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Review article

The brain effects of cannabis in healthy adolescents and in adolescents with schizophrenia: a systematic review

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ABSTRACT

Cannabis is widely used in adolescence; however, the effects of cannabis on the developing brain remain unclear. Cannabis might be expected to have increased effects upon brain development and cognition during adolescence. There is extensive re-organisation of grey (GM) and white matter (WM) at this time, while the endocannabinoid (eCB) system, which is involved in the normal physiological regulation of neural transmission, is still developing. In healthy adolescent cannabis users there is a suggestion of greater memory loss and hippocampal volume changes. Functional studies point to recruitment of greater brain areas under cognitive load. Structural and DTI studies are few, and limited by comorbid drug and alcohol use. The studies of cannabis use in adolescent-onset schizophrenia (AOS) differ, with one study pointing to extensive GM and WM changes. There is an intriguing suggestion that the left parietal lobe may be more vulnerable to the effects of cannabis in AOS. As in adult schizophrenia cognition does not appear to be adversely affected in AOS following cannabis use. Given the limited number of studies it is not possible to draw firm conclusions. There is a need for adequately powered, longitudinal studies.

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Contents

1. Introduction

Cannabis is the most common drug of misuse in Western countries (Murray et al., 2008). In a UK birth cohort – the Avon Longitudinal Study of Parents and Children (ALSPAC) – the prevalence of one per week cannabis use amongst 15–16 year olds was

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Table 1
NeuroImaging Studies of Cannabis Use in Adolescents.

Study	Average age of users (years) ± S.D.	Average age of controls (years) ± S.D.	Cannabis users (number)	Non-abusing controls (number)	Length of abstinence		Method	Observations in cannabis users compared to controls
					Minimum (days)	Average (days)		
Normal adolescents								
Abdullaev et al. (2010)	19.5 ± 0.8	19.7 ± 1.4	14	14	2	Unknown	Functional MRI	Stronger activation of the right prefrontal cortex
Ashtari et al. (2009) and 2011)	19.3 ± 0.8	18.5 ± 1.4	14	14	90	200	Structural MRI and DTI	Smaller right hippocampal volume correlated with cannabis use. Reduced fractional anisotropy, increased radial diffusivity, and increased trace in fronto-temporal connexions
Bava et al. (2009)	17.9 ± 0.9	17.8 ± 0.8	36	36	1	52.1	DTI	Lower FA in left superior longitudinal fasciculus (SLF), left postcentral gyrus, bilateral crus cerebri, and inferior frontal and temporal white matter tracts. FA was increased in the right occipital, internal capsule, and SLF regions. In particular. frontal-parietal circuitry affected.
Cheetham et al. (2011)	16.4 ± 0.6	16.5 ± 0.5	28	93	Unknown	Unknown	Structural MRI	Smaller orbitofrontal cortex volumes at age 12 predicted initiation of cannabis use by age 16 years
Cohen et al.(2011)	22.7 ± 2.4	Unknown	17	Unknown	Unknown	Unknown	Structural MRI	Increased grey matter reduction in lobule III with younger age of onset (although overall regional grey matter was in normal range)
Dekker et al. (2010)	Early use: 20.9 ± 2.9 Late use: 22.2 ± 2.3	21.1 ± 2.8	E: 10 L: 8	10	Unknown	Unknown	Structural MRI and DTI	Age of onset appeared independent of white matter changes
DeLisi et al. (2006)	21.1 ± 2.9	23.0 ± 4.4	10	10	Unknown	Unknown	Structural MRI	No significant change in any measured brain structures
Jacobsen et al.; (2007)	17.3 ± 1.1	17.0 ± 1.1	20	25	14	30	Functional MRI	During high verbal working memory load, nicotine withdrawal selectively increased task-related activation of posterior cortical regions and was associated with disruption of frontoparietal connectivity.
Jacobus et al. (2009)	16–19	16–19	14	14	23	Unknown	DTI	Higher FA in **4 regions**
Jacobus et al. (2012)	17.7 ± 0.7	17.5 ± 0.8	23	23	28	Unknown	DTI	Reduced CBF in including the left superior and middle temporal gyri, left insula, left and right medial frontal gyrus, and left supramarginal gyrusand increased CBF in the right precuneus at baseline which reverted to normal at 4 weeks.
Lopez-Larson et al. (2011)	17.8 ± 1.0	17.3 ± 0.8	18	18	Unknown	Unknown	Structural MRI	Decreased as well as increased cortical thickness in **specific areas**
McQueeny et al. (2011)	Male: 17.9 ± 0.9 Female: 18.2 ± 0.9	M: 17.7 ± 0.9 F: 17.9 ± 0.7	M: 27 F: 8	M: 36 F: 11	28	Unknown	Structural MRI	Compared to same-sex controls, female users demonstrated larger right amygdala volumes, male users had similar volumes
Medina et al.; (2009)	Male: 18.1 ± 0.8 Female: 18.2 ± 0.6	M: 17.7 ± 1.1 F: 18.5 ± 0.5	M: 12 F: 4	M: 10 F: 6	28	Unknown	Structural MRI	Compared to same-sex controls, female users demonstrated larger PFC volumes, male users had smaller volumes
Medina et al. (2010)	18.11 ± 0.7	18.0 ± 1.0	16	16	28	Unknown	Structural MRI	Larger inferior posterior vermis volumes
Padula et al. (2007)	18.1 ± 0.8	17.9 ± 1.1	17	17	28	Unknown	fMRI	More activation in right basal ganglia, right and left parietal lobes
Peters et al. (2009)	22.4 ± 2.6	22.6 ± 3.4	35	21	Unknown	Unknown	DTI	Use before age 17 associated with increased directional coherence in bilateral uncinate fasciculus, anterior internal capsule and frontal white matter
Rais et al. (2010)	21.8 ± 3.9	24.7 ± 6.7	19	31	Unknown	Unknown	Structural MRI	Excessive cortical thinning in 5 areas

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