Structural brain correlates of age of first alcohol and cannabis use: A magnetic resonance imaging study in healthy males

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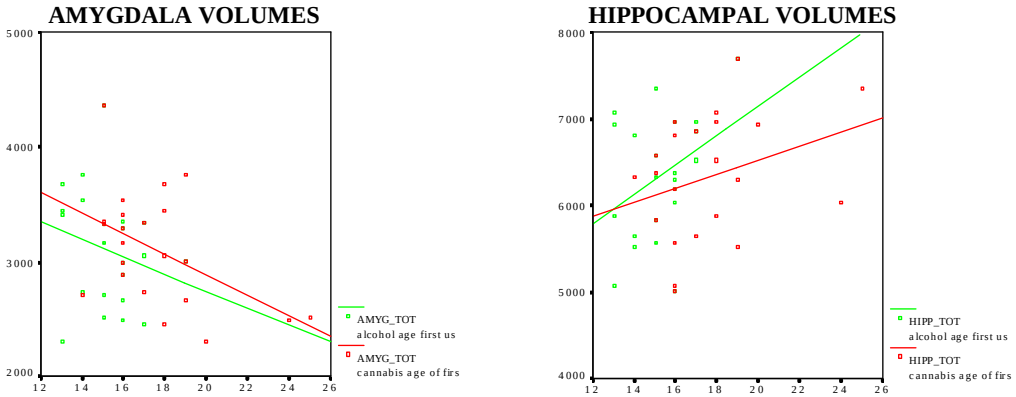
Background: Adolescence is a period during which there exist dynamic changes and maturational processes occurring within the brain that promote the acquisition of skills and behaviours necessary for independent living. In particular, changes occur within cortical and subcortical brain regions that regulate drive, affect and cognition (Wood et al., in press; Pine 2002; Luna et al., 2001). Disturbances within these same regions are associated with many psychiatric conditions, including substance use related disorders. Whilst the majority of teenagers experiment with alcohol and drugs, for most this is brief or recreational and typically they do not suffer long-term consequences. However, the true extent of the consequences and factors associated with drug and alcohol use, even social/recreational use, is still unclear (see Wilson et al., 2000).

Method: In this study, we used high-resolution structural MRI in 22 males (M age 23.3; SD 6.7; Range 16-41 years old) with a lifetime history of both alcohol and cannabis use. None of the subjects nor their first-degree relatives met diagnostic criteria for current or lifetime history of DSM-IV axis one disorders including substance use disorders. The volumes of the hippocampus and amygdala, as well as whole brain volumes were computed using manual tracing and automated techniques.

Results: Three separate linear regression analyses with hippocampal, amygdala and whole brain volumes as the dependent variables and age and intra-cranial volume (ICV) as covariates were performed. This revealed that age of first cannabis use (*p=0.001*), age of first alcohol use (*p=0.044*), and ICV (*p=0.008*) were all significant predictors of amygdala volumes. That is, earlier age of cannabis and alcohol use were independently predictive of larger amygdala volumes. As expected, ICV was also a significant predictor of whole brain and hippocampal volumes, but there was no significant effect of age of first cannabis or alcohol use on these measures. Visual inspection of the data for hippocampus shows that despite the fact that there was no significant association with age of first use, the nature of the relationship was in the opposite direction to that of the amygdala (i.e. earlier age of use was associated with smaller hippocampal volumes).



Discussion: The present results suggest that there is an association between age of first cannabis and alcohol use and regionally specific (e.g., amygdala) brain volumes, even within healthy 'recreational/social' users with no history of psychiatric illness nor formal diagnosis of a substance use disorder. This in interesting in the context of the increasing evidence that: (i) drug and alcohol use has been associated with subsequent development of affective disorders such as major depression and bipolar disorder (Patton et al 2003); (ii) affective disorders are associated with increased amygdala and decreased hippocampal volumes (Frodl et al., 2003; Altshuler et al., 2000), and that; (iii) compared with the mature adult, adolescents have an increased sensitivity to the neurotoxic effects of drug and alcohol use (Pyapali et al., 1999). Together, these differential relationships of cannabis and alcohol use on specific regions of the brain central nervous system have significant implications for the maturation of cognitive/executive control systems, as well as for the development of future psychopathology, especially in individuals who are already vulnerable. However, the relationship between drug and alcohol use and structural brain change is complex and poorly understood. For example, it unclear whether early use of cannabis leads to larger amygdala and smaller hippocampal volumes or that larger amygdala and smaller hippocampal volumes leads to an earlier age of drug and alcohol use. Clearly, further research is needed in this area to elucidate the consequences and associated factors related to drug and alcohol use.

References

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