Published in final edited form as:

Addict Behav. 2011 July ; 36(7): 773–776. doi:10.1016/j.addbeh.2011.02.006.

Explaining associations between cannabis use disorders in adolescence and later major depression: A test of the psychosocial failure model

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Abstract

Aims—Cannabis use disorders (CUDs) in adolescence are associated with increased risk for later major depressive disorder (MDD). The goal of this study was to examine the “psychosocial failure” explanation for this association: the possibility that psychosocial consequences of CUDs in adolescence account for the increased risk for later MDD.

Methods—Participants ($n=1252$) were drawn from the community-based sample of the Minnesota Twin Family Study and were assessed at ages 17, 20, and 24. CUDs and MDD were assessed via structured interview. “Psychosocial failure” was defined as educational failure (high school dropout), occupational failure (persistent unemployment), or engagement in crime.

Results—Psychosocial failure partially mediated the association between CUDs in adolescence and later MDD.

Conclusions—The adverse psychosocial consequences of CUDs in adolescence partially—but not fully—account for the observed association between early CUDs and later MDD.

Keywords

Cannabis dependence; Cannabis abuse; Major depression; Longitudinal; Adolescence; Mediation

1. Introduction

Heavy and/or frequent cannabis use in adolescence is associated with increased risk for later major depressive disorder (MDD; Degenhardt et al., 2003; Hayatbakhsh et al., 2007; Patton et al., 2002; van Laar et al., 2007). This association tends to remain significant after accounting for potential confounding variables (Patton et al., 2002; Hayatbakhsh et al., 2007; van Laar et al., 2007; but see Harder et al., 2008 and Pedersen, 2008). The effect may

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Contributors

Dr. Iacono designed the Minnesota Twin Family Study, the longitudinal study from which these data were drawn. Dr. Marmorstein designed this data analysis project, in collaboration with Dr. Iacono. Dr. Marmorstein conducted the literature review, ran the analyses, and wrote the first draft of the manuscript. Both Dr. Iacono and Dr. Marmorstein contributed significantly to the revision of the manuscript and both authors have approved the final manuscript.

Conflict of Interest

The authors have no conflicts of interest to disclose.

be particularly strong among adolescents (Schneider, 2008) but does not appear to be present for light or infrequent cannabis use (Degenhardt et al., 2003).

Three mechanisms have been proposed to explain this association (Degenhardt et al., 2003; Hayatbakhsh et al., 2007; Patton et al., 2002; van Laar et al., 2007): (1) biological effects (cannabis causes changes in neurotransmitter systems that increase the likelihood of depression); (2) shared vulnerabilities (common genetic and/or environmental vulnerabilities predispose some people to both problems); and (3) adverse psychosocial consequences of cannabis use (educational failure, unemployment, and crime mediate this association). We know of no human research directly addressing possible biological mechanisms (#1). However, research on rats indicates that long-term cannabinoid consumption may alter the responsiveness of the serotonin system in ways consistent with those observed in depression (Hill et al., 2006) and placebo-controlled trials in humans have demonstrated that cannabinoids can lead to dysphoria among cancer patients (Tramer et al., 2001). Cross-sectional research with adults suggests that shared vulnerabilities (#2) may contribute to this association (Lynskey et al., 2004), though mood disorders aggregate separately from cannabis use disorders (CUDs) within families (Merikangas et al., 2009). Although heavy drug use in adolescence has negative psychosocial consequences (e.g., Fergusson & Horwood, 1997; Kandel et al., 1986; Lynskey and Hall, 2000), we know of no previous research addressing the possibility that psychosocial consequences of heavy/frequent cannabis use mediate the association between this use and later MDD (#3).

We investigated the possibility that negative psychosocial consequences of CUDs in adolescence mediated the association between adolescent CUDs and early adulthood MDD, a possibility that we term the “psychosocial failure model” (#3, above). Specifically, we analyzed whether educational failure, unemployment, and crime (the three psychosocial consequences suggested in the literature; Degenhardt et al., 2003; Hayatbakhsh et al., 2007; Patton et al., 2002; van Laar et al., 2007) mediated the association between CUDs in adolescence and later MDD (while adjusting for the effects of earlier MDD and gender). Because it is plausible that more than one of the explanatory models accounts for the association, we expected to find evidence for partial mediation—the mediational path would be significant, but that a significant association between early CUDs and later MDD would remain even after accounting for psychosocial failure. In supplemental analyses, we examined whether adjusting for (1) conduct disorder (CD) and (2) parental MDD would affect the results, due to the associations between these factors and both CUDs and MDD and the fact that both of these factors could predict MDD in early adulthood (the dependent variable) after controlling for the effect of adolescent MDD.

2. Methods

2.1 Participants

Participants were drawn from the Minnesota Twin Family Study, a longitudinal community-based study of twins and their parents. All twins born in the state of Minnesota during target birth years were identified, and over 82% of those meeting inclusion criteria participated. They first were assessed at age 17 ($n=578$ males, 674 females) and re-assessed at 20 and 24. At 20, 83% and 94% of males and females, respectively, returned to the study; at 24, 92% and 94% of the original sample of males and females, respectively, returned. The University of Minnesota IRB approved this study, and informed consent and assent were obtained.

The sample was 98% white. Average socioeconomic status corresponded to parental occupations such as small business owners and clerical and sales workers. For more information regarding the study design and participant characteristics, see Iacono et al. (1999) and Iacono and McGue (2002).

2.2 Measures

2.2.1 Psychosocial failure—A participant was considered to experience “any psychosocial failure” if he/she experienced educational failure (not graduating from high school or earning a GED by 20), occupational failure (at 20 or 24, a period of unemployment of at least 6 months or more during a period that he/she wanted to work), or crime (in trouble with the police, aside from traffic stops, at any assessment). We also considered two psychosocial failure subtypes: educational or occupational failure (due to these being developmental variants on similar problems), and engaging in crime. The column headings in Table 1 include the prevalence of psychosocial failure.

2.2.2 MDD and CUDs—The Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al., 1987) was used to assess MDD at 17, 20, and 24. Lifetime definite (meeting all DSM-III-R criteria) or probable (missing one symptom) diagnoses of MDD at 17 were used as a measure of adolescent MDD; if a participant endorsed definite or probable MDD occurring since the last assessment at 20 or 24 (thereby indicating that he/she had MDD between the initial assessment at 17 and the third assessment at 24), this was considered to indicate MDD in early adulthood. Bereavement and organic rule-outs were applied. Therefore, MDD diagnoses were not made based on depressive episodes that were substance-induced. The Substance Abuse Module of the Composite International Diagnostic Interview (CIDI-SAM; Robins et al., 1987; Robins et al., 1988) was used to assess lifetime DSM-III-R diagnoses of cannabis abuse and cannabis dependence at age 17. If a participant endorsed experiencing definite cannabis abuse or probable or definite cannabis dependence, he or she was considered to have a CUD. Table 1 presents prevalences of these diagnoses (see column 1 and row 1).

2.2.3 CD and Parental MDD—A modified version of the SCID was used to assess CD. All symptoms had onsets prior to age 15. If a participant endorsed probable or definite DSM-III-R CD, he or she was considered to have CD (17.6%). Lifetime MDD in parents was assessed using the SCID. If either parent reported a history of definite or probable MDD (38.6%), parental MDD was considered present.

2.2.4 Infrequent cannabis use—At 17, if participants endorsed using cannabis at least once per year but not more than once per month, they were considered to engage in infrequent cannabis use (3.9%). Sixty-five percent of these participants used marijuana at least once per year but less than once per month, while 35% used it about once per month but less than 2–3 times per month.

2.3 Statistical Analyses

Phi correlations were conducted to describe associations among the diagnoses and psychosocial failure.

All other analyses in the study were conducted using generalized estimating equations to adjust for the presence of correlated observations (twins nested within families; Liang & Zeger, 1986). The logit link function was used, as appropriate with binary data (diagnosis present/absent). To examine whether similar associations between adolescent CUDs and later MDD were found in our sample as in other samples, we first entered CUD at 17, MDD at 17, and gender as independent variables and MDD after age 17 as the dependent variable. This analysis was then repeated using infrequent cannabis use instead of CUD.

The primary analyses were conducted in four stages. First, to examine whether CUDs in adolescence predicted psychosocial failure, we entered CUDs at 17 (with MDD at 17 and gender) as the independent variable and psychosocial failure as the dependent variable.

Second, to examine whether psychosocial failure predicted MDD, we entered psychosocial failure (with MDD at 17 and gender) as the independent variable and MDD after 17 (i.e., subsequent to the baseline assessment) as the dependent variable. Third, to examine whether CUDs in adolescence continued to predict later MDD once psychosocial failure was adjusted for, we entered CUDs at 17 and psychosocial failure (with MDD at 17 and gender) as the independent variables and MDD after 17 as the dependent variable. Fourth, to formally assess for mediation, we conducted Sobel tests using the parameter estimates (and associated standard errors) from the models using CUDs in adolescence to predict psychosocial failure and those using psychosocial failure to predict later MDD. A significant Sobel value indicated that the mediational path (indirect effect) was significant—i.e., that a significant portion of the CUD-MDD link could be explained by the joint effects of CUD on psychosocial failure and psychosocial failure on MDD.

We repeated these primary analyses considering the psychosocial failure subtypes—educational/occupational failure and crime—instead of the “any psychosocial failure” variable to assess differences according to type of psychosocial problem.

Finally, we repeated the primary analyses twice, adjusting for the effects of (1) CD and (2) parental MDD.

3. Results

All measures were significantly correlated with each other (Table 1).

Adjusting for adolescent MDD and gender, CUDs in adolescence were associated with an approximately 3-fold increase in risk for later MDD ($OR=2.95$, $CI=1.62-5.37$). To alleviate possible concerns about how robust this main effect was, we repeated the analysis examining the association between CUDs at 17 and MDD between 17 and 24 adjusting simultaneously for sex, MDD by 17, parental MDD, alcohol use disorders by 17, nicotine dependence by 17, and CD. The association remained significant ($OR=2.62$ ($CI: 1.22-5.65$)) even after accounting for these possible confounding influences. Infrequent marijuana use in adolescence was associated with any psychosocial failure ($OR=2.65$, $CI=1.42-4.95$) but not with increased risk for later MDD ($OR=.52$, $CI=.19-1.40$).

Table 2 presents odds ratios representing risks of: (1) psychosocial failure among people with CUDs in adolescence; (2) MDD after 17 among people with psychosocial failure; and (3) MDD after 17 among people with CUDs in adolescence, adjusting for the effect of psychosocial failure. All analyses adjusted for MDD in adolescence and gender. If the effect of CUDs in adolescence became non-significant once psychosocial failure was adjusted for, this would indicate that psychosocial failure fully mediated the association between adolescent CUDs and later MDD. The Sobel test indicates whether the mediational path was significant.

These results indicate that partial mediation was present—psychosocial failure mediated the association between CUDs in adolescence and later MDD, but the link between these disorders remained significant even once the effect of psychosocial failure was accounted for. This pattern of results was similar when subtypes of psychosocial failure were examined, though the Sobel coefficient for educational/occupational failure was only significant at a trend level ($p=.06$). This pattern of results remained similar when CD and parental MDD were adjusted for, though the Sobel coefficient in the analyses adjusting for CD was only significant at a trend level ($p<.07$).

4. Discussion

The results of this study indicate that the adverse psychosocial consequences of CUDs in adolescence—educational failure, unemployment, and crime—partially mediate the association between CUDs in adolescence and later MDD. Specifically, the mediational path linking adolescent CUDs to psychosocial consequences to later MDD was significant; however, even after these psychosocial consequences were adjusted for, early CUDs continued to significantly predict later MDD. Therefore, the adverse psychosocial consequences of CUDs in adolescence partially—but not fully—account for the observed association between early CUDs and later MDD. These results are consistent with our hypothesis that other factors, such as shared vulnerabilities and biological effects of cannabis use, likely also contribute to this association.

When psychosocial consequences were divided into two categories (educational/occupational problems and crime), the pattern of results was similar. We also conducted supplemental analyses adjusting for CD and parental MDD, and these yielded similar results, indicating that the findings of this study are not simply due to the joint correlations between these factors and CD or parental MDD.

The pattern of CUDs but not infrequent use of cannabis predicting increased risk for MDD is consistent with other research (Degenhardt et al., 2003). This implies that there is a threshold for cannabis misuse that must be exceeded before increased risk for MDD becomes apparent.

This study had limitations. Although the sample was representative of the state of Minnesota at the time the participants were born, it was predominantly Caucasian. Although our definition of psychosocial failure captured the concepts referred to in prior literature, we do not know to what degree they fully embrace aspects of psychosocial failure that could influence these results.

Thus, although adverse psychosocial consequences of having CUDs in adolescence are related to risk for later MDD, these consequences do not fully account for the observed association between CUDs in adolescence and later MDD. Future research examining biological mechanisms and shared vulnerabilities models, and/or other possible adverse psychosocial consequences, will be helpful in increasing our understanding of this association.

Acknowledgments

Role of Funding Sources

This study was supported by grants AA09367 from the National Institute on Alcohol Abuse and Alcoholism, and DA022456, DA05147 and DA016892 from the National Institute on Drug Abuse. NIAAA and NIDA had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

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Table 1

Correlations between MDD and CUD diagnoses and psychosocial failure

	MDD after 17 (13.9%)	Any Psychosocial failure (21.3%)	Educational/ occupational failure (7.8%)	Crime (15.6%)
CUD at 17 (6.6%)	.14***	.17***	.12***	.21***
MDD after 17		.10**	.08**	.07*
Any Psychosocial failure			.56***	.83***
Educational/occupational Failure				.09**
Crime				--

*
 $p < .05$;**
 $p < .01$;***
 $p < .001$;

MDD=major depressive disorder; CUD=cannabis use disorder

Table 2

Odds ratios (95% confidence intervals) representing associations between CUDs in adolescence, psychosocial failure, and later MDD^a

Independent Variables	Dependent Variables		Sobel ^b (SE)
	Psychosocial failure (type varies by model)	MDD after 17	
Model 1: Psychosocial failure (any)			
CUD at 17	3.66*** (2.20–6.08)		
Psychosocial failure		1.97** (1.32–2.94)	
CUD at 17 adjusting for psychosocial failure		2.54** (1.40–4.60)	2.78** (.32)
Model 2: Educational/occupational failure			
CUD at 17	3.17** (1.71–5.91)		
Educational/occupational failure		1.82* (1.06–3.13)	
CUD at 17 adjusting for educational/occupational failure		2.79** (1.54–5.09)	1.86 [§] (.37)
Model 3: Crime			
CUD at 17	5.40*** (3.12–9.36)		
Crime		1.87** (1.16–3.01)	
CUD at 17 adjusting for crime		2.54** (1.38–4.68)	2.37* (.45)

[§] $p=.06$;

* $p<.05$;

** $p<.01$;

*** $p<.001$;

MDD=major depressive disorder; CUD=cannabis use disorder; SE=standard error. The prevalences of the variables in this table are: CUD by 17=6.6%; MDD after 17=13.9%; any psychosocial failure=21.3%; educational/occupational failure=7.8%; crime=15.6%.

^a all models adjust for MDD by age 17 and gender

^b values presented are the Sobel test statistic and its associated standard error, with the significance level indicated by accompanying asterisks.