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Kroon, E.; Kuhns, L.; Cousijn, J.

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The short-term and long-term effects of cannabis on cognition: recent advances in the field

Emese Kroon[1,2], Lauren Kuhns[1,2] and Janna Cousijn[1,2]

The aim of this review is to discuss the most recent evidence for the short-term and long-term effects of cannabis on cognition. The evidence that cannabis intoxication is associated with short-term impairment across several basal cognitive domains, including learning and (episodic) memory, attentional control, and motor inhibition is increasing. However, evidence regarding the effects of long-term heavy cannabis use on cognition remains equivocal. Cannabis research suffers from difficulties in measuring cannabis exposure history, poor control over potential subacute effects, and heterogeneity in cognitive measures and sample composition. Multidisciplinary collaborations and investment in studies that help overcome these difficulties should be prioritized.

Addresses
[1] Neuroscience of Addiction (NofA) Lab, Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands
[2] The Amsterdam Brain and Cognition Center (ABC), University of Amsterdam, Amsterdam, The Netherlands

Corresponding author: Kroon, Emese (e.kroon@uva.nl)

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Introduction

Recent global changes in cannabis legislation parallel increases in use and decreases in harm perception [1,2]. Yet, there is still little conclusive evidence on the effects of cannabis use. This review specifically focuses on the effects of cannabis use on cognition. Cognition encompasses our thoughts and shapes our behaviour, and refers to distinct but partially overlapping processes such as learning, memory, attention, inhibition, decision-making, and emotion regulation. Cannabis contains over a hundred different cannabinoids including Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD [3]). Although the mechanisms are unclear, cannabinoids like THC and CBD potentially affect cognition through interactions with the endogenous cannabinoid system in the brain [4]. This system in-turn regulates many other neurotransmitter systems including the dopamine system often implicated in substance use disorders (SUD [5]). Moreover, like in other SUDs, the development of Cannabis Use Disorder (CUD) may also be related to pre-existing cognitive deficits [6]. Given the rapidly developing evidence base, we will discuss the most recent evidence for the effects of cannabis intoxication (short-term) and heavy cannabis use (almost daily use, long-term) on cognition (Table 1). We thereby start with basal cognitive functions, moving towards more complex cognitive functions and the role of affective processes therein.

Cannabis and cognition: current knowledge and recent advances

Learning and memory

Cannabis intoxication impairs learning and memory in a dose-dependent manner, although significant individual differences exist [7,8,9•]. Studies in heavy cannabis users are less consistent, but learning and immediate recall deficits are most commonly reported in active cannabis users [10••]. A recent longitudinal study [11•] in adolescent cannabis users suggests a causal link between cannabis exposure and immediate, but not delayed recall in an episodic memory task. Furthermore, another recent study showed that trial-by-trial verbal learning rates were slower in cannabis users compared to controls, and these learning rates were associated with altered functionality of the parahippocampal gyrus, thalamus and midbrain regions [12•]. While altered feedback processing may play a role in learning deficits observed in alcohol and other substance users, this may not necessarily be the case in cannabis users [13]. Furthermore, impairments may not be relegated to only memory of real experiences. Kloft *et al.* [14•] showed that cannabis intoxication increased susceptibility to false memory, an effect that appeared most prominent at immediate compared to delayed recall.

Subacute intoxication effects likely contribute to the described effects in cannabis users. The effects of cannabis on memory performance and related alterations in brain activity fade with abstinence [10••]. In line with this, working memory performance and functionality of the underlying brain network was only found to be impaired in individuals with a positive urine screen for THC [15•]. Despite the heterogeneous and potential timebound nature of the observed deficits, cannabis use-related learning and memory problems could seriously impact daily functioning of heavy cannabis users, including performance in school or at work. A combination of psychological, neurological, and neurobiological research [16••] is crucial to further elucidate the apparent

Table 1

Summary of current evidence for short-term and long-term effects of cannabis on cognition

	Short-term effects		Long-term effects		Suggested reading	
Domain	Evidence	Potential moderators	Evidence	Potential moderators	Reviews	Recent evidence
Learning and memory	**Sufficient** evidence that THC/cannabis impairs (non)-verbal learning and episodic memory. **Limited** evidence for impairment of other types of learning and memory.	Dose ↑ Early onset ↑ Heavy history ↓ Low THC:CBD ratio ↓	**Sufficient** evidence for impairments in current heavy users. **Insufficient** evidence for lasting effects after abstinence. Indications of (partial) recovery.	Subacute THC/cannabis effects ↑ Early onset ↑ Heavy history ↑ Comorbid mental health issues↑	[7,8,10••,16••]	[11•,12•,13,14•,36,37•]
Working memory	**Inconsistent** evidence that THC/cannabis impairs working memory.	–	**Inconsistent** evidence for long-term working memory deficits in current heavy users. **Limited** evidence for recovery after abstinence.	Subacute THC/cannabis effects ↑ Heavy history ↑ Early onset ↑ Task complexity ↑	[7,8,10••]	[15•]
Attentional control	**Sufficient** evidence that THC/cannabis impairs attentional control.	Dose ↑ Heavy history ↓	**Sufficient** evidence for impairments in sustained and divided attention in current heavy users. **Insufficient** evidence for lasting effects after abstinence. Indications of (partial) recovery.	Subacute THC/cannabis effects ↑ Early onset ↑ Heavy history ↑	[29,42••,52]	[9•]
Motor inhibition	**Sufficient** evidence that THC/cannabis impairs inhibition of ongoing responses (stop-signal task). **Inconsistent** results with other inhibition tasks.	Dose ↑	**Limited** and **inconsistent** evidence for impairments in current heavy users.	–	[29,42••,52]	[9•]
Cognitive biases	**Limited** evidence for cannabis-related approach bias and attentional bias.	–	**Sufficient** evidence for attentional bias, but **insufficient** evidence for approach bias in current heavy users. **No evidence** to support or refute lasting effects after abstinence.	Heavy history ↑ CUD severity ↑ THC ↑ Craving ↑	[24••,53]	[22,23,26•]
Emotion processing	**Consistent**, but **limited** evidence that THC/cannabis impairs emotion recognition, particularly for negative emotions.	Low THC:CBD ratio ↓	**Limited** evidence for impaired emotion identification/recognition in current heavy users. **No evidence** to support or refute lasting effects after abstinence.	–	–	[41•]
Decision making	**Insufficient** evidence that THC/cannabis impairs decision-making.	–	**Insufficient** and **inconsistent** evidence for impairments in current heavy users.	Cognitive subdomain	[29,43,53]	[11•]

This table is an adaptation and update of the table presented in Kroon *et al.* [31], focussing on the existing knowledge and most recent evidence for short-term and long-term effects of cannabis on cognition. The short-term effects column includes results from intoxication studies, while the long-term effects column includes evidence for the effects of longer periods of heavy (near daily) cannabis use on cognition.
THC = Δ9-tetrahydrocannabinol; CBD = cannabidiol.

complexity of mechanisms underlying the effects of cannabis on memory.

Attention

Similar to learning and memory, cannabis intoxication consistently results in a THC-dose-dependent reduction of the capacity to orient attention towards task-relevant stimuli [17–19]. In heavy compared to occasional cannabis users, tolerance to the acute effect of cannabis on attentional control was related to reduced responsiveness of the reward system after intoxication [20•]. This may relate to the general tolerance to cognitive impairments by cannabis intoxication often observed in heavy users [7,8,17,18,21]. Heavy cannabis users also develop an attentional bias towards cannabis and related objects that may interfere with other attentional processes [e.g. Ref. [22]. but see Ref. [23]). Although effect sizes were small, a recent meta-analysis showed evidence for an attentional bias towards cannabis-related words and pictures in heavy cannabis users [24••]. Attentional bias has been linked to the severity of CUD [25] and might reflect an involuntary early perceptual bias, supported by increased amplitude and earlier peak of the N1 component in response to distracting cannabis stimuli [26•].

Inhibition

Cannabis use, and drug use in general, has often been associated with poor inhibitory control. With regards to motor inhibition, cannabis intoxication consistently and dose dependently reduces the ability to inhibit an ongoing motor response, as measured with the stop-signal task (e.g. Refs. [27,28]). In contrast, inhibition before a response is initiated, as measured with the go/no-go task, may not be impaired by intoxication [28]. Findings on the effects of heavy cannabis use on motor inhibition are less consistent [29]. However, aside from potential problems caused by impairments in motor control due to cannabis intoxication [30], motor inhibition might not well-reflect the daily life inhibition problems present in most substance users. Indeed, slower proactive inhibitory control-related processes, such as those measured with the classical Stroop were found to relate to cannabis craving [23].

Decision-making

More complex cognitive functions such as decision-making heavily rely on the integrity of the basal cognitive functions discussed above and deficits in any of those might in turn result in risky decisions like substance use. The complexity of the processes involved may explain the inconsistent findings on the effects of cannabis intoxication and heavy use on decision-making [29,31]. Nonetheless, progress has been made and recent studies provide new insight into how heavy cannabis use and the context in which decisions are made affect risky decision-making. For example, a recent study on financial delay discounting (preferring immediate small rewards over delayed bigger rewards) observed a positive relationship between increased delay discounting and frequency of cannabis use [32]. Interestingly, Gilman *et al.* [33] found that heavy cannabis using adolescents compared to controls differed on risk taking in the social, safety, and ethical domains, but not the financial domain. In general, risky decision-making in heavy cannabis users seems associated with increased sensitivity to immediate gain accompanied by decreased loss sensitivity [34,35].

The importance of context and emotion

The previously discussed findings highlight the need for a more fine-grained investigation of cognitive subprocesses and their interactions, as well as the importance of the context in which cognition is measured. While cannabis use by a popular peer may bias decision-making in an occasional user, for individuals with a CUD, decision-making may be particularly compromised when confronted with cannabis-related cues. As with attentional bias, cannabis-related cues may also activate an approach bias towards cannabis in heavy cannabis users [25]. Moreover, acute stress may influence cognitive performance. For example, acute stress affects prospective memory performance in both heavy cannabis users and controls, but the effects are larger in heavy cannabis users [36]. On the other hand, increased working memory capacity seems to protect heavy cannabis users from craving under stressful circumstances [37•]. Taken together, potential cognitive deficits in heavy cannabis users may manifest themselves depending on contextual factors.

The impact of cannabis use on emotion processing is an important factor to consider herein. Although data is limited, cannabis intoxication may negatively affect emotion recognition [38]. This seems to be most apparent for negative emotions and appears to be related to reduced brain activity in reward and cognitive control related brain areas when presented with negative faces [39,40]. A recent study focusing on gender differences identified complex interactions between gender and cannabis use patterns in relation to the early processing of emotional stimuli (EEG, ERP: P1 and P3 [41•]). This highlights the general importance of assessing gender differences in the effects of cannabis use. This is a particularly relevant issue in the domain of emotion processing research because of the high rates of comorbidity between cannabis use and disorders associated with emotion processing (e.g. anxiety) and the commonly reported gender difference in the prevalence of these disorders.

Field wide difficulties and future directions

Aside from the classic confounders such as polysubstance use and comorbid mental health problems, as well as a lack of longitudinal data limiting our understanding of the causal relationship between cannabis and cognition, cannabis research is facing significant difficulties which have been brought to attention by the majority of recent reviews on the topic [10••,24••,42••,43]. While overcoming these difficulties is of utmost importance, clear solutions are still lacking.

First, the vast majority of studies on the long-term effects of heavy cannabis use on cognition share one confounding factor: the abstinence period. Studies show that THC metabolites are detectable in the plasma of heavy cannabis users for over a week [44] and even longer detectability is possible due to THC's lipophilic characteristics [45]. In line with this, cannabis-use-dependent neurocognitive impairments can be detected for as long as 28 days after cessation [46]. Hence, studies in current heavy cannabis users struggle to differentiate subacute from long-term effects. Although this confound should be acknowledged and more wide-spread assessment of THC metabolites is warranted, subacute effects should not always be seen as a problem in itself. After all, the mix of acute, subacute, and long-term effects represent what a current heavy cannabis user is dealing with in daily life. Nevertheless, more knowledge of the potential for recovery after abstinence and the role of CUD severity in recovery is needed.

Second, problems with quantifying use are often reported and pose a true problem for comparability across studies. Variable definitions of heavy cannabis use and the lack of standard cannabis units are recurrent problems. While both problems might reflect semantics, and defining categories for frequency and heaviness of use might indeed primarily require discussion, developing a standard unit is extremely complicated. Recently, attempts were made to develop a standard unit of cannabis [47,48••], but the complexity and variability in cannabis products and routes of administration hampers practicality. Cannabis contains over a hundred different types of cannabinoids and the THC:CBD ratio differs significantly between region and even between batches [49]. Poor knowledge about exposure history in most studies complicates research even further. To improve our knowledge base, accessible and more reliable methods to quantify cannabis use are needed. However, even then, research in most countries heavily relies on changes in local legislation to allow for these methods to be used.

Third, there are methodological problems that plague comparability in systematic reviews and meta-analyses. While increasing the amount of research will increase the power of these types of reviews, studies are rarely replicated and the variability between measures to assess the same cognitive construct remains a problem [24••,42••,43]. An increase in power will not reflect an increase in knowledge when this heterogeneity problem is not solved. In line with this, it remains important to be aware of the risks of assuming that similar tasks measure the same construct like is often done when aggregating results from stop-signal and go/no-go task [50].

Finally, it may be that the effects of heavy cannabis use on cognition are indeed mixed. The same dose of THC may result in impairments in some, while leading to improvement in others [51]. These individual differences are likely to depend on a large variety of moderating factors including THC:CBD ratio, differences in THC metabolization, poly-substance use, severity of cannabis dependence, age of onset, gender, and mental health. In turn, the combined effects of these factors might vary with the context under which cannabis is consumed and cognition is assessed.

Conclusion

The rapid increase of research into cannabis and its effects on cognition has provided us with answers as well as questions. While there is increasing evidence that cannabis intoxication negatively affects basal cognitive functions like episodic memory, attentional control, and motor inhibition, results on the long-term effects of heavy cannabis use, and potential recovery after abstinence, remain equivocal for most cognitive domains. Despite a slow start, cannabis research is breaking ground. Nevertheless, field-wide difficulties in quantification, methods of measuring cognitive constructs, and the influence of subacute effects seriously hamper the road ahead and require attention now. Multidisciplinary collaboration and investment in studies that solve these problems should be prioritized.

Conflict of interest statement

Nothing declared.

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