen in users on word list learning after 2 weeks of abstinence and on verbal working memory after 3 weeks. While attention processing speed was similar between groups, attention accuracy remained deficient throughout the 3 week abstinence period. These results implicate possible hippocampal, subcortical and prefrontal cortex abnormalities.

2010 Koskinen et al conducted a meta-analysis of the rate of cannabis use disorders (CUDs) in clinical samples of patients with schizophrenia. 35 studies were examined. The median current rate of CUDs was 16%(10 studies) and the median lifetime rate was 27.1% (28 studies). The median rate for CUDs was markedly higher in first episode vs long-term patients (current 28.6%/22.0%, lifetime 44.4%/12.2% respectively) and in studies where more than two thirds of the participants were male, than in the other studies (33.8%/13.2%). CUDs were also more common in younger samples than in the others (current 38.5%/16.0% lifetime 45.0%/17.9%). Conclusion: Approximately every 4th schizophrenia patient in our sample of studies had a diagnosis of CUDs. CUDs were especially common in younger and first-episode patient samples as well as in samples with a high proportion of males.

2011 Ali and others looked at the social contagion effect of marijuana use among adolescents. Their findings indicate that peer effects are important determinants of marijuana use even after controlling for potential biases. A 10% increase in the proportion of close friends and classmates that use cannabis increases the probability that an individual chooses to use marijuana by 5%.

2011 Buckner et al studied social anxiety and marijuana-related problems. The relationship between current (past 3 months) marijuana-related problems and 2 aspects of social anxiety (fear in social situations and social avoidance) among 102 current users was examined. Although both conditions were significantly correlated with marijuana-related problems, only social avoidance was uniquely related to marijuana problems after controlling for social fear, sex, negative effect, alcohol problems and marijuana use frequency. Sex moderated the relationship between social avoidance and marijuana related problems such that men with greater social avoidance exhibited the greatest severity of marijuana related problems. They conclude: Avoidance of social situations appears robustly related to marijuana-related problems.

2011 Feb, Solowij N and others studied verbal learning and memory in adolescent cannabis users, alcohol users and non-users aged 16 to 20. 181 adolescents took part. They found that cannabis users performed significantly worse than alcohol users and non-users on all performance indices. The degree of impairment was associated with the duration, quantity, frequency and age of onset of cannabis use, but unrelated to alcohol or any other drug use. The earlier the onset, the worse the memory performance.

Conclusions: Despite relatively brief exposure, adolescent cannabis users relative to their age-matched counterparts demonstrated similar memory deficits to those reported in adult long-term heavy uses. The results indicate that cannabis adversely affects the developing brain and reinforce concerns regarding the impact of early exposure.

2011 March Feinstein et al found that MS patients using marijuana to relieve pain were 'hurting' their thinking skills. The study used 25 patients and 25 controls. The users scored significantly lower on tests of attention, thinking speed and gauging space between objects. About 40 to 60% of people with MS have problems with decision making, thinking and reasoning. Pot smoking may be making this worse.

2011 June Fontes et al found that regular cannabis users, if they start before the age of 15 perform worse on brain tests than those who start later. 104 chronic cannabis users, of whom 49 had started before the age of 15, took part in a series of tests involving, executive functionng, attention, perseverance, ability to form abstract concepts, visual and motor skills and mental flexibility. There was no difference between the groups or controls in terms of IQ. The early onset group performed significantly worse on attention, impulse control and executive functioning.

Dr Maria Fontes said, 'We know that adolescence is a period in which the brain appears to be particularly vulnerable to the neurotoxic effects of cannabis'.

Gruber et al 2011 looked at age of onset of marijuana use and executive function. Age of onset, frequency, and magnitude of MJ use were all shown to impact cognitive performance. Findings suggest that earlier MJ onset is related to poorer cognitive function and increased frequency and magnitude of MJ use relative to later MJ onset. Exposure to MJ during a period of neurodevelopmental vulnerability, such as adolescence, may result in altered brain development and enduring neuropsychological changes.

2011 Crean and others conducted a review of executive functions and cannabis use. These are their conclusions: The trajectory of effects of cannabis on executive functions follows an interesting pattern of recovery of some functions and persisting deficits in others. The acute effects of cannabis use are evident in attentional and information processing abilities with recovery of these functions likely after a month or more of abstinence. Decision-making and risk-taking problems aren't necessarily evident immediately after smoking; however, if cannabis use is heavy and chronic, impairments may emerge that do not remit with abstinence, particularly if heavy use was initiated in adolescence such that maturation of executive functions was not achieved. Acute cannabis use impairs inhibition and promotes impulsivity, and over a period of abstinence, these deficits are most evident in tasks that require concept formation, planning and sequencing abilities. Working memory is significantly impaired following acute exposure to cannabis; however, these deficits resolve with sustained abstinence. Evidence is less clear in regards to verbal fluency abilities; however, research suggests that chronic, heavy use may impact verbal fluency abilities even after long-term abstinence. The long-term effects of cannabis on executive function is most clearly demonstrated when studies use chronic, heavy cannabis users, as opposed to light, occasional users. Yet even occasional cannabis use can acutely impair attention, concentration, decision-making, inhibition, impulsivity and working memory.

2012 Kucewicz looked at the fact that brain activity becomes uncoordinated and inaccurate during altered states of mind leading to neurophysiological and behavioural impairments reminiscent of schizophrenia. This study tested whether the detrimental effects of cannabis on memory and cognition could be the result of 'disorchesrated' brain networks. An agonist of THC was used on rats and completely disrupted co-ordinated brain waves across the hippocampus and prefrontal cortex. (like 2 sections of an orchestra playing out of sync. The rats became unable to make decisions while navigating round a maze.

2012 March Han et al found that acute cannabinoids can impair the working memory (the ability to retain and use information over short periods of time). A previously unknown signalling mechanism between neurons and non-neuronal cells called astrocytes (always thought to be merely supporting and protecting cells of neurons) has been found. 'Our study provides compelling evidence that astrocytes control neurons and memory, the supporting actor has become the leading actor' said Zhang, one of the authors. It was discovered that THC weakened the synapses between neurons in the hippocampus, crucial for memory formation, and this was controlled by the previously undiscovered CB1 receptors on the astrocytes.

2012 August, Zalesky et al (Australia) Looked at the effect of long-term cannabis use on axonal fibre connectivity. 59 people who had been using marijuana for 15 years on average were compared with scans (MRI) of 33 people who had never used the drug. The white matter in brains (complex wiring system) continues to develop over a lifetime. Changes to the volume, strength and integrity of the white matter were measured. Dr Seal, the lead researcher said there was a reduction in the volume of white matter of more than 80% of the users studied. The average age of initiation was 16 but there were some who had started at 10 or 11 – they were more seriously affected. Dr Seal said, 'This is the first study to demonstrate the age at which regular cannabis use begins is a key factor in determining the severity of the brain damage……We don't know if these changes are irreversible but we do know that these changes are quite significant……These people can have trouble learning new things and they are going to have trouble remembering things'.

2012 August, Meir et al as part of the long-running Dunedin Study, found that the IQ of children hooked on cannabis in their teens, and continuing to take it, fell by an average of 8 points (equivalent to dropping from average IQ to the lower third of the population). More than 1,000 children were put through a battery of tests at ages 13, 14 and then 38. None had tried cannabis when the research started making it easier to observe the effects of cannabis. Interviews on cannabis use were conducted at 18, 21,26, 32 and 38. Attention and memory were also harmed. Tests normally used to spot the early signs of Altzeimers were conducted and adolescent cannabis users fared worse. The effects on IQ could still be seen in those who had not touched cannabis for a year. Small falls in IQs were seen in those who never or occasionally used the drug and those who had started to use it as an adult.

2013 Jan Rogeberg (edited by Iverson) challenged the Meir paper above:

Correlations between cannabis use and IQ change in the Dunedin cohort are consistent with confounding from socioeconomic status

Abstract

Does cannabis use have substantial and permanent effects on neuropsychological functioning? Renewed and intense attention to the issue has followed recent research on the Dunedin cohort, which found a positive association between, on the one hand, adolescent-onset cannabis use and dependence and, on the other hand, a decline in IQ from childhood to adulthood [Meier et al. (2012) *Proc Natl Acad Sci USA* 109(40):E2657–E2664]. The association is given a causal interpretation by the authors, but existing research suggests an alternative confounding model based on time-varying effects of socioeconomic status on IQ. A simulation of the confounding model reproduces the reported associations from the Dunedin cohort, suggesting that the causal effects estimated in Meier et al. are likely to be overestimates, and that the true effect could be zero. Further analyses of the Dunedin cohort are proposed to distinguish between the competing interpretations. Although it would be too strong to say that the results have been discredited, the methodology is flawed and the causal inference drawn from the results premature.

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Specifically, the new study (Rogeberg) uses simulation models to suggest that other factors, such as socioeconomic status, may account for the downward IQ trend seen in the Meier et al. study. Indeed, when discussing traits like IQ, it would be surprising for one factor to be 100 percent causal. The strengths of the Meier et al study are that it is longitudinal in nature and that it controlled for a number of factors including years of education, schizophrenia, and other substance abuse. That said, observational studies in humans cannot account for all potentially confounding variables. In contrast, animal studies—though limited in their application to the complex human brain—can more definitively assess the relationship between drug exposure and various outcomes. They have shown that exposure to cannabinoids during adolescent development can cause long-lasting changes in the brain's reward system as well as the hippocampus, a brain area critical for learning and memory. The message inherent in these and in multiple supporting studies is clear. Regular marijuana use in adolescence is known to be part of a cluster of behaviors that can produce enduring detrimental effects and alter the trajectory of a young person's life—thwarting his or her potential. Beyond potentially lowering IQ, teen marijuana use is linked to school dropout, other drug use, mental health problems, etc. Given the current number of regular marijuana users (about 1 in 15 high school seniors) and the possibility of this number increasing with marijuana legalization, we cannot afford to divert our focus from the central point: regular marijuana use stands to jeopardize a young person's chances of success—in school and in life.

Madeline Meier, a psychologist at the Duke Transdisciplinary Prevention Research Center in Durham, North Carolina, who co-wrote the original paper with her colleagues, says that Røgeberg's ideas are interesting. However, she points out that the authors of the first *PNAS* paper restricted their analysis to individuals in middle-class families and those with low or high socioeconomic status. The outcome suggests that the decline in IQ cannot be attributed to socioeconomic factors alone.

In their original analysis, Meier says, she and her colleagues controlled for socioeconomic status and found that in all socioeconomic categories, the IQs of children who were not heavy users remained unchanged from adolescence to adulthood. Therefore, she says, socioeconomic status does not influence IQ decline.

Science experts defend the Meier paper:

http://www.sciencemediacentre.co.nz/2012/08/28/teen-cannabis-use-and-iq-experts-respond/

2012 September Long et al, ' The system of the brain responsible for mediating effects of cannabis, the endo-cannabinoid system, is most vulnerable to the drug during adolescence' .Dr Leonora Long said, ' During adolescence the endo-cannabinoid system in the brain undergoes a lot of change, and interfering with these changes by using cannabis could have consequences for the development of healthy brains in adults. Cannabis use is common among teens and adolescents, and adolescence is a time when adult behaviours and decision-making are developing. so this discovery is very significant. The endocannabinoid system is involved in appetite, pain sensation, mood and memory, and affects the way neurons in the brain communicate with each other.

2013 Blakemore SJ looked at cannabis and the adolescent brain. She supported the research by Meir in August 2012 about IQ resulting from The Dunedin Study.

2013 Raver and others found that adolescent cannabinoid exposure permanently suppresses cortical oscillations in adult mice, thus permanently altering working-memory performance in adults. 'To our knowledge, ours is the first study to demonstrate a direct link between cannabinoid exposure specifically during adolescence and abnormal electrophysiological activity in the adult neocortex, as well as to report a differential vulnerability of cortical regions that parallels their maturational state at the time of drug exposure'.

2013 Mechoulam and Parker looked at CBD effects. They found CBD opposes some but not all forms of behavioural and memory disruption caused by THC in male Rhesus monkeys.

2013 Dominquez and others examined the duration of untreated psychosis in adolescents: ethnic differences and clinical profiles. 940 new first-episode psychosis cases aged 14-35 (136 adolescent onset versus 804 adult onset individuals). Age of onset, family mental heath history, duration of untreated psychosis (DUP), suicidality and substance use info, were all collected at entry. Adolescents had significantly greater median DUP (179 days) than adults (81 days).Among adolescent ethnic groups, Median DUP whites – 454 days (DOH Target =3 months), black - 103 days, Asian and mixed - 28.5 days. Younger onset and higher lifetime cannabis users were associated with longer treatment delay.

2013 Bloomfield et al compared dopamine synthesis capacity in 19 regular cannabis users who experienced psychotic-like symptoms when they consumed cannabis with 19 non-user, sex and age matched control subjects. The results surprised them. Cannabis users had reduced dopamine synthesis capacity in the striatum and its associative and limbic sub-divisions compared with the controls. These results were seen in those users meeting abuse or dependence criteria. Dopamine synthesis capacity was negatively associated with higher levels of cannabis use and positively associated with age of onset of use, but not with cannabis induced psychotic-like symptoms. They concluded, ' these findings indicate that chronic cannabis use is associated with reduced dopamine synthesis capacity and question the hypothesis that cannabis increases the risk of psychotic disorders by inducing the same dopaminergic alterations seen in schizophrenia.

Professor Sir Robin Murray commented:

'Acute TCH increases striatal dopamine but we have known for some time that chronic dependence on drugs such as amphetamine or alcohol seems to depress striatal dopamine levels. Because dopamine is involved in reward this drives them to take more drugs to try and increase their dopamine back to normal. So this paper shows that cannabis acts like other drugs of abuse in that if you keep taking it your dopamine levels become low.

Recently it was reported by Dr Anissa Abi-Dharghum cannabis dependent people with psychosis symptoms also had low striatal dopamine but if they were given amphetamine they developed exacerbation of their psychosis even with a tiny increase in striatal dopamine (within normal limits). So it may be that the cannabis users who develop psychosis may have somehow developed a supersensitive dopamine system. This could be because of an abnormality further downstream. For example, you know that we have shown an effect of the gene AKT1. This has a role in post-receptor signalling i.e. after the dopamine receptor. So, it is possible that a person with the AKT1 risk variant might have so sensitive a dopamine system that psychotic symptoms might ensue even with a small change in striatal dopamine.

So the above remains a possibility. An alternative is that an effect on the CB1 receptor directly affects AKT without going through the Dopamine system.

Another alternative is something entirely different that we can't even speculate about. So the bottom line is that we don't have a definitive answer. But at least people are now seriously looking at these question.

2014 Lisdahl K, director of the brain imaging and neuropsychology lab at University of Wiskonsin-Milwaukee, in a presentation to American Psychological Association's 122nd Annual Convention said that: 'Frequent marijuana use (around once/week) can have a significant negative effect on the brains of teenagers and young adults, including cognitive decline, poor attention and memory, and decreased IQ. Abnormalities in the brain's gray matter (assoc with intelligence) have been found in 16 – 19 year olds who increased use over the past year.

2014 Battistella et al looked at the Long-term Effects of Cannabis on Brain Structure. Regular smokers were compared with occasional smokers matched by years of cannabis smoking. Regular cannabis use is associated with reduction of gray matter volume in the medial temporal cortex, temporal pole, para hippocampal gyrus, insula and orbitofrontal cortex. These are areas rich in cannabinoid CB1 receptors and functionally associated with motivational, emotional and affective processing. These changes correlate with the frequency of cannabis use before inclusion in the study. Age of onset also influences the magnitude of these changes. Significant gray matter volume reduction could result either from heavy consumption unrelated to the age of onset or instead from recreational cannabis use initiated at an adolescent age. In contrast, the larger gray matter volume detected in the cerebellum of regular smokers without any correlation with the monthly consumption of cannabis may be related to developmental processes occurring in adolescence (lack of pruning).

2014 Homel et al looked at associations between longitudinal trajectories of marijuana use from adolescence to young adulthood (15-25) and PSE (Post Secondary Education) experiences. They concluded that 'Frequent marijuana use from adolescence to young adulthood may close off opportunities for entering PSE. Occasional users may create delays in starting and finishing PSE among less-at-risk young people'.

2014 Silins et al investigated adolescent use and the consequences for young adults using 3 large long-running studies involving 3765 individuals in Australia and New Zealand (Australian Temperament Project, the Christchurch Health and Development Study and the Victorian Adolescent Health Cohort). Findings included: teenagers using cannabis daily before age 17 were 60% less likely to complete high school/university compared with never-users. They were also 7 times more likely to attempt suicide and 8 times as likely to use other illicit drugs. The authors linked frequency of use with 7 developmental outcomes to the age of 30: completing high school, obtaining a university degree, cannabis dependence, use of other illicit drugs, suicide attempts, depression and welfare dependence. A clear association was found wit frequency of use in adolescence and poor outcomes across most measures, even after controlling for socio-economic status, mental illness etc. Risk increased as amount taken rose.

2014 Mokrysz et al looked at educational and intellectual performance of 2612 children between the ages of 8 and 15, the IQs of these children were noted at these ages. Cannabis use was investigated for its role in educational performance. They found no relationship between canabis use and lower IQ at age 15. Heavier cannabis users (at least 50 times by age 15) did show marginally impaired educational abilities (exam results 3% lower).

The study was criticised: cannabis use was self-reportedand the measure of IQ at age 15 was an abbreviated versaion of the standard Wechsler IQ test.

Dr Madeline Meir (Dunedin Study) says,

“This new paper looks interesting. It does not relate in any way to our findings from The Dunedin Study, however. Our finding was that adults who were long-term dependent on cannabis and those who used cannabis 4 or more times/week during the 20 years after adolescence, had lost 8 IQ points by age 38.

Those who had lost the most IQ points were those who had started their cannabis use youngest, as teens. There is no reason to expect that teens who have used cannabis only 50 times would already show a loss of IQ points by age 15. The ALSPAC (Avon Longitudinal Study of Parents and Children) would need at least 20 more years of follow up, and data on cannabis dependence, before it could be compared to the Dunedin Study”.

2014 Conroy et al looked at the impact of marijuana use on self-rated cognition in young adult men and women. Forty eight young adults participated (22 female) mean age 22.3 years. There was a significant relationship between greater number of minutes of marijuana use and higher levels of self-related cognitive difficulties. Gender was not significant.

2014 Ehrenreich et al looked at marijuana use from Middle to High School and co-occurring problem behaviours, teacher –related academic skills and sixth grade predictions. 619 randomly selected students were assessed annually from 6th to 12th grade. They were grouped : Abstainer (65.6 %), Sporadic (13.9 %), Experimental (11.5 %), and Increasing (9.0 %). Compared to Abstainers, students in the Sporadic, Experimental and Increasing trajectories reported significantly more co-occurring problem behaviors of alcohol use, cigarette smoking, and physical aggression. Sporadic and Experimental users reported significantly less smoking and physical aggression, but not alcohol use, than Increasing users. Teachers consistently rated Abstainers as having better study skills and less attention and learning problems than the three marijuana use groups. Compared to Abstainers, the odds of dropping out of high school was at least 2.7 times higher for students in the marijuana use trajectories. Dropout rates did not vary significantly between marijuana use groups. In sixth grade, being male, cigarette smoking, physical aggression and attention problems increased the odds of being in the marijuana use trajectories. Multiple indicators-student self-reports, teacher ratings and high school dropout records-showed that marijuana was not an isolated or benign event in the life of adolescents but part of an overall problem behavior syndrome.
Stiby et al looked at the educational outcomes of adolescent cannabis and tobacco smokers at age 16. The sample was drawn from The Avon Longitudinal Study of parents and Children (1,155 individuals). GCSE results in English and Mathematics were investigated. Both weekly cannabis use and daily tobacco use were associated at age 15 with subsequent adverse educational outcomes.

2015 Smith et al discovered that teens who were heavy marijuana smokers (16-17 year olds at start daily for around 3 years) had an abnormally-shaped hippocampus and performed poorly on long-term memory tasks. The hippocampus is important to long-term memory (remembering life events). The brain abnormalities were observed during the individuals’ early twenties, two years after they had stopped smoking marijuana. Young adults who abused cannabis as teenagers performed about 18% worse on long-term memory tests than those who had never abused cannabis. There were 97 participants who used no other drugs. The study also found that young adults with schizophrenia who abused cannabis as teens, performed about 26% more poorly on memory tests than young adults with schizophrenia who had never abused cannabis.

2015 Dudok and others carried out cell-specific super-resolution imaging to reveal nanoscale organisation of cannabinoid signalling. They found that recreational smoking of cannabis can dramatically reduce the number of molecules ensuring the fine-tuning of brain functions and significantly interferes in the two-way communication between neurons.Research showed that the number of receptors in synapses receiving endocannabinoid molecules decreased dramatically by around 85% after a six-day THC treatment, with total regeneration taking as long as six weeks. These findings indicate that cell type-specific nano-scale analysis of endogenous protein distribution is possible in brain circuits and identify previously unknown molecular properties controlling endocannabinoid signalling and cannabis-induced cognitive dysfunction.

2015 April Riba et al found that cannabis consumers show greater susceptibility to false memories. Chronic consumers show more difficulties than the general population in retaining new information and recovering memories. Chronic use also causes distortions in memory, making it easier for imaginery or false memories to appear. On occasion the brain can remember things that never happened. This can occur even weeks after consumption has stopped.

2015 Jacobus et al studied Neuropsychological performance in adolescent marijuana users with co-occuring alcohol use over 3 years. Adolescent marijuana users with concomitant alcohol use (MJ + ALC, n = 49) and control teens with limited substance use histories (CON, n = 59) were given neuropsychological and substance use assessments at project baseline, when they were ages 16-19. They were then reassessed 18 and 36 months later. MJ + ALC users performed significantly worse than controls, across time points, in the domains of complex attention, memory, processing speed, and visuospatial functioning. Earlier age of marijuana use onset was associated with poorer processing speed and executive functioning by the 3-year follow-up. They concluded that frequent marijuana use throughout adolescence and into young adulthood appeared linked to worsened cognitive performance. Earlier age of onset appears to be associated with poorer neurocognitive outcomes that emerge by young adulthood, providing further support for the notion that the brain may be uniquely sensitive to frequent marijuana exposure during the adolescent phase of neurodevelopment.
2015 Olivier and Ulf investigated cannabis access and academic performance. Discrimination against legality was introduced on terms of nationality. 54,000 course grades of students in Maastricht were examined before and after ‘legal’ cannabis. The academic performance of students no longer legally permitted to buy cannabis increased substantially. Effects were stronger for women and low performers.

2015 Becker et al found longitudinal changes in white matter microstructure after heavy cannabis use. 23 young adults(18-20 years), regular users were paired with 23 age, sex and IQ matched non-using controls. Onset of cannabis use was before 17.Reduced longitudinal growth in several areas of the brain. Greater amounts of cannabis use correlated with greater longitudinal reduction, as was relatively impaired performance on a measure of verbal learning. Heavy cannabis use in adolescence and early adulthood alters ongoing development of white matter microstructure, contributing to functional impairment.

2015 Arria et al used a large longitudinal cohort study of college students to test the direct and indirect effects of marijuana use on college grade point average (GPA) and time to graduate, with skipping classes as a mediator of these outcomes. The results showed a significant path from baseline marijuana use frequently to skipping classes at baseline to lower first semester GPA to longer time to graduate. Over time the rate of change in marijuana use was negatively associated with rate of change of GPA, but did not account for any additional variance in graduation time. Percentage of classes skipped was negatively associated with GPA at baseline and over time.

2015 Rigucci et al investigated the effect of high-potency cannabis on the microstructure of the corpus callosum (crucial part of brain responsible for communication between the two brain hemispheres, composed of white matter fibres, called axons). They found ‘the more cannabis you smoke and the higher the potency the worse the damage will be’. They examined the white matter in the brains of 56 people who reported a first episode psychosis at the South London and Maudsley NHS Foundation Trust, and 43 healthy participants from the local area. They also discovered that ‘frequent use of high potency cannabis significantly affects the structure of white matter fibres in the brain whether you have psychosis or not’. The worst damage (lesions) was seen in the most posterior part of the corpus callosum.

2016 Auer et al looked at the association between lifetime marijuana use and cognitive function in middle age. 5115 black and white men and women between 18 and 30 were followed up over 25 years. After excluding current users and adjusting for potential confounders, cumulative lifetime exposure to marijuana remained significantly associated with worse verbal memory.

2016 Nunez et al investigated heavy cannabis use and cognitive function in first episode psychosis. They found that haeavy cannabis consumption seems to impair verbal memory in first psychotic episode patients Heavy users also peformed worse than medium users in other neurocognitive tests. Non-users performed better than all cannabis users in the arithmetic test.

2016 Suerken et al investigated the academic outcomes among college students. 'Five marijuana trajectory groups were identified: non-users (69.0%), infrequent users (16.6%), decreasing users (4.7%), increasing users (5.8%), and frequent users (3.9%). Decreasing users and frequent users were more likely to drop out of college and plan to delay graduation when compared to non-users. All marijuana user groups reported lower GPA (Grade Point Averages), on average, than non-users.

These results identify marijuana use patterns that put students at risk for poor academic performance in college. Students who use marijuana frequently at the beginning of the college career are especially at risk for lower academic achievement than non-users.

2016 Dahlgren et al examined whether marijuana use could predict the cognitive performance of executive function. They included earlier age at onset, higher frequency, and increased magnitude of use. They found that marijuana smokers had poorer executive function relative to control participants, a between-group difference that was primarily driven by individuals with early onset of marijuana use (before age 16; n = 21); significance remained even when controlling for frequency and magnitude of use. Further, earlier age at marijuana onset and increased marijuana use predicted poorer neurocognitive performance, and perseverative errors on the WCST (Wisconsin Card Sorting Test) significantly predicted marijuana group membership.

2016 D'Amico et al looked at adolescent alcohol and marijuana use in connection with academic and health problems. A total of 6509 adolescents completed 7 surveys between 2008 and 2015. Those who use both alcohol and marijuana during middle and high school are more likely to have poorer academic performance and mental health. They also had poorer academic functioning, being less prepared for school and have more delinquent behaviour. Non-white youth tend to experience poorer functioning than white youth. Confounding factors may be racial discrimination, parental involvement or neighbourhood quality.

2016 Silveira et al investigated 'laziness' in cannabis users. They tested the hypothesis that THC impairs a relevant cognitive function for long-term success, namely willingness to exert cognitive effort for greater rewards, and that CBD could attenuate such decision-making impairments.
29 male Long–Evans rats performing the rat cognitive effort task (rCET) received acute THC and CBD, independently and concurrently, in addition to other cannabinoids. Rats chose between 2 options differing in reward magnitude, but also in the cognitive effort (attentional load) required to obtain them. They found that THC decreased choice of hard trials without impairing the animals' ability to accurately complete them. In contrast, CBD did not affect choice. Co-administration of 1:1 CBD:THC modestly attenuated the deleterious effects of THC in "slacker" rats. Only male rats were investigated, and the THC/CBD co-administration experiment was carried out in a subset of individuals. They concluded that: These findings confirm that THC, but not CBD, selectively impairs decision-making involving cognitive effort costs. However, co-administration of CBD only partially ameliorates such THC-induced dysfunction.

2016 Plunk et al looked at medical cannabis legalization and school drop-out rates. Data from the 2000 Census and 2001–2014 American Community Surveys were restricted to individuals who were of high school age (14–18) between 1990 and 2012 (*n* = 5,483,715). 'Medical Marijuana Laws (MML) were associated with a 0.40 percentage point increase in the probability of not earning a high school diploma after completing the 12th grade (from 3.99% to 4.39%). High school MML exposure was also associated with a 1.84 and 0.85 percentage point increase in the probability of college non-enrollment and degree non-completion, (from 31.12% to 32.96% and 45.30% to 46.15%, respectively). Years of MML exposure exhibited a consistent dose response relationship for all outcomes. MMLs were also associated with 0.85 percentage point increase in daily marijuana use among 12th graders (up from 1.26%)'. They concluded that 'Medical marijuana law exposure between age 14 to 18 likely has a delayed effect on use and education that persists over time'.

2016 Hebert-Chatelain et al looked at memory loss and cannabis and its relationship to mitochondrial harm. Mitochondria are small organelles in most cells responsible for energy regulation. Research has shown that cannabis can cause memory loss. The researchers found that chemicals in cannabis attach to CB1 receptors in mitochondria in brain cells in the hippocampus where memory processing occurs. It is suggested that memory loss may be due to cannabis use and its impact on these organelles. They suggest their findings indicatethat chronic use of the drug could cause permanent damage to mitochondria leading to long-term or permanent memory loss.

2016 Powell-Booth et al looked at the impact of cannabis on the neuro-cognitive performance of Jamaican adolescents. The sample consisted of 62 male students – 30 cannabis users and 32 non-users, between 13 and 17 years of age. There was a significant difference between the performance of cannabis users and non-users on all tests of learning, memory and attention.

2017 Meda et al Looked at the longitudinal influence of alcohol and marijuana use on academic performance in college students. The longitudinal 2-year Brain and Alcohol Research in College Students provided the data. 1142 freshman students completed monthly alcohol and marijuana surveys. 3 clusters emerged 1. No/low users of both, 2. medium-high alcohol /no marijuana and 3. medium-high users of both. Group 2 demonsrate low GPAs (Grade Point Average) compared to non-users, but the difference becomes non significant over time. Group 3 students score lower at outset and this continues over the 2-year time scale.

2017 Williams et al looked at academic ability in children in relation to cigarette, alcohol and cannabis use. Data from 7 years of the longitudinal Study of Young People in England, 2004 - 2010 was used. Ages were 13/14 to 19/20. 6059 (3093 females) provided information about academic ability and health at age 11. High v low academic ability reduced the risk of persistent cigarette smoking in early adolescence. High v low ability increased the risk of occasional and persistent regular alcohol drinking in early adolescence and persistent but not occasional regular alcohol drinking in late adolescence. High academic ability was also positively associated with occasional and persistent cannabis use in late adolescence. They concluded that: High childhood academic ability at age 11 is associated with reduced risk of cigarette smoking but increased risk of drinking alcohol regularly and cannabis use. These associations persist into adulthood providing evidence against the hypothesis that high academic ability is associated with temporary 'experimentation' with substance use.

2017 Filbey et al investigated the age of starting use of marijuana and whether it had long-term effects on brain development. 'Although groups (early onset >16 and later onset >16) did not differ by onset status, groups diverged in their correlations between cannabis use and cortical architecture. Among early-onset users, continued years of MJ use and current MJ consumption were associated with thicker cortex, increased GWR (gray/white matter border contrast) and decreased LGI(Local Gyrification Index) Late-onset users exhibited the opposite pattern. This divergence was observed in all three morphological measures in the anterior dorso-lateral frontal cortex'. 'Divergent patterns between current MJ use and elements of cortical architecture were associated with early MJ use onset. Considering brain development in early adolescence, findings are consistent with disruptions in pruning. However, divergence with continued use for many years thereafter suggests altered trajectories of brain maturation during late adolescence and beyond'.

2017 Patte et al looked at marijuana and alcohol use as predictors of academic achievement. 26,475 grade 9-12 student with at least 2 years of linked longitudinal data were tested for the likelihood of responses to measures of academic goals, engagement, preparedness, and performance when shifting from never using alcohol or marijuana at baseline to using them at varying frequencies at follow -up. 'Students who began using alcohol or marijuana were less likely to attend class regularly, complete their homework, achieve high marks, and value good grades, relative to their abstaining peers. Changing from abstaining to rare/sporadic-to-weekly drinking or rare/sporadic marijuana use predicted aspirations to continue to all levels of higher education, and initiating weekly marijuana use increased the likelihood of college ambitions, while more regular marijuana use reduced the likelihood of wanting to pursue graduate/professional degrees, over high school.

2017 Melchior et al studied early cannabis initiation and educational attainment. 'Analyses are based on data collected among TEMPO cohort study participants (France, 2009, n = 1103, 22-35 years). Participants were previously assessed in childhood (1991) and adolescence (1999); additionally, their parents had taken part in a longitudinal epidemiological cohort study (GAZEL). Early cannabis initiation was defined as use at age 16 or earlier. Educational attainment was defined as the completion of a high-school degree ('Baccalauréat'). Early (up to and including age 16 years) and late (after age 16 years) cannabis-use initiators were compared with non-users. In age- and sex-adjusted analyses, early cannabis initiators were more likely than non-users to have low educational attainment [odds ratio (OR): 1.77. Late cannabis initiators did not have lower educational attainment than non-users. Early cannabis use and educational attainment appeared more strongly associated in young women than in young men.

2017 Castellanos-Ryan et al looked at adolescent cannabis use and neurocognitive performance. 'The main objective of this prospective longitudinal study was to investigate bidirectional associations between adolescent cannabis use (CU) and neurocognitive performance in a community sample of 294 young men from ages 13 to 20 years. The results showed that in early adolescence, and prior to initiation to CU, poor short-term and working memory, but high verbal IQ, were associated with earlier age of onset of CU. In turn, age of CU onset and CU frequency across adolescence were associated with (a) specific neurocognitive decline in verbal IQ and executive function tasks tapping trial and error learning and reward processing by early adulthood and (b) lower rates of high-school graduation. The association between CU onset and change in neurocognitive function, however, was found to be accounted for by CU frequency. Whereas the link between CU frequency across adolescence and change in verbal IQ was explained (mediated) by high school graduation, the link between CU frequency and tasks tapping trial and error learning were independent from high school graduation, concurrent cannabis and other substance use, adolescent alcohol use, and externalizing behaviors. Findings support prevention efforts aimed at delaying onset and reducing frequency of CU'.

2017 Meier et al looked at the association between adolescent cannabis use and neuropsychological decline in a longitudinal co-twin control study. Abstract: Participants were 1989 twins from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally representative birth cohort of twins born in England and Wales from 1994 to 1995. Frequency of cannabis use and cannabis dependence were assessed at age 18. Intelligence quotient (IQ) was obtained at ages 5, 12 and 18. Executive functions were assessed at age 18. Compared with adolescents who did not use cannabis, adolescents who used cannabis had lower IQ in childhood prior to cannabis initiation and lower IQ at age 18, but there was little evidence that cannabis use was associated with IQ decline from ages 12-18. For example, adolescents with cannabis dependence had age 12 and age 18 IQ scores that were 5.61 ($t = -3.11$, $P = 0.002$) and 7.34 IQ points ($t = -5.27$, $P < 0.001$) lower than adolescents without cannabis dependence, but adolescents with cannabis dependence did not show greater IQ decline from age 12-18 ($t = -1.27$, $P = 0.20$). Moreover, adolescents who used cannabis had poorer executive functions at age 18 than adolescents who did not use cannabis, but these associations were generally not apparent within twin pairs. For example, twins who used cannabis more frequently than their co-twin performed similarly to their co-twin on five of six executive function tests ($Ps > 0.10$). The one exception was that twins who used cannabis more frequently than their co-twin performed worse on one working memory test (Spatial Span reversed; $\beta = -0.07$, $P = 0.036$). Short-term cannabis use in adolescence does not appear to cause IQ decline or impair executive functions, even when cannabis use reaches the level of dependence. Family background factors explain why adolescent cannabis users perform worse on IQ and executive function tests.

2018 Mouro et al investigated the harm done to the brain by cannabis and cannabis-based drugs. A new study led by Ana Sebastião, group leader at Instituto de Medicina Molecular João Lobo Antunes and Professor of Faculdade de Medicina of Universidade de Lisboa (iMM, FMUL; Portugal) and her team in collaboration with researchers from the University of Lancaster (UK), shows that the long-term use of either cannabis or cannabis-based drugs impairs memory. The study now published in the *Journal of Neurochemistry* reveals the implications for both recreational users and people who use the drug to combat epilepsy, multiple sclerosis and chronic pain. Through the legalisation in several countries of cannabis or cannabis-based drugs, there is an increased number of long-term users and more potent varieties are available for recreational users. It is already known that heavy, regular cannabis use increases the risk of developing mental health problems including psychosis and schizophrenia. However, there is still little understanding of the potential negative side effects of long-term cannabinoid exposure. Now, the research group led by Ana Sebastião in collaboration with Neil Dawson and his team at Lancaster University studied the effects of a specific cannabinoid drug (named WIN 55,212-2) and found that mice exposed for long-term to the drug had "significant memory impairments" and could not even discriminate between a familiar and novel object. Also, brain imaging studies showed that the drug impairs function in key brain regions involved in learning and memory. Moreover, the long-term exposure to the drug impairs the ability of brain regions involved in learning and memory to communicate with each other, suggesting that this underlies the negative effects of the drug on memory. "Importantly, our work clearly shows that prolonged cannabinoid intake, when not used for medical reasons, does have a negative impact in brain function and memory. It is important to understand that the same medicine may re-establish an equilibrium under certain diseased conditions, such as in epilepsy or multiple sclerosis, but could cause marked imbalances in healthy individuals. As for all medicines, cannabinoid-based therapies have not only beneficial disease-related actions, but also negative side effects", says Ana Sebastião. A previous study from the same team has showed that acute exposure to cannabinoids results in recognition memory deficits, an effect that can be prevented by the use of a drug of the family of caffeine. "These results are very important for the development of pharmacological strategies aiming to decrease cognitive side effects of currently used cannabinoid-based therapies, which proved effective against several nervous system disorders", explains Ana Sebastião. "This work offers valuable new insight into the way in which long-term cannabinoid exposure negatively impacts on the brain. Understanding these mechanisms is central to understanding how long-term cannabinoid exposure increases the risk of developing mental health issues and memory problems; only its understanding will allow to mitigate them", says Neil Dawson.

2018 Morin et al conducted a population-based analysis of the relationship between substance use and adolescent cognitive development. Abstract: Alcohol and cannabis misuse are related to impaired cognition. When inferring causality, four nonexclusive theoretical models can account for this association: 1) a common underlying vulnerability model; 2) a neuroplasticity model in which impairment is concurrent with changes in substance use but temporary because of neuroplastic brain processes that restore function; 3) a neurotoxicity model of long-term impairment consequential to substance use; and 4) a developmental sensitivity hypothesis of age-specific effects. Using a developmentally sensitive design, the authors investigated relationships between year-to-year changes in substance use and cognitive development. A population-based sample of 3,826 seventh-grade students from 31 schools consisting of 5% of all students entering high school in 2012 and 2013 in the Greater Montreal region were assessed annually for 4 years on alcohol and cannabis use, recall memory, perceptual reasoning, inhibition, and working memory, using school-based computerized assessments. Multilevel regression models, performed separately for each substance, were used to simultaneously test vulnerability (between-subject) and concurrent and lagged within-subject effects on each cognitive domain.Common vulnerability effects were detected for cannabis and alcohol on all domains. Cannabis use, but not alcohol consumption, showed lagged (neurotoxic) effects on inhibitory control and working memory and concurrent effects on delayed memory recall and perceptual reasoning (with some evidence of developmental sensitivity). Cannabis effects were independent of any alcohol effects.Beyond the role of cognition in vulnerability to substance use, the concurrent and lasting effects of adolescent cannabis use can be observed on important cognitive functions and appear to be more pronounced than those observed for alcohol.

2018 Schuster et al looked at abstinence from cannabis for a month and memory. Eighty-eight adolescents and young adults (aged 16–25 years) who used cannabis regularly were recruited from the community and a local high school between July 2015 and December 2016. Participants were randomly assigned to 4 weeks of cannabis abstinence, verified by decreasing 11-nor-9-carboxy-Δ9-tetrahydrocannabinol urine concentration (MJ-Abst; n = 62), or a monitoring control condition with no abstinence requirement (MJ-Mon; n = 26). Attention and memory were assessed at baseline and weekly for 4 weeks with the Cambridge Neuropsychological Test Automated Battery. ***:*** Among MJ-Abst participants, 55 (88.7%) met a priori criteria for biochemically confirmed 30-day continuous abstinence. There was an effect of abstinence on verbal memory ($P = .002$) that was consistent across 4 weeks of abstinence, with no time-by-abstinence interaction, and was driven by improved verbal learning in the first week of abstinence. MJ-Abst participants had better memory overall and at weeks 1, 2, 3 than MJ-Mon participants, and only MJ-Abst participants improved in memory from baseline to week 1. There was no effect of abstinence on attention: both groups improved similarly, consistent with a practice effect. This study suggests that cannabis abstinence is associated with improvements in verbal learning that appear to occur largely in the first week following last use. Future studies are needed to determine whether the improvement in cognition with abstinence is associated with improvement in academic and other functional outcomes.

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