

Cannabis förlängda effekt på det kognitiva systemet

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Sammanfattning: Cannabis långsiktiga effekt på exekutiva funktioner tycks ge en hindrande påverkan även efter 3 veckors (och längre) avhållsamhet. Emedan de grundläggande uppmärksamhets och korttidsminnesfunktionerna i stort sätt har normaliserats så kvarstår mätbara brister i beslutsfunktionen, konceptskapande och planering. Studierna avseende brister i Verbalt Flöde ger för närvarande blandat resultat. De individer som har använt cannabis under lång tid har störst kvarstående brister.

Den kliniska bilden visar:

- att den passiva perioden efter det akuta tillståndet, tenderar att bli längre och längre, ju oftare man brukar cannabis. Kliniskt kan man se den förlängda effekten efter ett bruk 3 gånger per vecka i 6 månader.
- att när detta passiva och "sega" tillstånd blir för utmärkande så ger den akuta effekten cannabisrökaren en känsla av att bli "normal".

En förklaring kan vara att efter en viss tid i eliminationsprocessen så ger THC inte den psykoaktiva aktiva effekten, utan GABA påverkan medför en nedreglering av aktiviteteten i de exekutiva funktionerna och påverkar såvitt vi kan förstå idag inte belöningssystemet excitatoriskt. Effekten blir då en nedreglering av aktiviteten det kognitiva systemet. Antagligen påverkas detta av hur ofta man använder cannabis.

Cannabis påverkan

De olika tillstånden som cannabinoiderna ger individen är

1. Akut påverkan som har två faser
 - Högdos effekt = utåtriktad och aktiv
 - Lågdos effekt = inåtriktad och aktiv
2. Förlängd påverkan som utvecklas i förhållande till frekvens och tid i missbruk på grund av ackumulering av aktivt THC
 - Lågdos effekt = inaktiv

Hjärnbarken, särskilt frontalloben, hippocampus, cerebellum och basala ganglierna har hög täthet av cannabisreceptorer. Receptorerna sitter framförallt vid utflödeskärnorna i dessa områden. Receptorernas placering indikerar en involvering i kognitiv funktion, speciellt exekutiv funktion. Cannabinoiderna förstärker GABA systemets hindrande aktivitet och försvagar därigenom individens förmåga att utnyttja sin intellektuella kapacitet. Hjärnans

neuropsykologiska nätverk fragmenteras. Därför påverkas fronto-limbiska bindningar, fronto-temporala bindningar och Precuneus. Forskningen har visat att följande kognitiva funktioner påverkas negativt: verbalt flöde, uppmärksamhet, koncentration, exekutiv funktion (Crean, 2011). Detta har också studerats inom Brain Imaging forskningen.

Om man jämför resultaten från Brain Imaging studier med resultat från studier som har använt neuropsykologiska instrument så ser man dessutom att de neuropsykologiska instrumenten uppvisar en tröghet i normalisering av funktion trots att systemet har återställts, vilket innebär att vi måste ta hänsyn till den enskilde individens kognitiva kapacitet (Lundqvist, T. 2009).

Forskning som stödjer en förlängd påverkan är

- Agurell et al 1986.
- Johansson, G 1988.
- Bergamaschi MM et al. 2013. **Konklusion:** Cannabinoider kan upptäckas i blod hos kroniskt dagliga cannabisbrukare efter en månads bibehållen abstinens. Detta stämmer överens med det tidsförlopp som har rapporterats i studier som mäter kvardröjande neurokognitiv funktion.

Det har sedan 70-talet funnits studier som indikerar att cannabinoiderna ger en toleransutveckling (abstinenssymtom) och att om man skulle blockera CB1-receptorn så skulle det med stor sannolikhet ge abstinenssymtom som liknar det vid opiatmissbruk (djurstudier). Därför kan man anta att cannabinoidernas elimineringsprocess till stor del släcker ut abstinensen (Jones R.T, 1981 och Bergamaschi MM et al. 2013).

När det gäller skador på sikt

visar flera studier att vissa delar av hjärnan förändrats i storlek hos personer som rökt cannabis i tio år eller längre och att dessa förändringar är bestående längre än den residuala (kvardröjande) effekten (21 dagar), (*t.ex. Solowij et al 2002*)

En möjlig förklaring är att cannabinoiderna förorsakar en sänkning av aktiviteten i de delar av hjärnan som ska utföra intellektuella aktiviteter på hög nivå. Detta medför en negativ påverkan på de tankefunktioner som vi behöver för att hantera vår vardag (Fontes et al. 2011 och Meier et al 2006).

Lundqvist (1995a) ordnade de kognitiva funktioner enligt psykologisk psykometri. De nedan beskrivna kognitiva kvaliteterna är inte oberoende av varandra. Tvärtom, ett samarbete dem emellan är nödvändigt. De är olika aspekter på ett tema, kognitiv kontroll och hantering av beteendemönster och kapaciteten är relaterad till exekutiv funktion. Effekten medför att cannabisrökaren ofta upplever sin personliga historia som hölj i dimmoln.

- *Den språkliga förmågan blir sämre.* Den kroniske missbrukaren (KM) får allt svårare att hitta ord och förstå vad andra menar, orden förlorar sin kvalitet. KM tänker konkret och blir kvalitativt avskärmd från sin omedelbara omgivning.

- *Förmågan att dra korrekta slutsatser blir sämre.* KM märker att misstag upprepas men förmågan att förstå vad det beror på försämras. Orsaken kopplas inte till cannabisrökningen.
- *Flexibiliteten i tanken minskar.* KM lyssnar inte så mycket på vad andra tycker utan har sina åsikter klara och nyanserar sällan dessa. Det innebär att KM talar *till* och inte *med* andra.
- *Minnet blir sämre.* Det medför att KM brister i uppmärksamheten, koncentration och svårigheter att hålla en röd tråd i samtal eller i en upplevelse. Missbruket påverkar också långtidsminnet, både vad det gäller omvärlden och personligt färgade (episodiskt minne) händelser.
- *Förmågan att sätta samman en helhet av delar blir sämre.* KM får svårare att urskilja vad som är väsentlig information, att känna att ”det är jag som tycker så”. Känslan av att leva i ett sammanhang och sträva mot hälsa försämras.
- *Förmågan att kunna orientera sig i rummet blir sämre.* KM lever ofta sin egen värld och är inte så intresserad av vad som händer runt omkring honom eller henne. KM bryr sig mindre om relationer mellan människor och planerar inte sin dag.
- *Helhetsminnet brister (Gestaltminne).* KM har svårigheter att återskapa mönster, vilket t ex kan leda till att man kan gå vilse i sin egen stad, likaså att man har tilltagande svårigheter att komma ihåg vilka relationer olika personer har till varandra. KM har ofta svårigheter att komma ihåg rutiner och hur man ska uppföra sig i olika situationer.

Den kvalitativa nedregleringen av dessa kognitiva funktioner normaliserades efter sex veckors avhållsamhet och behandling med KBT teknik.

Dessa sju kognitiva funktionerna är en central del i behandlingstekniken som beskrivs i Haschavvänjningsprogrammet (HAP). I metoden illustreras de som normalfunktion och vad som händer under cannabisinflytande. HAP är en metod som innehåller KBT, MI, MET och Återfallsprevention. dvs. (Lundqvist 1995b).

Det finns nu metaanalyser som har återgetts i sammanställningar. Den som tydligast har fokuserat på den förlängda effekten är Crean (2011). Hennes review återges här på sitt originalspråk.

An evidence based review of acute and long-term effects of cannabis use on executive cognitive function

Previously published reports (Pope et al., 2001; 2002) using traditional neuropsychological assessment methods typically show a resolution of deficits by 28 days of abstinence. However, as neuroimaging technology has improved, more recent reports show subtle, long-term effects of cannabis on cognition and brain functioning (Bolla et al., 2005). In addition, newly published reports suggest that the deficits change as a function of the quantity of cannabis consumed and duration of use (Solowij et al., 1995; 2002; Grant et al., 2003). Adolescents who started smoking between the ages of 14–22 years old and stopped by age 22 had significantly more cognitive problems at age 27 than their non-using peers (Brook et al., 2008). In addition, adult cannabis users who began smoking before the age of 17, but not users who began smoking after the age of 17, had significant impairments in measures of executive functioning, including abstract reasoning, verbal fluency, and verbal learning and memory compared to non-using controls (Pope et al., 2003).

Summary of the Residual Effects of Cannabis on Executive Functions Investigations on the residual effects of cannabis on executive functioning show that recently abstinent cannabis users (7 hours to 20 days) may experience impairment in certain aspects of executive functioning. Attention, concentration, inhibition and impulsivity may or may not continue to be impaired during the interval associated with the elimination of THC and its metabolites from the brain. Decision-making and risk-taking capabilities have not been thoroughly studied during this period, but a single study by Whitlow et al. (2004) suggests that these abilities are impaired. In contrast to the acute effects of cannabis in working memory, deficits as a function of residual cannabis effects have not been found. Findings for verbal fluency are somewhat mixed, but may be due in part to sample differences in degree of cannabis exposure. Studies showing the greatest deficits in executive functioning used subjects who had been smoking heavy amounts of cannabis for long periods of time. It is likely that residual impairments are linked to the duration and quantity of cannabis use.

Long-term effects of cannabis on executive functioning (3 weeks or longer since last use).

The long-term effects of cannabis use have received the greatest research attention in recent years. Nevertheless, this area of the literature has been fraught with inconsistencies in findings and is complicated by discrepant definitions of what constitutes “long-term effects.” For the purpose of this review, long-term effects refer to 21+ days since last using cannabis, which ensures that both the acute and residual effects of cannabis in the brain have been eliminated. Only a handful of researchers have examined these long-term effects of cannabis use on executive functions, as reviewed below.

Attention and Concentration: In five of seven studies, no attention or concentration impairments were found in subjects who had remained abstinent from 28 days to one year (Lyons et al., 2004; Pope et al., 2001; 2002; 2003; Verdejo-Garcia et al., 2005). Conversely, of the two remaining studies, Solowij (1995) examined cannabis users abstinent from 6 weeks to 2 years and found significant impairment in selective attention and concentration. Likewise, Bolla and colleagues (2002) found long-term deficits in attention and concentration in a sample of heavy, chronic cannabis users, abstinent for approximately 28 days. It is possible that these disparate findings are attributable to impairment in basic information processing skills rather than higher level attentional abilities. Information processing has not been examined in long-term cannabis abstinence.

Decision-Making and Risk-Taking: Another cognitive construct recently examined in abstinent cannabis users is decision making and risk-taking. One study compared cannabis users, cocaine users, and control subjects who were abstinent 25 days and found a trend towards significant impairment in decision-making and risk-taking in the cannabis group compared with non-cannabis using controls and no differences in performance when compared with the cocaine group (Verdejo-Garcia et al., 2006).

Inhibition and Impulsivity: The majority of research assessing the long-term effects of cannabis on inhibition and impulsivity have used two different tests: the Stroop Test or the Wisconsin Card Sort Test (WCST). Studies using the Stroop test have consistently found no significant differences between cannabis and control groups (Lyons et al., 2004; Pope et al., 2001; 2002; 2003; Verdejo-Garcia et al., 2005). In contrast, studies using the WCST have all found significant differences (Bolla et al., 2002, Pope et al., 2001; 2002; 2003), with the exception of Lyons et al. (2004). That study examined male monozygotic twins who used varying amounts of cannabis (>1 time/wk for a minimum of 1 year versus < 5 times in their

life time) and found no differences between the siblings. The Stroop test requires active selection and, as a result, may require inhibition of some aspects of attention to produce the appropriate response (Kosmidis et al., 2006) whereas the WCST requires additional functions such as conceptualizing, developing, and testing hypotheses, as well as inhibition (Huguelet et al., 2000). Both tests require the ability to perform set shifting and maintenance. It is possible that the discrepant findings in the cannabis literature may represent intact set shifting and maintenance but impairment in concept formation, planning and sequencing.

Working Memory: The only known study to analyze the long-term effects of cannabis on working memory is Vardejo-Garcia and colleagues (2005). This study did not find any significant differences between abstinent cannabis users and polysubstance abusers. Perhaps studies using a control group may yield more definitive findings in this area.

Verbal Fluency: Pope et al., (2001; 2002; 2003) examined verbal fluency after 28 days of abstinence. Performance differences between groups reported in the earlier studies were nonsignificant; however, the most recent study showed significant differences between groups on verbal fluency. This later study divided the cannabis groups based on age of onset (early and late) and compared their performance with a control group. Early onset cannabis users (who began smoking before age 17) demonstrated significant impairments in verbal fluency compared with controls. These findings suggest that age of onset, and possibly years of use, mediates the impact of long-term effects of cannabis on verbal fluency.

Summary of the Long-Term Effects of Cannabis on Executive Functions Cannabis appears to continue to exert impairing effects in executive functions even after 3 weeks of abstinence and beyond. While basic attentional and working memory abilities are largely restored, the most enduring and detectable deficits are seen in decision-making, concept formation and planning. Verbal fluency impairments are somewhat mixed at this stage. Similar to the residual effects of cannabis use, those studies with subjects having chronic, heavy cannabis use show the most enduring deficits.

Executive Function Measured	Acute Effects	Residual Effects	Long-Term Effects
Attention/Concentration	Impaired (light users) Normal (heavy users)	Mixed findings	Largely normal
Decision Making & Risk Taking	Mixed findings	Impaired	Impaired
Inhibition/Impulsivity	Impaired	Mixed findings	Mixed findings
Working Memory	Impaired	Normal	Normal
Verbal Fluency	Normal	Mixed findings	Mixed findings

Note: Acute Effects denotes 0–6 hours after last cannabis use;
Residual Effects denotes 7 hours to 20 days after last cannabis use;
Long-Term Effects denotes 3 weeks or longer after last cannabis use.

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