bulletin series 26 – August 2015

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bulletin

Cannabis use and cognition

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A large body of evidence shows that cannabis use acutely affects cognition[1-4]. This is particularly the case for verbal learning and memory[2], which refers to the ability to learn and remember verbal information such as a list of words, and response inhibition[1], which is suppression of actions that are inappropriate or interfere with goal completion. The effects of acute cannabis administration on these and other domains of cognition vary according to a number of factors, most notably, whether participants are occasional or regular users and the dose administered[1, 2, 5].

Outside of acute intoxication, regular cannabis users display a number of cognitive deficits compared with non-using controls, but research remains mixed in terms of the nature of cognitive deficits, who may be more susceptible (e.g., those who begin using cannabis in early adolescence, long-term heavy users, etc.), and the timeframe of impairment.

This bulletin summarises research on the acute effects of cannabis use on cognition, and reviews existing investigations of cognitive impairment in cannabis users at different points of abstinence. Finally, it raises the issue of the need to better control for pre-existing differences in cognition and/or cognition-related variables that may predispose individuals to earlier and/or heavier cannabis use to better understand the relationship between cannabis use and cognition.

Acute effects of cannabis use on cognition

Research has consistently shown administration of cannabis or delta-9-tetrahydrocannabinol (THC), the active component in cannabis, adversely affects verbal learning and memory. This effect appears to be dose and time dependent and most consistent among occasional cannabis users. For instance, a recent study[2] investigated the effects of a low and a high dose of THC (7.5mg vs 15mg) against placebo on 15 male participants, who were not frequent users of cannabis, over a period of 48 hours. Administration of 15mg THC has a negative effect on verbal learning at two hours and six hours post-administration, which was no longer present from eight hours onwards. The lower THC dose was similar to the placebo condition across time. Verbal memory was impaired by the higher THC dose at two hours post-administration, but this difference was no longer apparent at six hours onwards. Again, this effect was not seen at the lower THC dose. By eight hours, all THC cognitive effects had dissipated and by 24 hours, plasma levels were undetectable. In contrast, acute administration of THC has not reliably been found to impair verbal learning and memory in regular users[4]. The relative lack of impairments found in verbal learning and memory following acute use among regular and heavy cannabis users (compared to infrequent users) may suggest that tolerance to these effects develops following repeated use[3].

Unlike verbal learning and memory, acute impairments found on measures of response inhibition following THC administration are evident in both occasional and regular users[1]. For instance, in a study by Ramaekers et al (2008), occasional and frequent users of cannabis were compared across a range of cognitive measures before and after acute exposure to THC. Occasional users were negatively affected by THC on a number of tasks, including a critical tracking task (designed to assess perceptual motor control), a divided attention task (which measures the ability to perform two tasks simultaneously), and a stop signal task (used to measure response inhibition). The frequent user group showed THC-related impairments only in response inhibition. The finding of impaired response inhibition following acute THC exposure in regular users of cannabis has been replicated by other researchers[6]. Importantly, such findings indicate that regular use may lead to tolerance to the effects of THC for some cognitive functions but not others, such as response inhibition. The ability to suppress or terminate a response that is no longer appropriate or interferes with current goals is crucial to being able to adapt ongoing behaviour to suit changing environments and goals. Failure to do so (due to impaired response inhibition) may have very serious consequences in certain situations, such as while driving.

Studies have also found deficits following acute THC or cannabis administration on non-verbal memory tasks, working memory, executive functioning, and reward-related decision-making[5, 7], though such findings are somewhat less consistent than for verbal learning/memory and response inhibition, even across studies that examine the acute effects of cannabis in occasional users only. Finally, acute cannabis exposure does not appear to significantly impair simpler cognitive tasks, such as simple reaction time measures, or verbal fluency measures[2, 7].

Non-acute effects (12 hours and above)

People who use cannabis regularly, especially adolescents or adults who began using cannabis in early adolescence, typically display a number of cognitive deficits compared to occasional users and non-users when tested days, even weeks, after the period of acute intoxication. For instance, a recent study by Becker et al (2014) compared 35 college students who used cannabis daily (and had started using it before the age of 17 years) to 35 non-using students on a variety of cognitive tasks such as verbal learning and memory, executive planning, sustained attention, spatial working memory, and reward-related decision-making. Cannabis users showed significant impairments in verbal memory and reward-related decision-making compared to the non-using controls. Importantly, participants had been asked to not use cannabis for a period of 12 hours prior to testing so the results are unlikely to be the result of acute intoxication or withdrawal. Non-acute impairments in verbal learning and memory (persisting to varying extents) have also been documented in other studies using adolescent8, young-adult populations[9], adolescent-onset[10] and long-term heavy cannabis using adults[11].

It appears that different domains of cognition undergo varying levels of improvement following cessation of cannabis use. For instance, a recent study[8] investigated the cognitive changes undergone during a three-week period of abstinence from cannabis in a group of adolescent heavy cannabis users compared to a control group (who had used cannabis less than five times in their lifetime). The cannabis group showed significant deficits compared to the control group in the areas of verbal learning and memory at three days of abstinence, but these improved over time and were comparable to the control group at three weeks. In contrast, selective attention deficits that were present in the cannabis group compared to the control group at three days persisted throughout the entire three week testing period. Non-acute selective attention deficits in adolescent or young adult cannabis users have been documented in other studies[12, 13] and have been found to be associated with cannabis use frequency[14]. Interestingly, comparison of cannabis-using and non-using adults on behavioural measures of selective attention have largely failed to show such differences[10, 15].

In adults, relatively long-lasting cognitive impairment throughout abstinence from cannabis appears to occur mainly in the domain of verbal memory[10]. A study by Pope et al (2003)[10] investigated cognitive impairment and changes over a period of abstinence in a group of adult heavy cannabis users (daily smokers who smoked more than 5000 times in their lifetime) compared to a control group (who had used cannabis no more than 50 times in their lifetime). The cannabis group showed significant deficits compared to the control group one week following abstinence in the areas of verbal learning and memory, with verbal memory deficits persisting for up to one month, while verbal learning deficits improved and no longer differed from controls at one month of abstinence. However, when the authors controlled for 'premorbid' IQ, the verbal memory impairment found after one month of abstinence disappeared. The authors thus argued against the idea of cannabis having led to long-lasting cognitive deficits, as when they controlled for premorbid IQ (via current verbal IQ), group differences were no longer significant at the one month time point. Their argument, however, was based on the erroneous assumption that verbal IQ is stable over time and unaffected by cannabis use, thus a reliable indicator of premorbid IQ. This assumption has been challenged by recent longitudinal studies showing IQ, including verbal IQ, undergoes a significant decline over time as a result of persistent cannabis use[16]. To the extent that current verbal IQ does not reflect premorbid IQ in long-term cannabis users, Pope et al's (2003) lack of a finding of verbal memory impairment at one month abstinence after controlling for verbal IQ should be interpreted with caution.

That said, research does indicate there may be pre-existing factors related to cognition that could account for differences found in cognition between cannabis users and non-users. In other words, some group differences in cognition may not be the result of cannabis use per se, but may be due to pre-existing group differences. For instance, reduced cognitive inhibition (ability to suppress/ignore irrelevant information) in early adolescence has been found to predict greater cannabis use by late adolescence[17]. Thus, the relatively persistent selective attention deficits found in adolescent cannabis users[8] may in fact have preceded cannabis use. Similarly, reward-related decision-making has been found to predict subsequent heavy drinking in males[18] and ecstasy uptake in females[19], opening the possibility that related impairments among cannabis users[e.g., 20] might have preceded cannabis use. Inhibitory and reward-related cognitive processes need to be better investigated (alongside 'traditional' cognitive functions) in prospective longitudinal studies before concluding that long-term and/or early onset cannabis use leads to long-term cognitive impairments.

Summary

Findings of cognitive impairment are more consistent in studies examining acute exposure to cannabis or THC, especially in relation to response inhibition and verbal learning and memory. The latter acute effects are specific to occasional users and are not typically found among regular users. The former, i.e., acute deficits in response inhibition following exposure to THC, appear to apply to both occasional and regular users.

Findings of non-acute cognitive impairment related to cannabis use are largely mixed in terms of the type of deficit found and its persistence following cessation. More longitudinal studies that commence prior to the onset of cannabis use, measure a range of diverse cognitive functions and cannabis use parameters, and also take into account cognition-related personality differences (e.g. impulsivity), are needed to better understand the long-term effects of cannabis use and to untangle these effects from those of other variables that predispose young people to earlier and/or heavier use. Lastly, there appears to be a gap in the literature examining cognition in older cannabis using adults (› 50) and thus a lack of understanding of how cannabis use may affect age-related cognitive changes over time in this group.

References

1. **Ramaekers, J., Kauert, G., Theunissen, E., Toennes, S. W. & Moeller, M. (2008).** Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. *Journal of Psychopharmacology.*
2. **Curran, V., Brignell, C., Fletcher, S., Middleton, P. & Henry, J. (2002).** Cognitive and subjective dose-response effects of acute oral Δ9-tetrahydrocannabinol (THC) in infrequent cannabis users. *Psychopharmacology 164,* 61-70.
3. **Hart, C., van Gorp, W., Haney, M., Foltin, R. W. & Fischman, M. W. (2001).** Effects of Acute Smoked Marijuana on Complex Cognitive Performance. *Neuropsychopharmacology 25,* 757-765.
4. **Hart, C. L., Ilan, A. B., Gevins, A., Gunderson, E. W., Role, K., Colley, J. & Foltin, R. W. (2010).** Neurophysiological and cognitive effects of smoked marijuana in frequent users. *Pharmacology Biochemistry and Behavior 96,* 333-341.
5. **Weinstein, A., Brickner, O., Lerman, H., Greemland, M., Bloch, M., Lester, H., et al. (2008).** A study investigating the acute dose— response effects of 13 mg and 17 mg Δ 9- tetrahydrocannabinol on cognitive—motor skills, subjective and autonomic measures in regular users of marijuana. *Journal of Psychopharmacology 22,* 441-451.
6. **Metrik, J., Kahler, C. W., Reynolds, B., Mc Geary, J. E., Monti, P. M., Haney, M., De Wit, H. & Rohsenow, D. J. (2012).** Balanced placebo design with marijuana: Pharmacological and expectancy effects on impulsivity and risk taking**.** *Psychopharmacology 223,* 489-499.
7. **Morrison, P. D., Zois, V., McKeown, D. A., Lee, T. D., Holt, D. W., Powell, J. F., Kapur, S. & Murray, R. M. (2009).** The acute effects of synthetic intravenous Δ9-tetrahydrocannabinol on psychosis, mood and cognitive functioning. *Psychological Medicine 39*, 1607-1616**.**
8. **Hanson, K. L., Winward, J. L., Schweinsburg, A. D., Medina, K. L., Brown, S. A. & Tapert, S. F. (2010).** Longitudinal study of cognition among adolescent marijuana users over three weeks of abstinence. *Addictive Behaviors 35,* 970-976.
9. **Gonzalez, R., Schuster, R. M., Mermelstein, R. J., Vassileva, J., Martin, E. M. & Diviak, K. R. (2012).** Performance of young adult cannabis users on neurocognitive measures of impulsive behavior and their relationship to symptoms of cannabis use disorders. *Journal of Clinical and Experimental Neuropsychology 34,* 962-976.
10. **Pope, H. G., Gruber, A. J., Hudson, J. I., Cohane, G., Huestis, M. A. & Yurgelun-Todd, D. (2003).** Early-onset cannabis use and cognitive deficits: what is the nature of the association? *Drug and Alcohol Dependence 69,* 303-310.
11. **Solowij, N., Stephens, R. S., Roffman, R. A. & et al. (2002). C**ognitive functioning of long-term heavy cannabis users seeking treatment. *Jama 287,* 1123-1131.
12. **Abdullaev, Y., Posner, M. I., Nunnally, R. & Dishion, T. J. (2010).** Functional MRI evidence for inefficient attentional control in adolescent chronic cannabis abuse. *Behavioural Brain Research 215*, 45-57.
13. **Medina, K. L., Hanson, K. L., Schweinsburg, A. D., Cohen-Zion, M., Nagel, B. J. & Tapert, S. F. (2007).** Neuropsychological functioning in adolescent marijuana users: subtle deficits detectable after a month of abstinence**.** *Journal of the International Neuropsychological Society 13,* 807-820.
14. **Lisdahl, K. M., Wright, N. E., Medina-Kirchner, C., Maple, K. E. & Shollenbarger, S. (2014).** Considering Cannabis: The Effects of Regular Cannabis Use on Neurocognition in Adolescents and Young Adults. *Current Addiction Reports 1,* 144-156.
15. **Harding, I. H., Solowij, N., Harrison, B. J., Takagi, M., Lorenzetti, V., Lubman, D. I., Seal, M. L., Pantelis, C. & Yücel, M. (2012).** Functional connectivity in brain networks underlying cognitive control in chronic cannabis users. *Neuropsychopharmacology 37,* 1923-1933.
16. **Meier, M. H., Caspi, A., Ambler, A., Harrington, H., Houts, R., Keefe, R. S., et al. (2012).** Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proceedings of the National Academy of Sciences 109,* E2657-E2664.
17. **Squeglia, L. M., Jacobus, J., Nguyen-Louie, T. T. & Tapert, S. F. (2014).** Inhibition during early adolescence predicts alcohol and marijuana use by late adolescence. *Neuropsychology 28,* 782-790.
18. **Goudriaan, A. E., Grekin, E. R. & Sher, K. J. (2011).** Decision Making and Response Inhibition as Predictors of Heavy Alcohol Use: A Prospective Study. *Alcoholism: Clinical and Experimental Research 35,* 1050-1057.
19. **Schilt, T., Goudriaan, A., Koeter, M., van den Brink, W. & Schmand, B. (2009).** Decision making as a predictor of first ecstasy use: a prospective study. *Psychopharmacology 203,* 519-527.
20. **Becker, M. P., Collins, P. F. & Luciana, M. (2014).** Neurocognition in college-aged daily marijuana users. *Journal of Clinical and Experimental Neuropsychology 36,* 379-398.