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**The health effects of recreational cannabis use: A comment on the review by Hall**

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The past 20 years have seen a significant increase in research on the antecedents and consequences of cannabis use in young adults. At the beginning of this period there was a relative paucity of evidence concerning both: a) factors that increased the risk of cannabis use and dependence; and b) consequences of early and heavy cannabis use on health and adjustment. However, our understanding of these issues has increased dramatically over this period. The current state of knowledge of the effects of cannabis use on health and psychosocial functioning amongst young people is well-summarised in Hall's scholarly review of the evidence (1). Hall attributes this increase in knowledge to the contribution of a series of well-designed epidemiological studies, and in particular the evidence provided by longitudinal birth cohorts during a period of time in which regular cannabis use was relatively common.

In his review, Hall shows that there is now substantial evidence to suggest that cannabis use by young people is associated with a range of adverse health and psychosocial outcomes, including increased risks of: motor vehicle accidents; cannabis dependence; psychotic symptomatology; lower levels of educational attainment; use of other illicit drugs; cognitive impairment; and chronic bronchitis. In most cases, Hall shows that these linkages have both an age and dose-response gradient, such that these risks are stronger for those individuals who begin using cannabis at a younger age, and for those who use cannabis more heavily.

While Hall provides an excellent review of the evidence, an important issue that is not discussed concerns the future direction of research on cannabis. We are of the view that there are three areas of research that are of high priority:

1. *The role of neurophysiological factors.* Whilst there is growing evidence of the adverse impacts of cannabis on educational achievement, cognitive functioning and related outcomes, less is known about the extent to which these linkages are due to the long-term effects of cannabis on the brain. There is growing evidence from both animal and human studies that the use of

cannabis can lead to changes in neurophysiological structure and functioning. These changes include: alterations to the function of cannabinoid receptor CB1 (2); gray matter volume reduction (3); inhibition of synaptic pruning (4); reduction of hippocampal and amygdala volume (5); reductions in axonal connectivity (6); and reduced cerebral blood flow (7). These effects are particularly important during adolescence (8), and may explain the linkages between adolescent cannabis use and later educational and cognitive impairment. Developing a clear understanding of how cannabis affects the brain, and the consequences of this for later cognitive and related functioning is an area of high research priority.

2. *Genes and environment.* A second important issue concerns the extent to which cannabis use and dependence is influenced by genetic factors. In particular, evidence from twin studies has suggested the presence of quite substantial heritability ( $h^2$ ) for cannabis dependence, with estimates ranging from .44 to .78 (9, 10). For this reason, further research into the genetic factors that cause people to be susceptible to cannabis use and dependence may increase understanding of the effects of cannabis on psychosocial functioning.

In addition, there has been some evidence to suggest that the associations between cannabis use and psychotic symptomatology may be influenced by gene x environment interactions. Specifically, Caspi and colleagues found evidence that carriers of the COMT valine158 allele were at greater risk of psychotic symptomatology after using cannabis (11). However, these findings have not been replicated by other studies (12-15), and further studies have examined other possible gene by environment interactions in the linkages between cannabis use and psychotic symptomatology (16-18). It is clear that further research on possible gene x environment interactions is needed not only to elucidate the linkages between cannabis and psychosis, but also to explore the role of genetic factors in linkages between cannabis and other psychosocial outcomes.

3. *The changing legal environment and the use of cannabis.* Finally, perhaps the most important issue relating to cannabis concerns the extent to which changes in the legislation regarding cannabis have effects on population rates of consumption, and particularly rates of consumption by vulnerable young people. Recent changes to cannabis legislation in the USA and elsewhere (19) provide a number of natural experiments of both the risks and benefits of: a) legalizing medical marijuana; b) decriminalizing marijuana; and c) legalizing the supply of cannabis. The next decade will provide an opportunity to document both the benefits and risks associated with the changing legal landscape regarding cannabis use. Given the emerging evidence concerning the adverse effects of cannabis use, and the fact that the legalisation of the drug could arguably increase the level of risk posed by cannabis use (19), it is critical that these changes in cannabis legislation are monitored and evaluated through well-designed studies that are able to assess the impact of these law changes both at the individual and the population level.

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