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Effects of major depressive disorder and attention-deficit/hyperactivity disorder on the outcome of treatment for cocaine dependence

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Abstract

Co-occurring psychiatric disorders have been associated with poor prognosis among substance-dependent patients, but few studies have examined this association among patients with cocaine dependence (CD). We compared baseline characteristics and treatment outcome between cocaine-dependent patients with major depressive disorder (MDD; n = 66), those with attention-deficit/hyperactivity disorder (ADHD; n = 53), and those with CD without comorbid disorders (CD alone; n = 48) who had been randomized to the placebo arms of clinical trials with venlafaxine, methylphenidate, and gabapentin, respectively. The three groups differed significantly in racial makeup, with more Caucasians and Hispanics among patients with MDD and those with ADHD but more African Americans among those with CD alone. The groups did not differ significantly in treatment retention, with retention rates ranging from 42% to 47%; neither did they differ in the rates of achieving 2 consecutive weeks of urinalysis-confirmed abstinence, with rates ranging from 40% to 50%. Using logistic regression for repeated measures with general estimating equations, modeling the likelihood of a cocaine-positive week over time in treatment, we found the diagnostic group to interact with the baseline level of cocaine use and time. Among cocaine-dependent patients who achieved abstinence at baseline, those with MDD and those with ADHD had better outcome over time as compared with patients with CD alone. However, among patients with cocaine-positive urine specimens at baseline, those with MDD and those with ADHD were associated with poor outcome as compared with patients with CD alone. The findings suggest that diagnosis and treatment of co-occurring disorders such as depression and ADHD may be important components of treatment planning for CD and that the baseline level of cocaine use should be included as a covariate in studies evaluating the impact of such treatment. Published by Elsevier Inc.

Keywords: ADHD; Major depressive disorder; Cocaine dependence; Treatment retention; Treatment outcome

1. Introduction

Major depressive disorder (MDD) and attention-deficit/hyperactivity disorder (ADHD) are common psychiatric disorders among cocaine-dependent individuals seeking treatment (Clure et al., 1999; Levin, Evans, & Kleber, 1998; Rounsaville & Carroll, 1991). The lifetime prevalence rates of MDD in the general population are notable, with rates ranging from 13% to 16% (Hasin, Goodwin, Stinson, & Grant, 2005; Kessler et al., 2003), whereas the rates of MDD in treatment-seeking cocaine-abusing individuals are higher, ranging from 15% to 30% (Charney, Palacios-Boix, Negrete, Dobkin, & Gill, 2005; Kilbey, Breslau, & Andreski, 1992; McLean et al., 1999; Rounsaville & Carroll, 1991). Similarly, Kessler et al. (2006) found that the rate of adult ADHD in the US population is 4.4%, whereas recent prevalence studies on substance-dependent samples seeking treatment have obtained rates ranging from

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15% to 24% (King, Brooner, Kidorf, Stoller, & Mirsky, 1999; Levin et al., 1998; Schubiner et al., 2000), suggesting that these disorders merit clinical attention in substance abuse treatment settings. Despite this, there remain only limited data characterizing the impact of these co-occurring psychiatric disorders on treatment outcome in cocaine-dependent patients.

Few placebo-controlled trials have examined the pharmacological treatment of depression or ADHD in cocaine-dependent adults, and, to date, the findings have been mixed. Some studies suggested that depressed cocaine-dependent individuals receiving an antidepressant medication have greater improvement in their depressive symptoms as compared with those receiving placebo, as well as trends toward improvement in some measures of cocaine use (McDowell et al., 2005; Nunes et al., 1995), whereas other studies found no advantage for antidepressants (Cornelius et al., 1998; Schmitz et al., 2001). Two controlled trials with the stimulant methylphenidate among cocaine-dependent adults with ADHD (Levin, Evans, Brooks, & Garawi, 2006; Schneider et al., 2001) found greater improvement in at least some measures of ADHD symptoms for those receiving active medication as compared with those receiving placebo. Neither trial found methylphenidate to be different from placebo on global measures of cocaine use outcome, such as the overall proportion of cocaine-positive urine specimens, although Levin et al. (epub, 2006a) did find a greater reduction in cocaine-positive urine specimens over time on methylphenidate using a repeated measures linear model.

There are even fewer data regarding how well psychotherapeutic approaches work for cocaine-dependent individuals with ADHD or MDD (Rounsaville, 2004). Information can be gleaned from the double-blind trials referenced above in which cognitive–behavioral interventions were provided, along with the medication. For most pharmacological trials targeting cocaine-dependent individuals with psychiatric comorbidities, retention rates are lower than 50% (McDowell et al., 2005; Schmitz et al., 2001; Schubiner et al., 2002), demonstrating that cocaine-dependent individuals with psychiatric comorbidities are difficult to retain in treatment. In these trials, less than 25% in either the active medication groups or the placebo groups achieved a prolonged period of abstinence or had a proportion of cocaine-negative urine specimens exceeding 50% (Evans et al., 2007; McDowell et al., 2005; Schmitz et al., 2001; Schubiner et al., 2002). Furthermore, these data suggest that cognitive–behavioral therapy, in addition to the pharmacotherapy, is not substantially enhancing retention or abstinence. This is consistent with other studies suggesting that cognitive–behavioral therapy has a modest impact on abstinence and treatment retention (Carroll, 1997). It is less clear whether cocaine-dependent individuals with psychiatric comorbidity are more difficult to retain in treatment trial or have poorer treatment responses as compared with those without psychiatric comorbidity.

Longitudinal naturalistic studies examining the impact of co-occurring depression on the outcome of drug or alcohol abuse in general have also produced conflicting findings. A number of studies have shown MDD, or psychiatric severity in general, to be associated with poorer substance use outcome or treatment retention (Carroll, Power, Bryant, & Rounsaville, 1993; Charney et al., 2005; Dodge, Sindelar, & Sinha, 2005; Greenfield et al., 1998; Hasin et al., 2002; Kosten, Rounsaville, & Kleber, 1987; Rounsaville, Dolinsky, Babor, & Meyer, 1987; Rounsaville, Kosten, Weissman, & Kleber, 1986), whereas other studies suggested that there is no negative impact on treatment retention or perhaps even a positive impact of depression on retention in treatment (Agosti, Stewart, & Quitkin, 1991; Brown et al., 1998; McKay et al., 2002; Rounsaville et al., 1987; Siqueland et al., 2002). In one review of this literature, Hasin, Nunes, and Meydan (2004) concluded that MDD tends to confer a poor prognosis but that the impact of depressive symptoms, measured with cross-sectional scales, is less clear. This suggests the importance of careful clinical history taking and diagnosis of a depressive disorder. Rounsaville (2004) suggested that the varied results may be explained by the fact that the low energy, impaired cognition, and anhedonia of depression may have a negative impact on the effectiveness of treatment, whereas, on the other hand, the pain of depressive symptoms may motivate patients to remain engaged in treatment. It is worthy of note that few of these naturalistic studies focused specifically on cocaine-dependent individuals.

Naturalistic studies assessing the impact of ADHD on outcome in cocaine-dependent individuals have also been limited. Two studies found that cocaine-abusing adults with ADHD are less likely to complete and/or do well with substance abuse treatment (Carroll et al., 1993; Levin, Evans, McDowell, Brooks, & Nunes, 2002), whereas King et al. (1999) found no prognostic impact of ADHD in methadone maintenance treatment patients. Methadone maintenance treatment patients may be less likely to drop out of treatment because of the reinforcing effects of methadone. Deficits in attention and memory have been found to be associated with high dropout rates among cocaine-dependent patients without ADHD (Aharonovich et al., 2006).

We concurrently conducted three clinical trials with medications for patients with cocaine dependence (CD) and MDD, those with CD and ADHD, and those with CD without co-occurring disorders. Other than differing co-occurring diagnoses and medications being tested, these studies were similar in their inclusion and exclusion criteria and other methodological features, including that all patients received weekly and individualized manual-guided cognitive–behavioral relapse prevention therapy, a commonly used psychological platform in pharmacological research trials. By comparing the placebo groups across these three trials, we have the opportunity to evaluate the impact of co-occurring MDD or ADHD on treatment outcome for cocaine-dependent patients undergoing standard psychosocial outpatient treat-