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Author Manuscript
Faculty of Biology and Medicine Publication

This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Published in final edited form as:

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serveur académique lausannois

UNIL | Université de Lausanne
Faculté de biologie
et de médecine

Is the relationship between major depressive disorder and self-reported alcohol use disorder due an artificial one?

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Running head: Major depressive disorder and alcohol use disorder

Key-words: Alcohol use; confounder; negative thinking pattern; youth.

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Abstract

Aims. Many studies have suggested a close relationship between alcohol use disorder (AUD) and major depressive disorder (MDD). This study aimed to test whether the relationship between self-reported AUD and MDD was artificially strengthened by the diagnosis of MDD. This association was tested comparing relationships between alcohol use and AUD for depressive people and non-depressive people.

Methods. As part of the Cohort Study on Substance Use Risk Factors, 4,352 male Swiss alcohol users in their early twenties answered questions concerning their alcohol use, AUD, and MDD at two time points. Generalized Linear Models for cross-sectional and longitudinal associations were calculated.

Results. For cross-sectional associations, depressive participants reported a higher number of AUD symptoms (β = 0.743, p < .001) than non-depressive participants. Moreover, there was an interaction (β = -0.204, p = .001): the relationship between alcohol use and AUD was weaker for depressive participants rather than non-depressive participants. For longitudinal associations, there were almost no significant relationships between MDD at baseline and AUD at follow-up, but the interaction was still significant (β = -0.249, p < .001).

Conclusions. MDD thus appeared to be a confounding variable in the relationship between alcohol use and AUD, and self-reported measures of AUD seemed to be overestimated by depressive people. This result brings into question the accuracy of self-reported measures of substance use disorders. Furthermore, it adds to the emerging debate about the usefulness of substance use disorder as a concept, when heavy substance use itself appears to be a sensitive and reliable indicator.

Is the relationship between major depressive disorder and self-reported alcohol use disorder an artificial one?

Introduction

The associations between alcohol use disorder (AUD) and major depressive disorder (MDD) are a well-studied topic: many studies have suggested a close relationship between these two major health problems (Blow et al., 2007; Boden and Fergusson, 2011; Conner et al., 2009; Davis et al., 2008). One systematic review (Boden and Fergusson, 2011) reported a moderate association between AUD and MDD, with adjusted odds ratios (OR) ranging from 1.03 to 4.21. Several studies have examined the causal relationship between AUD and MDD. The most plausible explanations have been that: 1) AUD increases the risk of MDD because it induces social difficulties and physical health problems (Foster et al., 1999); 2) the two disorders are linked by common genetic factors (Kuo et al., 2010; Wang et al., 2004); 3) alcohol use causes metabolic changes which increase the risk of MDD (McEachin et al., 2008); 4) individuals with MDD use alcohol as a coping strategy and for mood enhancement (Grant et al., 2009; Young-Wolff et al., 2009); and 5) the stigma associated with AUD worsens later psychiatric disorders, including the severity depression (Glass et al., 2014; Hatzenbuehler, 2009).

However, another issue may also explain the relationship between self-reported AUD and MDD: depressive individuals are known to exhibit negative thinking patterns (Ackermann and DeRubeis, 1991; Strunk and Adler, 2009; Strunk et al., 2006), i.e. to have inaccurate and negative views of themselves and their behaviors (Beck, 1967, 1976). Therefore, the judgments of depressive people are contaminated by a systematic negative bias: they give inaccurate descriptions of themselves, e.g. self-perception of their competencies, skills, and characteristics (Greenberg et al., 1992; Whitton et al., 2008). Depressive people may also be

able to make better judgments than non-depressive people under some circumstances (e.g. more accurate perception of task performance, no illusion of control bias), a phenomenon called "depressive realism" (Moore and Fresco, 2012). Therefore, one can wonder whether the associations between MDD and AUD, in self-reporting studies of the general population, are artificially enhanced because depressive individuals rate AUD items according to their negative views of themselves. Indeed, AUD is stigmatized (Glass et al., 2014; Nutt and Rehm, 2014; Rehm et al., 2013; Schomerus et al., 2011), and thus depressive people may well apply their negative views to this topic, just as they do to other aspects of their lives and personalities.

This study thus aimed to test whether the relationship between self-reported AUD and MDD was artificially strengthened by the diagnosis of MDD; it used a longitudinal design, as recent authors have suggested (Glass et al., 2014). To test the hypothesis, a robust and non-stigmatized indicator of AUD was needed and alcohol use itself seemed to be sufficiently accurate for this purpose; heavy alcohol use is associated with various measures of AUD (Bohn et al., 1995; Knight et al., 2002). Although alcohol use itself is not included as a criterion in the latest Diagnostic and Statistical Manual of Mental Disorders' (DSM-5, American Psychiatric Association, 2013) definition of AUD, it is clear that anyone with an AUD diagnosis consumes alcohol, and previous studies have reported that alcohol use itself should be a suitable criterion in future classifications (Nutt and Rehm, 2014; Rehm et al., 2013; Saha et al., 2007). Moreover, alcohol use alone is not stigmatized in the way that AUD is (Kandel, 1980; Nutt and Rehm, 2014; O'Grady, 2013). Indeed, depending on the population (*e.g.* youth), drinking alcohol can even be a socially desirable behavior.

If the diagnosis of self-reported AUD is contaminated by MDD diagnosis instead of being a 'real' association between MDD and AUD—whatever the causal pathway—we would expect: 1) a positive relationship between alcohol use and AUD in non-depressive people, *i.e.* the

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more alcohol people drink, the more symptoms of AUD they exhibit; and 2) this relationship to be lower, or even non-existent, in depressive people because of MDD's confounding effect on this association. We assumed that this contamination would occur at the same time, i.e. for concurrent MDD diagnosis and self-reported AUD. Thus, we expect that 3) in cross-sectional associations, MDD diagnosis will be associated with an increased number of symptoms of self-reported AUD, but 4) in longitudinal associations, MDD diagnosis will not predict the number of later symptoms of self-reported AUD.

Method

Participants and procedures

The data are part of the Cohort Study on Substance Use Risk Factors (C-SURF). C-SURF is a longitudinal study designed to assess substance use patterns among young Swiss men. Participants were enrolled in three of Switzerland's six army recruitment centres, located in Lausanne (French-speaking), Windisch, and Mels (German-speaking), and covering 21 of the country's 26 cantons (including all French-speaking ones). Because there is no pre-selection for conscription and participation in the recruitment procedure is obligatory in Switzerland, all Swiss men around 20 years old were eligible for inclusion in the present study. Assessment was carried out outside of the army environment. Indeed, army recruitment centers were used to inform and enroll participants but the study was independent of the army and of eligibility for military service.

Baseline data were collected between September 2010 and March 2012, and follow-up data were collected between January 2012 and April 2013, with an average of 15 ± 2.8 months between the two assessments. A total of 5,990 participants filled in the baseline questionnaire; 5,223 (87.2%) filled in the follow-up questionnaire. The sample presented in this study focused on alcohol users only (N = 4,598). Missing values were deleted listwise, and the final

sample consisted of 4,352 participants (94.7% of the alcohol users). A previous study about sampling and non-response bias by (Studer et al., 2013) reported a small non-response bias. Lausanne University Medical School's Clinical Research Ethics Committee approved the study protocol (No. 15/07).

Measures

DSM-5 alcohol use disorder. AUD was assessed at baseline and follow-up using the 11 criteria of alcohol dependence in DSM-5 (American Psychiatric Association, 2013). We used a continuous numbered scale of criteria (from 0 to 11) instead of a cut-off, partly because recent literature assumes alcohol dependence to be a concept with a more continuous dimension to it, rather than a categorical model (Kerridge et al., 2013), and partly because alcohol dependence may not yet have been diagnosed in such young populations.

Alcohol use. Participants completed an extended quantity-frequency (QF) measurement questionnaire of alcohol use at both baseline and follow-up. The extended QF questionnaire captures the variability in drinking habits better than with other instruments (Gmel et al., 2014), providing separate information on weekends and weekdays over the previous tlweve months. Choices for the usual number of weekend drinking days (Friday, Saturday, and Sunday) were 3 days, 2 days, or 1 day per weekend, 2-3 weekend days per month, and 1 weekend day or fewer per month. The same style of choices was given for weekday drinking days (Monday to Thursday), with the highest frequency category being four days per week. Quantities consumed per drinking day (in standard drinks containing approximately 10-12g of pure alcohol) were closed-ended (answer categories: 12 drinks or more (coded '13'), 9-11 drinks, 7-8 drinks, 5-6 drinks, 3-4 drinks and 1-2 drinks). Midpoints of the categories were used, and the measures were converted into a total number of drinks per week. As the distribution of the extended QF questionnaire was skewed, a log transformation was applied.

We also measured risky single-occasion drinking (RSOD) at baseline and follow-up using the standard measure from the Alcohol Use Disorder Identification Test (AUDIT), *i.e.* a quantity of six drinks or more on any one occasion in the previous 12 months. Weekly or more frequent RSOD was coded '1', and '0' otherwise.

The age of first alcohol use was also assessed.

Depression. The WHO's Major Depressive Inventory (ICD-10) was used to assess levels of depression at both baseline and follow-up (Bech et al., 2001; Olsen et al., 2003). This inventory is a twelve-item questionnaire that screens answers on a six-point scale coded from '0' (never) to '5' (all the time). The scoring procedure and cut-off described by Bech et al. (2001) were used to define MDD according to DSM-IV, using nine criteria (three criteria use two items and take the higher score of the two). A diagnosis of MDD was coded '1', and '0' otherwise.

Demographic covariates. Demographic covariates included language (French- or German-speaking), age, perceived family income as a proxy for level of income ('below average income', 'average income', 'above average income') and level of education attained ('lower secondary', 'upper secondary', 'tertiary').

Statistical analyses

Initial descriptive statistics were calculated, including prevalence rates of MDD and weekly RSOD, medians for the extended QF questionnaire, and means for the number of AUD symptoms.

Cross-sectional and longitudinal relationships were subsequently tested using Generalized Linear Models (GLM, Poisson regression). A first model regressed the number of AUD symptoms on the extended QF questionnaire (logged), MDD, and the interaction between the extended QF results and MDD. This regression was carried out once for cross-sectional

associations (baseline data) and once for longitudinal associations. For longitudinal associations, we adjusted for the number of AUD symptoms at baseline, and we added MDD at follow-up as a predictor. Extended QF questionnaire was not included in the model because of its collinearity with numbers of AUD symptoms. A second model tested the relationship between MDD and alcohol use, to see if MDD was a predictor of alcohol use. Again, this was calculated once for cross-sectional associations and once for longitudinal associations, adjusting for alcohol use at baseline for the longitudinal model.

All analyses were calculated controlling for age, educational attainment, financial situation, age of onset of alcohol use, RSOD, and language (baseline data).

We used two sensitivity analyses: the first one used the continuous score of MDD (logged because the distribution was skewed) instead of the dichotomous diagnosis of MDD, and the second one used a dichotomous variable of alcohol use instead of the continuous number of drinks per week. Drawing on Rehm et al. (2013), a variable with a cut-off of an average of at least 10g pure alcohol per day was created (*i.e.* seven drinks a week, coded '0' if participants drank less alcohol than the cut-off, and '1' otherwise). The results were the same as those presented below, with a little less statistical power for dichotomous alcohol use.

All analyses were conducted using SPSS 21 software.

Results

Participants' characteristics

The average age of participants was 19.9 ± 1.2 years old at baseline and 21.2 years old at follow-up. The average age of first alcohol use was 14.4 ± 1.8 years old. A total of 53.2% of participants were French-speaking. At baseline, almost half of the participants had a lower secondary level of education (49.5%), and 27.0% had a tertiary level of education. Only

13.4% had a perceived family income below average income, whereas 46.5% had a perceived family income above it.

Table 1 presents statistics for alcohol-related variables and MDD. Only a small proportion of participants met the criteria for major depression according to DSM-IV: 2.3% at baseline and 2.5% at follow-up (not shown in Table 1). The number of AUD symptoms was quite low: participants reported an average of 1.38 and 1.35 AUD symptoms at baseline and follow-up, respectively. Overall average alcohol use, as measured by the extended QF questionnaire, was less than six drinks a week. However, nearly a quarter of the participants reported weekly or more frequent RSOD.

Insert Table 1 about here

Associations between alcohol use and AUD controlling for MDD

In cross-sectional associations, all factors were significantly related to the number of AUD symptoms (see Table 2). As expected, the number of AUD symptoms increased as alcohol use increased (β = 0.583, p < .001). Depressive people reported a higher number of AUD symptoms (β = 0.743, p < .001), and the loading was higher for MDD than for alcohol use. More interestingly, the interaction between MDD and alcohol use was a negative one, meaning that the relationship between alcohol use and the number of AUD symptoms was weaker for depressive people than for non-depressive ones (β = -0.204, p = .001).

In longitudinal associations, alcohol use at baseline predicted the number of AUD symptoms at follow-up (β = 0.323, p < .001), but MDD at baseline did not predict later AUD (β = 0.017, p = .839). However, the interaction was significant (β = -0.249, p < .001). There was also a cross-sectional association between MDD at follow-up and the number of AUD symptoms at follow-up (β = 0.269, p < .001).

Insert Table 2 about here

Associations between alcohol use and MDD

The relationship between alcohol use and MDD was non-significant (not shown in Table 1): MDD did not predict alcohol use for either cross-sectional (β = -0.040, p = .631) or longitudinal associations (β = -0.136, p = .073).

Discussion

This study aimed to test whether MDD distorted self-reported measures of AUD.

First, in both cross-sectional and longitudinal associations, alcohol use measured using the number of drinks per week (*i.e.* extended QF questionnaire) was a predictor of AUD. This result was in line with previous studies showing both alcohol use and heavy alcohol use to be good indicators of AUD (Bohn et al., 1995; Knight et al., 2002; Rehm et al., 2013; Saha et al., 2007).

Beyond this result, in cross-sectional associations, there was an association between MDD and the number of AUD symptoms. Depressive participants reported more AUD symptoms than non-depressive participants, which may suggest an overestimation due to the negative thinking patterns of depressive people.

Moreover, the significant negative interaction between MDD and alcohol use on the number of AUD symptoms showed that the relationship between alcohol use and the number of AUD symptoms was weaker for depressive participants than for non-depressive participants. Being depressive weakened the link between alcohol use and AUD, and thus appeared to be a confounding variable. The fact that MDD was not significantly associated with alcohol use provides further support to this hypothesis.

As mentioned in the introduction, symptoms of AUD are stigmatized (Glass et al., 2014; Nutt and Rehm, 2014; Rehm et al., 2013; Schomerus et al., 2011), whereas alcohol use measured by the number of drinks consumed is not (Kandel, 1980; Nutt and Rehm, 2014; O'Grady, 2013). As depressive people are more likely to share negative and inaccurate views of themselves (Ackermann and DeRubeis, 1991; Beck, 1967, 1976; Strunk and Adler, 2009; Strunk et al., 2006), they may have quoted the criteria for diagnosing AUD in a pessimistic and negative way (*i.e.* significant positive principal effect of MDD), disconnected from 'real' alcohol use (*i.e.* significant negative interaction between alcohol use and MDD).

In longitudinal associations, there was no principal effect of MDD at baseline on the later number of AUD symptoms at follow-up, whereas MDD at follow-up was associated with concurrent number of AUD symptoms. Therefore, MDD's association with AUD, as highlighted in cross-sectional comparisons, was concurrent but not stable over time, even if the significant interaction suggested that previous MDD diagnosis still lowered the association between alcohol use and number of AUD symptoms. This result further supported the idea of a contamination by MDD diagnosis in self-reported surveys with long-term relationships being inconsistent.

This study had some limitations—the most important being that it only included men. To establish whether its findings were consistent for both sexes would require a study including women. Indeed, women are more likely to be depressive than men (Kessler et al., 1993; Piccinelli and Wilkinson, 2000). A second limitation was that no external diagnoses were included in the study. The actual clinical state of the participants would be required to decide whether self-reported AUD is really contaminated by MDD. Further investigations including both external and self-reported diagnoses are needed. A last limitation was that no direct measure of negative thinking patterns among depressive participants was assessed. Therefore,

it is possible that another component of MDD contribute to the overestimation of self-reported AUD. Future studies may also include a measure of negative thinking pattern.

In conclusion, this study suggested that the relationships between self-reported measures of AUD and MDD were distorted by MDD diagnosis. MDD diagnosis appeared as a confounding variable in the relationship between alcohol use and AUD. Self-reported measures of AUD may be overestimated because of the systematic negative bias and negative thinking patterns of depressive people. This result, therefore, not only questioned the accuracy of self-reported measures of substance use disorders, but it also added to the emerging debate about the usefulness of substance use disorder as a concept, especially when heavy substance use itself appears to be a sensitive and reliable indicator (Glass et al., 2014; Rehm et al., 2013). Labelling drinkers as 'dependent' may thus not be the best way to detect alcohol-related problems, reduce the burden of disease associated with alcohol use, and cure patients.

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Table 1. Descriptive statistics

	Overall 100% (N=4,352)		Major depressive disorder 2.3% (N=99)		No major depressive disorder 97.7% (N=4,253)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Alcohol use disorder, mean (SD)	1.38 (1.76)	1.35 (1.65)	3.03 (3.30)	2.11 (2.45)	1.35 (1.69)	1.33 (1.62)
Risky single-occasion drinking, % (n)	24.6 (1,069)	22.6 (983)	38.4 (38)	27.3 (27)	24.2 (1,031)	22.5 (956)
Extended QF, median (IQR)	5.67 (9.85)	5.85 (10.48)	7.00 (16.27)	5.85 (13.73)	5.67 (9.85)	5.85 (10.49)

SD, standard deviation; IQR, Interquartile range

Table 2. Adjusted[*] cross-sectional and longitudinal associations of AUD, major depressive disorder and alcohol use

	Cross-sectional associations		Longitudinal associations	
	β	p-value	β	p-value
Extended QF (logged)	0.583	< .001	0.323	< .001
Major depressive disorder	0.743	< .001	0.017	.839
Interaction extended QF × major depression	-0.204	.001	-0.249	< .001
Major depressive disorder (follow-up)	-	-	0.269	< .001

DV, dependent variable; AUD, alcohol use disorder; QF, quantity/frequency

[*]Adjusted for age, educational attainment, financial situation, onset of alcohol use, RSOD, and language for all models, and also the number of AUD symptoms at baseline for longitudinal associations.