Published in final edited form as:

Psychol Addict Behav. 2009 December ; 23(4): 613–619. doi:10.1037/a0017324.

A Stress-Coping Profile of Opioid Dependent Individuals Entering Naltrexone Treatment: A Comparison with Healthy Controls

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Abstract

Background—Stress is known to increase addiction vulnerability and risk of relapse to substance use.

Purpose & Method—We compared opioid dependent individuals entering naltrexone treatment ($n = 57$) with healthy controls ($n = 75$) on measures of stress, coping, and social support and examined the relative contribution of group membership, coping and social support to stress within the sample. Analyses of variance (ANOVA) and covariance (ANCOVA), and stepwise multiple regression were conducted.

Results—Compared with controls, opioid dependent subjects reported greater stress, less use of adaptive coping, but comparable use of maladaptive/avoidant coping. No group differences were found with respect to social support. Perceived stress was predicted by group membership, low social support and greater use of maladaptive/avoidant coping, and the prediction by social support and maladaptive/avoidant coping did not differ by group.

Conclusion—Opioid dependent individuals entering naltrexone treatment experience higher levels of stress and report less use of adaptive coping strategies when compared with controls. Group membership, maladaptive/avoidant coping and social support independently contribute to perceived stress. Findings suggest that novel treatment approaches that decrease maladaptive/avoidant coping and improve social support are important aspects of decreasing stress during early recovery from opioid addiction.

Keywords

Opioid dependence; naltrexone; stress; social support; coping

Abuse of heroin and prescription opioids remains a significant public health concern despite the availability of effective pharmacotherapies such as naltrexone, methadone, buprenorphine, and the buprenorphine/naloxone combination (Comer, Sullivan & Hulse, 2007). Of these medications, orally administered naltrexone is the only approved opioid antagonist that blocks the euphoric effects of opioids and which serves as a non-dependence-forming alternative to opioid agonists such as methadone and buprenorphine. The clinical utility of naltrexone follows

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from operant conditioning models of behavior which predict that opioid use will extinguish if not reinforced by opioid effects on brain reward circuits (Tucker & Ritter, 2000). Cognitively, naltrexone may deter opioid use by creating the expectancy that users will not experience the drug's effects.

Despite the strong theory in support of its use and the unequivocal pharmacologic effectiveness of naltrexone in blocking the actions of opioids, naltrexone has not lived up to its potential with treatment programs typically struggling with poor adherence and high drop-out rates (Comer *et al.*, 2007; Kirchmayer, *et al.* 2002; Rounsaville, 1995; Tucker & Ritter, 2000). Reasons given for poor adherence include naltrexone's absence of reinforcing properties, the requirement of a detoxification and an opioid-free period prior to initiation, adverse neuropsychiatric and gastrointestinal effects possibly caused by naltrexone itself, discomfort associated with protracted withdrawal symptoms (*e.g.*, nervousness; sleep difficulty), the absence of negative consequences for abrupt discontinuation, and a lack of genuine motivation to achieve abstinence (Comer *et al.*, 2007; Rounsaville, 1995; Tucker & Ritter, 2000).

Another possible contributor to the adherence problems associated with this form of treatment is that naltrexone treated opioid abusers in early recovery experience high levels of stress which may increase drug craving and relapse susceptibility. Indeed, stress plays a role in drug craving and addiction relapse (Sinha, 2008), and evidence suggests that naltrexone treated opioid abusers demonstrate vulnerability to stress induced craving and hyper-arousal responses despite opioid effects being blocked by four to six weeks of chronic naltrexone treatment (Hyman, *et al.* 2007). Considering that naltrexone does not protect against stress in opioid abusers, gaining a better understanding of stress-related factors (*e.g.*, coping, social support) that could be targeted to reduce stress-related vulnerability to addiction may improve treatment outcomes.

Stress is conceptualized as a relationship between an individual and his/her environment that is appraised as exceeding coping resources and has the potential to endanger well-being (Lazarus & Folkman, 1984). Stress plays a prominent role in the perpetuation of drug addiction (Goeders, 2003; 2004; Sinha, 2001; 2005; 2008; Turner & Lloyd, 2003; Wills, 1990) and may be particularly taxing during early recovery as opioid dependent individuals attempt to cope with stressors (*e.g.*, legal and relationship problems, job loss, financial debt) and unremitting protracted withdrawal symptoms without resorting to opioid use. Indeed, their overall level of stress, the manner by which they cope with their difficulties, and the strength of their social support networks (conceptualized as a coping resource for the purposes of the current study) may help determine their success at averting stress-related relapse and attaining a drug-free lifestyle.

Regarding personal coping resources, there is evidence that substance abusers who actively take steps to overcome problems (*e.g.*, through problem solving, conflict resolution, and healthy affect regulation) as compared with those who more commonly avoid facing problems or focus on venting emotions in response to stress (*e.g.*, yelling at others; slamming doors) typically meet with better outcomes (Beutler, Moos, & Lane, 2003; Eftekhari, Turner, & Larimer, 2004; Wills & Hirky, 1996). Supportive relationships may also facilitate recovery efforts (Broome, Simpson, & Joe, 2002; Ellis, Bernichon, Yu, Roberts, & Herrell, 2004; Havassy, Hall, & Wasserman, 1991; McMahon, 2001; Warren, Stein, & Grella, 2007) by assisting with coping and promoting less threatening interpretations of negative life events (Cohen, 2004; DeLongis & Holtzman, 2005; Ozbay, Johnson, Dimoulas, Morgan III, Charney, & Southwick, 2007), and moderating the impact that stress has on cravings (Ames & Roitzsch, 2000). For these reasons, assessment of perceived stress, coping, and social support at treatment entry may identify strengths and deficits that could help inform treatment planning and stress-focused intervention. Importantly, these are all factors that are amenable to change.

Thus, our study had two goals: The first was to compare opioid dependent individuals entering naltrexone treatment to healthy controls on measures of perceived stress, coping, and social support to identify their relative strengths and deficits. Our second goal was to examine the effects of coping and social support on stress within the sample and explore whether the relationship between social support/coping and perceived stress would be different for opioid dependent versus healthy control participants.

We hypothesized that: 1) opioid dependent individuals would report greater stress, less use of adaptive coping strategies (problem and emotion-focused coping), greater use of maladaptive/avoidant coping strategies, and less social support than healthy social drinking controls, and 2) social support and coping would be associated with perceived stress. We also examined the exploratory hypothesis that the relation between coping strategies/social support and perceived stress would be different for the opioid dependent versus healthy control individuals.

Method

Participants

Opioid dependent adults (age 18 or older) entering treatment for primary opioid dependence at a standard outpatient naltrexone treatment program and who were being recruited to participate in a study examining the effects of an experimental medication (lofexidine) on naltrexone treatment outcomes were included in analyses. Study exclusion criteria included: 1) regular use of anticonvulsants, sedatives/hypnotics, prescription analgesics, antihypertensives (including clonidine), antiarrhythmics, antiretroviral medications, and tricyclic antidepressants, 2) psychotic or otherwise severely psychiatrically disabled (*i.e.*, suicidal, homicidal, current mania), 3) significant underlying medical conditions such as cerebral, renal, thyroid or cardiac pathology, 4) abstinent from opiates for more than four weeks prior to naltrexone initiation, 5) medical problems that would preclude naltrexone treatment, such as laboratory evidence of significant hepato-cellular injury as evidenced by abnormal liver enzyme tests including SGOT and SGPT (> 3 times normal) or elevated bilirubin levels), and a history of cirrhosis, 6) hypotensive individuals with sitting blood pressure below 95 mm Hg systolic, 7) women who are pregnant, nursing or refuse to use a reliable form of birth control, and 8) ECG evidence at baseline screening of any clinically significant conduction abnormalities, including a Bazlett's QTc of > 450 msec for men and QTc > 470 msec for women.

Forty-one percent of those screened (109 out of 267) did not meet entry criteria. Others who did meet entry criteria did not participate in the study for a number of reasons (*e.g.*, they did not provide consent or withdrew their consent; they returned to opioid use; they did not show for treatment and were unable to be contacted; they elected to engage in alternative treatment).

The standard naltrexone treatment regimen enrolled patients who had recently completed opioid detoxification and were opioid free (as assessed by an opioid-free urine toxicology screen) upon presentation to the clinic. Initially, participants self-administered 25mg of naltrexone under observation on their first day of induction. Their dose was increased on subsequent days until they reached the optimum dosing schedule in which patients visited the clinic three times per week (Monday, Wednesday, and Friday) to self-administer naltrexone. One-hundred mg was self-administered on Mondays and Wednesdays and 150 mg was given on Fridays. Naltrexone self-administration was conducted at the clinic under observation of clinic staff in order to ensure medication compliance. All participants were assigned to receive naltrexone and individualized cognitive-behavioral psychotherapy with an experienced clinician. They were randomized to receive either lofexidine or placebo. Baseline study assessments used for the current study were administered during the first week of treatment with naltrexone and before study medications (lofexidine or placebo) had been administered.

Control subjects were recruited from advertisements in local newspapers. They were excluded if they met current or lifetime abuse or dependence criteria for alcohol or any other illicit drug. Individuals being treated for any psychiatric or medical condition were also excluded.

All participants gave written consent, and the Human Investigation Committee of the Yale University School of Medicine approved the two studies from which the data were collected. Demographics and sample characteristics are displayed in Table 1.

Measures

Perceived Stress Scale (PSS)—The PSS (Cohen, Kamarck, & Mermelstein, 1983) is a 14-item self-report questionnaire that assesses the degree to which recent life situations are appraised as stressful. Respondents are asked to indicate how often they have felt or thought a certain way in the past month (*e.g.*, “In the last month, how often have you been upset because of something that happened unexpectedly?”; “In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?”) on a five point scale that ranges from 0 (never) to 4 (very often). Responses are then summed to indicate the level of perceived stress. The PSS has demonstrated adequate internal and test-retest reliability (Cohen *et al.*, 1983).

COPE Questionnaire—The COPE (Carver, Scheier, & Weintraub, 1989) is a 53-item self-report measure of the different ways people tend to respond to stress. Participants are asked to indicate the extent to which they engage in various behaviors (“I try to come up with a strategy about what to do; I pretend that it has not really happened”) when faced with problems on a four point scale that ranges from 1 = “Don’t do this at all” to 4 = “Do this a lot.” As described in Carver *et al.* (1989), five scales (comprising 4 items each) measure aspects of *problem-focused coping* (active coping; planning; suppression of competing activities; restraint coping; and seeking of instrumental social support), five scales (comprising 4 items each) measure aspects of *emotion-focused coping* (seeking of emotional social support; positive reinterpretation; acceptance; denial¹; turning to religion), and three scales (comprising 4 items each) measure coping responses that are arguably “less useful” or counterproductive when coping with stress (focus on and venting of emotions; behavioral disengagement from continued efforts at dealing with the stressor; mental disengagement from continued efforts at dealing with the stressor). For our purposes, we referred to this final scale cluster as *maladaptive/avoidant coping*. One additional scale (comprising only 1 item) asks about the extent to which individuals use drugs or alcohol to think less about problems. This item was excluded from analyses because it comprised only 1 item and was not included under any of the three coping styles described in the original paper on the COPE (Carver *et al.* 1989). The development of the COPE questionnaire was based on theoretical models, and it has been widely used for research purposes (Hasking & Oei, 2002). Standardized Cronbach’s alpha was .89, .83, and .70 for problem-focused coping, emotion-focused coping, and maladaptive/avoidant coping respectively in a previous study using a drug dependent sample (Hyman, Paliwal, & Sinha, 2007).

Interpersonal Support Evaluation List (ISEL-The General Population Form)—

Social support data were collected via the Interpersonal Support Evaluation List (ISEL; Cohen

¹Carver *et al.* (1989) took a theoretically-based approach to the assessment of coping strategies and described denial as an emotion-focused coping strategy. The authors state that denial can help minimize distress and facilitate effective coping but that denial may create additional problems unless the stressor can advantageously be ignored. They also suggest that denial may be useful at the early stages of a stressful situation but impede coping if persistently relied upon for a particular stressor. We understand the controversy regarding this subscale and see that it could fit under emotion-focused or maladaptive/avoidant depending upon the situation and particular stressor at hand. Considering the ambiguity of this scale, we elected to list denial as an emotion-focused strategy as described by Carver *et al.* (1989).

& Hoberman, 1983; Cohen, Mermelstein, Kamarck, & Hoberman, 1985). The ISEL consists of 40 statements concerning the perceived availability of four social support resources that potentially have the ability to facilitate coping with stressful events. *Appraisal support* is the perceived availability of someone to go to for advice or guidance in coping with problems (e.g., “When I need suggestions for how to deal with a personal problem I know there is someone I can turn to.”). *Tangible support* is the perceived availability of instrumental or material resources that assist in coping with stressful situations (e.g., “If I needed a quick emergency loan of \$100, there is someone I could get it from.”). *Self-esteem support* is the perceived availability of a positive comparison when comparing one’s self to others (e.g., “I am able to do things as well as most other people.”). Finally, *belonging support* is the perceived availability of others with whom one can share activities (e.g., “If I wanted to have lunch with someone, I could easily find someone to join me.”). Respondents indicate whether each statement is true or false, and responses that indicate support are summed to calculate their level of perceived social support. The summary score combines data from all four subscales and was used in the present study as an overall measure of functional social support (Cohen *et al.* 1985). The ISEL has proven valid and reliable in a number of samples (Cohen *et al.* 1985).

Data Analysis

Comparison of Opioid Dependent Subjects and Controls on the Stress-related Measures

Prior to comparing groups on the stress-related measures (PSS, the three COPE composites, and the ISEL summary score), we examined whether demographic variables were associated with these measures using Analysis of Variance (ANOVA) and Pearson correlation. We considered age, gender, ethnicity, and years of education because they are known to have an effect on stress responses and/or stress-related coping (Birditt & Fingerman, 2003; Blanchard-Fields, 2007; Haarr & Morash, 1999; Lawrence, Ashford, & Dent, 2006; Lunsford *et al.* 2006; Meyer, Schwartz, & Frost, 2008; Ptacek, Smith, & Dodge, 1994). Any demographic associated with the stress-related measures was controlled for in group comparisons using Analysis of Covariance (ANCOVA). If none of the demographics was associated with a particular measure, we compared groups using ANOVA.

Influence of Coping and Social Support on Stress in Opioid Dependent Subjects and Controls

In studying the relationship between coping/social support and stress, we conducted a stepwise multiple regression. The 0.15 significance level was used for selection of variables into the model. The dependent variable was perceived stress. The predictor variables were problem-focused coping, emotion-focused coping, maladaptive/avoidant coping, social support, group (opioid dependent; healthy controls), and group X problem-focused coping, group X emotion-focused coping, group X maladaptive coping, and group X social support interactions. We also included demographic variables that were correlated with perceived stress in the regression model. If the interaction terms were significant, we conducted follow-up stepwise regressions predicting perceived stress from coping and social support for each group separately.

Results

Comparison of Opioid Dependent Subjects and Controls on the Stress-related Measures

Preliminary analyses to identify demographic covariates for group comparisons indicated that perceived stress was associated with gender and years of education. Problem-focused coping was associated with age, years of education, and ethnicity. Emotion focused coping was associated with years of education and ethnicity. Maladaptive/avoidant coping had no

relationship with demographic variables. Finally, perceived social support was associated with years of education.

While controlling for demographics associated with the stress-related measures of interest, comparative analyses indicated that opioid dependent subjects scored higher on perceived stress ($M = 32.4$, $SD = 6.9$) than healthy controls ($M = 19.5$, $SD = 7.4$); $F(1, 129) = 93.77$, $p < .0001$. They reported less use of problem-focused coping ($M = 46.4$, $SD = 10.8$) than healthy controls ($M = 56.5$, $SD = 8.8$); $F(1, 125) = 8.56$, $p = .004$, less use of emotion-focused coping ($M = 43.9$, $SD = 8.2$) than healthy controls ($M = 50.1$, $SD = 7.0$); $F(1, 126) = 3.83$, $p = .05$ and comparable use of maladaptive/avoidant coping ($M = 25.4$, $SD = 4.9$) as healthy controls ($M = 25.6$, $SD = 4.2$); $F(1, 130) = 0.04$, $p = .84$. Finally, opioid dependent patients reported comparable levels of social support ($M = 32.3$, $SD = 6.4$) as healthy controls ($M = 34.2$, $SD = 4.9$); $F(1, 129) = .45$, $p = .50$.

Predictors of Perceived Stress

We began by identifying demographic and stress-related variables that were associated with perceived stress (at the $p \leq .05$ level). Pearson correlations were used for continuous variables (the 3 coping factors, social support, age & years of education) and ANOVAs were used for categorical variables (gender & ethnicity). Results indicated that problem-focused coping was negatively associated with perceived stress ($r = -.31$, $p = .0003$), emotion-focused coping was negatively associated with perceived stress ($r = -.19$, $p = .03$), maladaptive/avoidant coping was positively associated with perceived stress ($r = .33$, $p = .0001$), perceived social support was negatively associated with perceived stress ($r = -.42$, $p < .0001$), and years of education was negatively associated with perceived stress ($r = -.43$, $p < .0001$). A gender difference was found with men reporting greater perceived stress ($M = 26.5$, $SD = 9.6$) than women ($M = 22.5$, $SD = 9.2$); $F(1, 130) = 5.53$, $p = 0.02$. Age and ethnicity were not significantly associated with perceived stress.

Using multiple stepwise regression, perceived stress was regressed on the linear combination of hypothesized predictors (the coping variables and social support), group, group X problem-focused coping, group X emotion-focused coping, group X maladaptive/avoidant coping, group X social support, gender, and years of education. Variables were entered into the model if they were significant at the $p \leq .15$ level. The final equation containing “group”, maladaptive/avoidant coping, and social support accounted for 61% of the variance in perceived stress [$R^2 = .61$; $F(3, 128) = 67.3$, $p < .0001$]. The partial R^2 values were then reviewed to assess the relative importance of the three variables in the prediction of perceived stress. These values were .44 for group ($F = 104.1$, $p < .0001$), .12 for maladaptive/avoidant coping ($F = 34.6$, $p < .0001$), and .05 for social support ($F = 16.5$, $p < .0001$), indicating that all of these variables explained a significant portion of the variance in perceived stress above and beyond the other predictors in the model. The demographic variables and the group X coping and group X social support interaction terms did not enter as significant predictors in the final model. Therefore, we did not analyze the relationship between coping/social support and stress separately in the opioid dependent and healthy control groups.

Is Social Support related to Maladaptive/Avoidant Coping?

As maladaptive/avoidant-coping and social support independently predicted stress, we also examined if there was any evidence that social support was related to maladaptive/avoidant coping. Results indicated that, in the full sample ($N = 132$), social support was significantly associated with maladaptive/avoidant coping ($r = -.29$, $p = .0006$).

Discussion

Opioid dependent individuals entering naltrexone treatment experience higher levels of stress than normal healthy controls. This finding is important because stress is known to perpetuate opioid craving and increase relapse susceptibility (Hyman *et al.* 2007; Sinha, 2001, 2007). This may be particularly salient during early recovery as stressors proliferate and before stress-coping responses are improved in the context of psychotherapy. Opioid dependent individuals also demonstrate less use of adaptive problem and emotion-focused coping strategies than healthy individuals, but these groups show comparable use of maladaptive/avoidant forms of coping and comparable levels of social support.

The level of perceived social support and extent to which maladaptive/avoidant coping strategies are typically used when facing problems was predictive of stress in the sample, and no group interaction effect was found. This finding suggests that social support may protect against stress whereas maladaptive/avoidant coping may exacerbate it, regardless of whether one is opioid dependent or a healthy control. Interestingly, although adaptive problem and emotion-focused coping differed between groups and were modestly correlated with stress, after controlling for social support, maladaptive/avoidant coping, and demographic factors, adaptive problem and emotion-focused coping were not related to stress. Together, these findings suggest that the extent to which an individual engages in maladaptive/avoidant forms of coping may be more important than the extent to which adaptive coping strategies are used in predicting his or her overall level of perceived stress. This finding is consistent with prior literature indicating that among coping efforts, avoidant coping has the strongest and most consistent relationship with distress (see Holahan, Moos, Jolahan, Brennan, & Schutte, 2005 for review). It may be that maladaptive/avoidant coping (*e.g.*, focusing on venting emotions; active disengagement from efforts at dealing with problems) is directly related to stress as a conditioned response (*i.e.*, escape/avoidance conditioning or the “fight or flight” response) whereas adaptive forms of coping (*e.g.*, planning; problem solving) are more deeply rooted in executive function and have a more indirect relationship with stress.

In addition to being a maladaptive response to stress, a maladaptive/avoidant coping style may also be implicated in the generation of future life stressors (Hammen, 1991). As stated by Holahan *et al.* (2005), “Cognitive avoidance may permit incipient stressors, such as financial or health problems, to fester and grow. Behavioral avoidance may actively promote new stressors, such as when emotional discharge aggravates strains in family or work relationships (p.659).” Indeed, these authors have found support for this hypothesis in a prospective study which showed an association between baseline avoidance coping and more chronic and acute life stressors four years later (Holahan *et al.* 2005).

Specific to the treatment of opioid dependence, our findings suggest that behavioral and/or pharmacological treatments that target maladaptive/avoidant coping, and social support may reduce distress and improve treatment outcomes. This approach may be more effective than simple administration of opioid agonists and partial agonists such as buprenorphine and methadone, both of which have been shown to reduce heroin seeking in rodents following heroin priming but which have not demonstrated effectiveness in relation to stress-induced reinstatement of drug seeking behavior (Leri, Tremblay, Sorge, & Stewart, 2004; Shaham & Stewart, 1996; Sorge, Rajabi, & Stewart, 2005).

For instance, a recent study found that opioid dependent patients treated with naltrexone and lofexidine, an alpha-2 adrenergic agonist, demonstrated lower heart rates and an attenuated stress and drug-cue induced opioid craving response as compared with those treated with naltrexone alone, and they also had higher opioid abstinence rates and better relapse outcomes (Sinha, Kimmerling, Doebrick, & Kosten, 2007). Another study found that a two-session

stress-management intervention (stress-inoculation training) delivered approximately one week apart to substance dependent individuals improved stress, stress-induced craving, and reports of ability to resist substance use (Back, Gentilin, & Brady, 2007). Our findings suggest that introducing more frequent and intensive stress-management training and/or stress-reducing medications (*e.g.*, lofexidine) at the outset of treatment with naltrexone may help improve outcomes. If maladaptive/avoidant coping is indeed a conditioned response to stress that also generates and perpetuates future life stressors, then exposure therapy techniques that confront individuals with stressful stimuli while disallowing maladaptive/avoidant coping responses may help to reduce harm expectancy, extinguish maladaptive/avoidant coping, and ultimately reduce stress (Hofmann, 2008). However, care should be taken to implement graded exposure techniques so as not to overwhelm patients and provoke an opioid relapse. Switching from orally administered naltrexone to long-acting injectable naltrexone formulations (Comer *et al.*, 2007) may also enhance treatment success by providing a longer period of non-reinforcement where stress resiliency can be enhanced through psychotherapeutic interventions. For those opioid dependent individuals who are unable to directly inhibit maladaptive/avoidant coping reactions, our data suggest that simply enhancing social support may temper maladaptive/avoidant coping and lead to stress reduction.

This study is not without limitations. First, the cross-sectional nature of the study precludes us from coming to a conclusion regarding the direction of the findings. While maladaptive/avoidant coping and social support may indeed affect stress, it is also possible that stress can increase one's use of maladaptive/avoidant coping and lead to behaviors (*e.g.*, angry outbursts; avoidance of others) that alienate or push away sources of social support. Certainly, both mechanisms may be in effect and result in a vicious cycle of stress and maladaptive behavior. Another limitation derives from difficulties measuring coping. While the COPE questionnaire is a popular measure that has been used extensively in previous research, various populations may use different coping strategies that may or may not be reflected in this particular scale, and the COPE appears to demonstrate good psychometrics in certain populations but not in others (Hasking & Oei, 2002). Furthermore, self-reports of how individuals tend to cope with stress may be very different from how they actually cope when faced with various stress-evoking situations. However, given that the maladaptive/avoidant coping scale was associated with stress, we advocate using this COPE scale for predicting stress in clinical and non-clinical populations.

Overall, the study findings suggest that stress is high and coping impoverished in opioid dependent individuals entering naltrexone treatment. This may be a factor contributing to poor treatment adherence, drop-out, and relapse. Our data also suggest that helping patients inhibit maladaptive/avoidant coping responses should be given higher priority than strengthening adaptive-coping responses when considering stress-focused treatment planning. Careful assessment of perceived stress, social support, and coping and more frequent and intensive stress-coping interventions conducted within and outside of the therapeutic context are warranted.

Acknowledgments

This study was supported by the National Institutes of Health (NIH) grants R01-DA18219 (RS), P50-DA16556 (RS), and K02-DA17232 (RS). We thank the staff at the Substance Abuse Treatment Unit (SATU) and Yale Stress Center for their assistance with this project. We also thank Dr. Benjamin Toll and Dr. Raquel Andres-Hyman for their comments.

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Table 1**Demographics & Sample Characteristics (N = 132)**

	Opioid Group (n=57)	Controls (n=75)	Significance
Age (<i>M, SD</i>)	27.4 (8.8)	31.5 (9.0)	$F = 6.52, p = 0.01$
Years of ed (<i>M, SD</i>)	12.5 (1.5)	14.9 (1.9)	$F = 61.9, p < 0.0001$
Gender (n, %)			$\chi^2 = 11.64, p = 0.0006$
Men	46 (81%)	36 (48%)	
Women	11 (19%)	39 (52%)	
Ethnicity (n, %)			$\chi^2 = 20.2, p = 0.0002$
Caucasian	52 (91%)	42 (56%)	
AA	3 (5%)	23 (31%)	
Hispanic	1 (2%)	8 (11%)	
Other	1 (2%)	2 (3%)	
Years of opioid use (<i>M, SD</i>)	7.1 (6.2)	Not applicable	
Age of first use (<i>M, SD</i>)	20.4 (5.7)	Not applicable	
Age of onset of regular (3× per week) use (<i>M, SD</i>)	22.5 (5.9)	Not applicable	
Co-morbid diagnoses (n, %)			
ETOH Abuse	4 (7%)	0 (0%)	
ETOH Dependence	3 (5%)	0 (0%)	
Cocaine Abuse	5 (9%)	0 (0%)	
Cocaine Dependence	12 (21%)	0 (0%)	
Cannabis Abuse	8 (14%)	0 (0%)	
Cannabis Dependence	9 (16%)	0 (0%)	
Mood Disorder	1 (2%)	0 (0%)	
Anxiety Disorder	8 (14%)	2 (3%)	

Note: The Structured Clinical Interview for DSM-IV Axis I Mental Disorders- (SCID-I: First, Spitzer, Gibbon, & Williams, 1995) was used to diagnose psychiatric and substance use disorders. The mood and anxiety sections of the SCID-I were not available on 12 opioid dependent individuals and one healthy control subject who dropped out prior to completion of those modules.