Associations between adolescent cannabis use and brain structure in psychosis

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ABSTRACT

Associations between cannabis use and psychotic disorders suggest that cannabis may be a contributory risk factor in the neurobiology of psychosis. In this study, we examined brain structure characteristics, total and regional gray matter density (GMD), using Voxel Based Morphometry, in psychotic individuals, stratified by history of cannabis use (total n = 109). We also contrasted GMD estimates in individual diagnostic groups (schizophrenia/bipolar I disorder) with and without history of adolescent cannabis use (ACU). Individuals with psychosis as a whole, both with and without history of ACU, had lower total and regional GMD, compared to healthy controls. ACU was associated with attenuated GMD reductions, compared to non-users, especially in the schizophrenia cases, who showed robust GMD reductions in fronto-temporal and parietal cortex, as well as subcortical regions. Notably, total and regional GMD estimates in individuals with psychosis and ACU were not different from controls with no ACU. These data indicate that the history of ACU in psychotic individuals is associated with attenuated GMD abnormalities. Future investigations targeting potential unique etiological and risk factors associated with psychosis in individuals with ACU may help in understanding of the neurobiology of psychotic disorders and novel treatment options for these individuals.

1. Introduction

According to the UNO World Drug Report, about 3.8 percent of the global population used cannabis in the past year, roughly the same proportion as in the last decade (United Nations Office on Drugs and Crime, World Drug Report 2017), making cannabis among the most frequently used illicit drugs in the world. In the US, the prevalence of cannabis use is on the rise and has reached 13.5% of the population (United Nations Office on Drugs and Crime, World Drug Report 2017). Cannabis use disorders are a common comorbidity for schizophrenia and related psychotic disorders, with a recent meta-analysis estimating current cannabis use at 16%, and lifetime cannabis use at 27%, with higher rates in males and in first episode schizophrenia individuals (Roskinen et al., 2010). Cross-sectional and longitudinal studies show a consistent relationship between cannabis use and psychotic disorders (Gage et al., 2016). Cannabis use prior to onset of psychosis (Semple et al., 2005) is associated with earlier onset of illness (Tosato et al., 2013). In addition, onset of cannabis use at younger ages (Large et al., 2011) and the frequent use of more potent strains of cannabis are associated with higher risk of developing psychosis (Di Forti et al., 2014). This temporal and dose response relationship between cannabis use and psychosis (Kraan et al., 2016) suggests that cannabis can be a contributory risk factor in the neurobiology of psychotic disorders. This clinical observation can also be found in basic neuroscience studies showing that the adolescent brain responds differently to cannabis use than the adult brain, making it susceptible to cannabis use and resulting in lasting effects on brain circuitry and morphology (Grigorenko et al., 2002; Kittler et al., 2000; Quinn et al., 2008; Reali et al., 2011; Rubino and Parolaro, 2016; Rubino et al., 2009).

An unexpected and intriguing observation is that premorbid cannabis use in schizophrenia is associated with better cognitive function, compared to individuals with schizophrenia without history of cannabis use (Hanna et al., 2016; Schnell et al., 2012; Yucel et al., 2012), though some studies have not supported this observation (Ringen et al., 2010). Schnell et al., (2012) have found less severe cognitive impairments and...
There was a higher proportion of Cannabis Dependence among HC-ACU compared to HC-NonACU ($\chi^2(2)= 3.91$, $p= 0.05$) and PSY-ACU compared to PSY-NonACU ($\chi^2(2)= 22.88$, $p= 0.001$).

We recently reported that in individuals with psychosis (schizophrenia/schizoaffective disorder) and cannabis use disorder (CBD), ACU was associated with less impaired global cognitive function, as measured by the Brief Assessment of Cognition in Schizophrenia (BACS), compared to cannabis non-users (Hanna et al., 2016). Further, we found that this effect on cognition was specifically driven by differences between the SZ with and without history of ACU, and not the BP, subgroups.

Here, we extended our work by examining brain structure characteristics—whole brain and regional gray matter density (GMD)—in...
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