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Evaluation of Cognitive Behavioral Therapy/Motivational Enhancement Therapy (CBT/MET) in a Treatment Trial of Comorbid MDD/AUD Adolescents

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Abstract

Objective—Behavioral therapies developed specifically for co-occurring disorders remain sparse, and such therapies for comorbid adolescents are particularly rare. This was an evaluation of the long-term (2-year) efficacy of an acute phase trial of manualized cognitive behavioral therapy/motivation enhancement therapy (CBT/MET) versus naturalistic treatment among adolescents who had signed consent for a treatment study involving the SSRI antidepressant medication fluoxetine and CBT/MET therapy for comorbid major depressive disorder (MDD) and an alcohol use disorder (AUD). We hypothesized that improvements in depressive symptoms and alcohol-related symptoms noted among the subjects who had received CBT/MET would exceed that of those in the naturalistic comparison group that had not received CBT/MET therapy.

Methods—We evaluated levels of depressive symptoms and alcohol-related symptoms at a two-year follow-up evaluation among comorbid MDD/AUD adolescents who had received an acute phase trial of manual-based CBT/MET (in addition to the SSRI medication fluoxetine or placebo) compared to those who had received naturalistic care.

Results—In repeated measures ANOVA, a significant time by enrollment status difference was noted for both depressive symptoms and alcohol-related symptoms across the two-year time period of this study, with those receiving CBT/MET demonstrating superior outcomes compared to those who had not received protocol CBT/MET therapy. No significant difference was noted between those receiving fluoxetine versus those receiving placebo on any outcome at any time point.

Conclusions—These findings suggest long-term efficacy for an acute phase trial of manualized CBT/MET for treating comorbid MDD/AUD adolescents. Large multi-site studies are warranted to further clarify the efficacy of CBT/MET therapy among various adolescent and young adult comorbid populations.

Keywords

Cognitive behavioral therapy; motivational enhancement therapy; comorbidity; adolescents; alcohol use disorder; major depression; follow-up

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1. Introduction

Behavioral therapies developed specifically for co-occurring disorders remain sparse (Carroll, 2004), and such therapies that have been designed and tested among comorbid adolescents are particularly rare. Our own group of researchers previously conducted a pilot study involving open label (not double-blind) fluoxetine in combination with CBT/MET therapy in adolescents with comorbid major depressive disorder (MDD) and an alcohol use disorder (AUD). Fluoxetine is a widely prescribed selective serotonin reuptake inhibitor (SSRI), which is a type of antidepressant medication. Fluoxetine has been approved by the Food and Drug Administration (FDA) for treatment of major depressive disorder among adolescents and adults. The results of that pilot study demonstrated efficacy for treatment during the acute phase trial and also at each of the yearly follow-up assessments of the five years follow-up period (Cornelius et al., 2001; Cornelius et al., 2004; Cornelius, Clark, et al., 2005; Cornelius, Clark, et al, 2007). However, that pilot study did not include a placebo comparison group or a naturalistic comparison group that did not receive verbal therapy, so it was unclear whether the improvements in depressive symptoms and in alcohol-related symptoms noted in that pilot study resulted from the fluoxetine, from the CBT/MET therapy, or from the passage of time.

More recently, our own research group conducted a first double-blind, placebo-controlled acute phase study of fluoxetine in comorbid MDD/ AUD youth (Cornelius, Bukstein, et al., 2009). The results of that study demonstrated large within-group improvements in both depressive symptoms and in drinking, but no significant differences were noted between the fluoxetine group and the placebo group on any of the outcome variables (Cornelius, Bukstein, et al., 2009). Thus, no efficacy was noted for fluoxetine for treating either the depressive symptoms or the alcohol-related symptoms of that adolescent comorbid population, despite the prominent clinical improvements noted across the subjects who participated in the treatment study. Since all persons in that study received CBT/MET therapy, it appeared that the prominent clinical improvements that had been noted may have resulted from CBT/MET therapy. A naturalistic (no protocol treatment) comparison group was collected for that study, but no assessments of the participants in that comparison group were made during the acute phase of the study, so no definitive assessment of the acute phase efficacy of the CBT/MET therapy could be made. However, a two-year follow-up evaluation was conducted involving both the subjects involved in the randomized acute phase study who had all received manualized CBT/MET therapy and the naturalistic comparison group, so a preliminary evaluation of the long-term efficacy of CBT/MET among comorbid youth could be made as a secondary data analysis. The current paper is the result of that analysis.

To date, no controlled studies other than our own recently published study have been conducted involving CBT/MET therapy among adolescents with comorbid Major Depressive Disorder/Alcohol Use Disorder. However, one previous controlled study of CBT therapy (in combination with a fluoxetine) trial was conducted by Riggs and colleagues (2007) among a broad sample of comorbid adolescents. That study by Riggs et al (2007) did not specifically address adolescents with comorbid major depression and an alcohol use disorder, but instead addressed the more heterogeneous population of adolescents with major depression in combination with any substance use disorder. The authors of that study concluded that fluoxetine and CBT had greater efficacy than did placebo and CBT on one but not both depression measures, and was not associated with greater decline in self-reported substance use. The authors of that article speculated that CBT therapy may have decreased the depressive symptoms of their study sample, but they could not make any

conclusions about the efficacy of the CBT therapy, because no comparison sample was available that had not received the CBT therapy.

Cognitive behavioral approaches, such as the CBT used in this study, are based on social learning models (Carroll, 2005: Deas, 2008). CBT emphasized a functional analysis of drug use, including the development of an understanding of drug use with respect to its antecedents (triggers) and consequences. CBT emphasized the recognition of high-risk situations and the acquisition of skills to cope with craving cues and other high-risk situations. CBT has been shown to be effective across a wide range of substance use disorders (Carroll, 1996; Irwin et al, 1999; Carroll, 2005), including substance use disorders in the presence of co-occurring mood disorders (Carroll, 2004) and substance use disorders involving adolescents (Kaminer et al., 2002; Deas, 2008).

Motivational enhancement therapy (MET), including the MET used in this study, is a brief intervention used to enhance an individual's engagement in therapy and motivation to make changes regarding substance use and high-risk behaviors (Miller et al., 1992; Miller & Wibourne, 2002; Carroll, 2004). This form of brief intervention is theoretically appealing for adolescents with substance use disorders because adolescents with those disorders are typically non-treatment-seeking, and need to be motivated to engage in treatment (Tevyaw & Monti, 2004). Primary tenets of MET include using an empathic nonjudgmental stance, performing reflective listening, avoiding arguments, and supporting self-efficacy for change (Deas, 2008). MET has been shown to be effective across a wide range of substance use disorders, with particularly strong support among alcohol abusing and dependent populations (Wilk et al., 1997; Carroll, 2005; Carroll et al., 2006). MET has also demonstrated effectiveness for treatment of substance use disorder among persons with comorbid psychiatric disorders (Swanson, et al, 1999; Baker et al., 2002), and for treating substance use disorders among adolescents ((Tevyaw & Monti, 2004).

In this report, we present data involving a two-year follow-up assessment in order to provide a first preliminary assessment of the long-term efficacy of CBT/MET among comorbid MDD/AUD youth. The outcome findings presented in this manuscript are the result of statistical comparisons between subjects who had received CBT/MET therapy versus those who had not received CBT/MET therapy during the acute phase study, but instead had received naturalistic care. Those who had received CBT/MET therapy included all subjects who had participated in the acute phase study, which included those who had received fluoxetine and those who had received placebo. We hypothesized that improvements in depressive symptoms and alcohol-related symptoms noted among the CBT/MET subjects would exceed the improvements noted in the naturalistic comparison group.

2. Method

2.1. Subjects

Before entry into this treatment protocol, the study was explained, and written informed consent was obtained from all subjects (or from a parent or guardian with child assent if the participant was a minor) after all procedures had been fully explained. The study was approved by the University of Pittsburgh Institutional Review Board. This study was conducted at the Western Psychiatric Institute and Clinic (WPIC) of the University of Pittsburgh Medical Center (UPMC). Subjects were recruited for participation in the treatment study through referrals from any of the WPIC treatment programs and by responding to newspaper, radio, and bus advertisements. During recruitment, the subjects were told that they were being recruited for a treatment study involving adolescents and young adults with a combination of depression and alcohol problems.

Study participants were required to be between 15 and 20 years of age at baseline to be included in the study. At the baseline assessment, participants were evaluated for the DSM-IV diagnoses of an alcohol use disorder (AUD) (alcohol abuse or alcohol dependence) and for major depressive disorder (MDD). The comorbid presence of both a current AUD and a current MDD was required for inclusion in the treatment study. Standardized diagnostic instruments were used to assess for current diagnoses of major depressive disorder and for alcohol abuse or dependence. The DSM-IV diagnosis of MDD was confirmed using the Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL) (Kaufman, et al., 1997; Puig-Antich, 1986). The DSM-IV diagnosis of an alcohol use disorder (alcohol abuse or dependence) was confirmed using the Substance Use Disorders Section of the Structured Clinical Interview for the DSM (SCID) (Spitzer, et al., 2003; Martin, et al., 2000). Faculty members from our alcohol research center have validated the SCID with adolescent substance abuse populations (Martin et al., 2000). In addition, minimum current levels of drinking and of depressive symptoms were also required for study inclusion, as noted on the Timeline Follow-back scale and the HAM-D-27, respectively (Cornelius, Bukstein, et al., 2009; Cornelius, Bukstein, et al., 2010). Minimum levels of drinking for study inclusion were defined as drinking at least 10 drinks over the month prior to baseline assessment, as demonstrated on the Timeline Follow-back scale. Minimum levels of depressive symptoms for study inclusion were defined as a HAM-D-27 score of greater than or equal to 15 at the baseline assessment. Persons who did not meet the criteria for inclusion in the treatment trial because of an inadequate number of diagnostic criteria for MDD (sub-threshold for MDD) were offered the option of participating in a naturalistic comparison group which did not involve protocol medication treatment or protocol therapy, but which did involve a long-term follow-up evaluation two years after completion of the study baseline, in order to provide a preliminary evaluation of the effect of the protocol CBT/MET therapy. Those persons in the naturalistic comparison group were referred to care in a dual diagnosis program near their home, and subsequently received care at the person's discretion, provided by non-protocol staff.

Exclusion criteria included a DSM-IV diagnosis of bipolar disorder, schizoaffective disorder, or schizophrenia. Persons with hyper- or hypothyroidism, significant cardiac, neurological, or renal impairment, and those with significant liver disease (SGOT, SGPT, or gamma-GTP greater than 3 times normal levels) were also excluded from the study. Persons who had received antipsychotic or antidepressant medication in the month prior to baseline assessment were excluded. Persons with any substance abuse or dependence other than nicotine dependence or cannabis abuse or dependence were excluded from the study. Persons with any history of intravenous drug use were excluded from the study. Persons were recruited into the study regardless of race, ethnicity, or gender. Other exclusion criteria were pregnancy, inability or unwillingness to use contraceptive methods, and an inability to read or understand study forms.

2.2 CBT/MET Therapy

Manual-based therapy was provided to all subjects in the acute phase treatment trial, including those who had received fluoxetine and those who had received placebo. Persons in the naturalistic comparison group did not receive manual-based therapy. That manual-based therapy consisted of Cognitive Behavior Therapy (CBT) for treatment of major depressive disorder and for treatment of the alcohol use disorder, and Motivation Enhancement Therapy (MET) for treatment of the alcohol use disorder. The CBT/MET therapy was provided during each protocol visit during the acute phase treatment trial, so persons who participated in the acute phase treatment trial received psychotherapy on nine occasions: baseline, week 1, week 2, week 3, week 4, week 6, week 8, week 10, and week 12.

The cognitive behavior therapy for treatment of alcohol use disorder used in this study utilized the widely used techniques described in the CBT manual utilized in Project MATCH (Kadden, et al., 1994). The Cognitive Behavior Therapy for depression used in this study utilized the widely used techniques of cognitive therapy that have been adapted for treatment of adolescent depression, as described by Brent and colleagues (1997). This therapy was chosen because cognitive behavioral therapy has been reported to be more efficacious than alternative psychosocial interventions for the acute treatment of adolescents with major depressive disorder (Birmaher, et al., 2000). The Motivation Enhancement Therapy used in this study was adapted after the Motivation Enhancement Therapy used in Project MATCH (Miller, et al., 1992).

Three therapists provided therapy during the acute phase of this study. The three therapists who conducted therapy for the acute phase of the study were all Master's level staff members with several years of experience in providing CBT/MET therapy to adolescents and young adults with comorbid MDD/AUD. They all participated in comprehensive training exercises prior to the beginning of the study to ensure standardization in therapeutic techniques. This training included extensive readings on CBT/MET therapy, viewing of CBT/MET tapes, and conducting practice therapy sessions which were viewed by all of the therapists. This process was overseen by a senior staff person with a doctorate in therapy in order to further standardize the therapy. They also participated in annual assessments of their training to ensure that no "drift" in therapy occurred.

2.3 Pharmacotherapy

Following completion of the baseline assessment, participants in the treatment trial were randomly assigned to receive fluoxetine or placebo administered in identical-looking opaque capsules. Active medication and matching placebo were prepared by the research pharmacy at the Western Psychiatric Institute and Clinic of the University of Pittsburgh Medical Center. Patient randomization was conducted by urn randomization, stratified by gender. All subjects were initially given 1 capsule (10 mg fluoxetine or placebo), which was increased after 2 weeks to 2 capsules (20 mg fluoxetine or placebo), which was the target dose of the study. The study was conducted in a double-blind fashion, though one study physician remained non-blinded in order to handle any problems which may have arisen. Ratings of alcohol use and symptom severity were conducted weekly for the first month, and biweekly for the second and third month of the 12-week acute phase study.

2.4 Assessment Procedures and Measures

Assessments for this study were completed by a Master's level staff member with several years of experience conducting assessments with comorbid adolescents. All assessors also completed a comprehensive clinical assessors training program, lasting between 2 and 3 months. All raters participating in the proposed treatment study must have demonstrated adequate levels of inter-rater reliability prior to administering ratings. Experiential training included observation of experienced assessors with independent coding of instruments (at least 5 sessions). Agreement with the interviewing clinician must have exceeded 90% for advancement to administering assessments with an assisting supervisor present. Prior to performing solo interviews, the assessor must have completed a minimum of two assessments with a supervisor present but not assisting, and coding must have achieved 90% agreement with the observing supervisor. After the completion of formal training, monitoring continues through periodic joint interview reliability evaluations with pairs of interviewers. Pill counts were used to ensure compliance with protocol medication. The validity of participant's self-reported drinking was assessed with breath alcohol levels. To ensure a high level of participation for these evaluations, a \$20.00 payment was made to patients completing each assessment (Festinger, et al., 2008).

Subjects' diagnoses were finalized after case presentations at diagnostic conferences, attended by two study faculty members and the assessors. This "best estimate" diagnostic procedure (which is utilized for the SCID and SCID II as well as for the K-SADS) is in accordance with the method described by Leckman and colleagues (1982), and was validated by Kosten & Rounsaville (1992).

Observer-rated depressive symptoms were assessed with the Hamilton Rating Scale for Depression (HAM-D-27) (Hamilton, 1960). The reliability and validity of the HAM-D are well established (Hamilton, 2008). Participant-rated depressive symptoms were assessed with the Beck Depression Inventory (BDI) (Beck, et al., 1961). The reliability and validity of this widely-used instrument are well established (Beck, et al., 2008). Drinking behavior was evaluated using the timeline follow-back method (TLFB) (Sobell LC, et al., 1988). The TLFB has demonstrated good reliability, validity, and clinical utility across a wide variety of populations (Sobell & Sobell, 2008). This instrument provided a daily tabulation of drinking behavior, thus providing detailed information on the quantity and frequency of this behavior. The primary alcohol use outcome variables included number of drinks per drinking day, the number of drinking days, and the number of heavy drinking days (defined as greater than or equal to 4 drinks per day for women and 5 for men).

2.5 Statistical Analysis

Descriptive statistics were calculated for all variables. Continuous baseline measures were compared by independent, 2-tailed *t* tests for continuous variables. Categorical baseline measures were compared by chi-square analysis, corrected for continuity. Statistical analyses were completed on an intent-to-treat basis. Outcome measures for depression and for drinking across treatment groups were compared by repeated measures analysis of variance. The outcome findings presented in this manuscript are the result of statistical comparisons between subjects who had received CBT/MET therapy during the acute phase study versus those who had received naturalistic care. Those who had received CBT/MET therapy included all subjects who had participated in the acute phase study, which included those who had received fluoxetine and those who had received placebo. All tests of significance were 2-tailed. An alpha level of less than or equal to 0.05 was used in the study. All analyses were conducted using the Statistical Package for the Social Sciences, version 15.0 (Norusis, 1992).

3. Results

A total of 118 persons signed informed consent to participate in the acute phase study and completed the baseline assessment. Of those persons, 50 met all the inclusion criteria to participate in the Acute Phase Treatment Study, including 22 males and 28 females. These participants included 43 Caucasians, 4 African-Americans, and 3 with mixed race. The mean age of those 50 persons was 19.5 + / - 1.6 years.

A total of 68 persons were excluded from participation in the acute phase trial. Those 68 persons included 36 males and 32 females; and included 53 Caucasians, 10 African-Americans, and 5 persons with mixed race. The mean age of those 68 persons was 19.4 + / - 1.4 years. The only factor that distinguished those who were enrolled in the acute phase study from those who were not enrolled in the study was the number of criteria that had been met for major depressive disorder. Specifically, the number of criteria met for MDD by those who had been enrolled in the acute phase study (mean 7.2 + / - 1.2) was higher than the number of criteria met for MDD by those who had not be enrolled in that study (mean 4.8 + / - 3.1, f=3.91, p=0.05). Thus, those who were not enrolled in the acute phase study were typically slightly sub-threshold for MDD. No other symptom severity factor or demographic factor significantly distinguished those who were enrolled from those who were not enrolled

in the acute phase study. Almost two-thirds (64%, N=75) of the persons who signed informed consent for possible participation in the protocol study subsequently completed the two-year follow-up assessment, including 48 who had participated in the treatment protocol and 27 from the comparison group.

In repeated measure analysis of variance, a significant time by enrollment status difference was noted for both depressive symptoms and alcohol-related symptoms across the two-year time period of this study. For example, a significantly greater improvement (decrease) in depressive symptoms was noted among those who had enrolled in the treatment trial (and thus had received CBT/MET therapy) as compared to those who had not enrolled in the treatment trial on number of DSM criteria for MDD (f=14.6, p=0.000), self-reported depressive symptoms, as measured on the Beck Depression Inventory (f=12.4, p=0.001), and on observer-rated depressive symptoms, as measured on the Hamilton Depression Rating scale (f=16.6, p=0.000). Also, a significantly greater improvement (decrease) in number of DSM criteria for an alcohol use disorder was noted among those who had enrolled in the treatment trial and had therefore received CBT/MET therapy, as compared to those who had not enrolled in the treatment trial (f=14.2, p=0.000). At baseline, the percentage of subjects with alcohol dependence who participated in the acute phase trial was not significantly different from the percentage with alcohol dependence in the naturalistic comparison group (81% vs. 78%, respectively). The percentage of subjects who met diagnostic criteria for alcohol dependence decreased in both treatment groups between baseline and the two-year follow-up assessment. However, the group that had participated in the CBT/MET therapy (as part of their protocol therapy) had a lower prevalence of alcohol dependence at the two-year follow-up than the group that had participated in naturalistic therapy (41% vs. 17%, chi-square=5.3, p=0.021). In contrast, no significant difference was noted between those receiving fluoxetine and those receiving placebo at any time point.

4. Discussion

Our study demonstrated that adolescents with comorbid major depression and an alcohol use disorder who had participated in manualized CBT/MET therapy during their acute phase treatment trial demonstrated greater improvement in depressive symptoms and in alcohol-related symptoms at the two-year follow-up assessment compared to outcomes noted in the naturalistic comparison group who had not received CBT/MET. In a previous publication from this same treatment study (Cornelius et al., 2009), no acute phase difference was noted between those who had been randomized to fluoxetine versus those who had been randomized to placebo. Consequently, treatment with protocol medication did not explain the improvement in depressive symptoms and in alcohol-related symptoms that was noted among those who had participated in the acute phase treatment trial. Consequently, the CBT/MET therapy which had been received by all of the participants in the acute phase treatment protocol apparently was the factor which led to their higher level of clinical improvement. That finding provides preliminary support suggesting efficacy for CBT/MET therapy for treating the depressive symptoms and the alcohol-related symptoms of comorbid MDD/AUD adolescents.

Our current tentative conclusions regarding the efficacy of CBT/MET therapy for comorbid AUD/MDD adolescents is consistent with the findings of Riggs and colleagues (2007), who speculated that CBT therapy may have contributed to their higher-than expected treatment response in their pharmacotherapy/CBT treatment trial of a mixed sample of comorbid adolescents. However, the Riggs study did not involve a comparison group that did not receive verbal therapy, so no definitive conclusions were drawn concerning the effectiveness of CBT therapy among their youthful comorbid population by the authors of that paper. The results described in our current manuscript are also consistent with the promising results of

our previous pilot study of open label fluoxetine in combination with CBT/MET therapy in comorbid MDD/AUD adolescents, which demonstrated acute phase and continuation efficacy for treatment at each of the yearly follow-up assessments of the five years followup period (Cornelius, Clark, et al., 2005; Cornelius, Clark, et al., 2007). However, that pilot study did not include a placebo comparison group or a naturalistic comparison group, so it had been unclear whether the improvements in depressive symptoms and in alcohol-related symptoms noted in that pilot study resulted from the fluoxetine or from the CBT/MET therapy. The results described in our current manuscript regarding the efficacy of CBT/MET therapy in comorbid MDD/AUD adolescents are also consistent with the results of our own recent study of adolescents with a comorbid major depression in combination with a cannabis use disorder (Cornelius, Bukstein, et al., 2010). Until the time when more definitive studies can be performed, the results of the current study in combination with the results from the Riggs study and from our own recent work suggest that psychological intervention should be considered first-line treatment for comorbid MDD/AUD adolescents, with pharmacotherapy offered to those who do not respond to this intervention alone. It is also noteworthy that the efficacy of CBT/MET could potentially mask significant medication effects in treatment studies in which CBT/MET therapy is used in both the medication arm and the placebo arm of the study.

The results of this study should be interpreted in light of some limitations. First, the sample in this study was limited to outpatient comorbid MDD/AUD adolescents. Consequently, it is unclear to what extent the results of this study generalize to the treatment of comorbid MDD/AUD adults or to comorbid adolescents in more intensive treatment settings, such as inpatient settings or partial hospital settings. Second, the sample size in the present study was limited. Large trials would be needed to more definitively evaluate the efficacy of CBT/MET therapy among comorbid MDD/AUD adolescents. Further studies are also warranted to clarify the utility of promising but unproven predictors of treatment response among comorbid populations, such as clinical predictors, neuroimaging-related predictors, and genetic predictors of treatment response among comorbid populations (Cornelius, Salloum, et al., 1997; Cornelius, Bukstein, et al., 2005; Cornelius & Clark, 2007; Cornelius, Aizenstein, et al., 2010; Cornelius, Ferrell, et al., 2010).

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Table 1

Symptom Severity at Baseline and at 2-Year Follow-Up

	CBT/MET $(n = 48)$	$\Gamma(n = 48)$	NO CBI/MET $(n = 27)$	E.1 $(n = 2/)$	
Baseline	Mean	s.d.	Mean	s.d.	Sig.
BDI Total	22.9	7.84	19.6	9.00	0.103
HAM-D 27	20.0	5.91	13.7	9.01	0.001
DSM alcohol abuse criteria count	1.2	1.04	6.0	1.11	0.239
DSM alcohol depend criteria count	4.0	1.58	3.0	2.22	0.023
DSM alcohol Abuse +Dependence criteria count	5.3	2.21	3.9	2.93	0.030
DSM current MDD criteria count	7.2	1.27	8.4	3.11	0.000
Total drinks per week	19.5	10.78	21.0	20.47	0.690
Days of alcohol use per week	3.0	1.42	2.9	1.81	0.724
Heavy drinking days per week	2.0	1.15	2.2	1.77	0.490
Average drinks per drinking occasion in past month	6.4	2.59	6.3	3.51	0.939
	CBT/MET $(n = 48)$	$\Gamma(n = 48)$	No CBT/MET $(n = 27)$	ET $(n = 27)$	
2 year follow-up	Mean	s.d.	Mean	s.d.	Sig.
BDI Total	6.1	8.02	12.3	10.16	0.005
HAM-D 27	3.7	5.34	6.7	7.53	0.043
DSM alcohol abuse criteria count	0.3	09.0	8.0	1.00	0.011
DSM alcohol depend criteria count	1.1	1.22	2.1	2.16	0.013
DSM alcohol Abuse + Dependence criteria count	1.4	1.65	2.9	2.68	0.004
DSM current MDD criteria count	1.7	2.77	2.3	2.77	0.367
Total drinks per week	11.5	13.75	16.9	16.79	0.133
Days of alcohol use per week	2.1	1.70	2.6	2.18	0.273
Heavy drinking days per week	1.0	1.37	1.7	1.72	0.095
Average drinks per drinking occasion in past month	4.7	2.91	5.6	3.53	0.208

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