Effects of Dextroamphetamine on Depression and Fatigue in Men With HIV: A Double-Blind, Placebo-Controlled Trial

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Background: This report documents findings from a small placebo-controlled trial of dextroamphetamine for depression and fatigue in men with the human immunodeficiency virus (HIV). Dextroamphetamine offers the potential for rapid onset of effect and activation properties, both of which are important to persons with medical illness and an uncertain, but limited, life expectancy.

Method: Primary inclusion criteria included the presence of a DSM-IV depressive disorder, debilitating fatigue, and no history of dependence on stimulants. The study consisted of a 2-week randomized, placebo-controlled trial, with the blind maintained until week 8 for responders, followed by open treatment through the completion of 6 months.

Results: Of 23 men who entered the study, 22 completed the 2-week trial. Intent-to-treat analysis indicated that 73% of patients (8/11) randomly assigned to dextroamphetamine reported significant improvement in mood and energy, compared with 25% (3/12) among placebo patients (Fisher exact test, $p < .05$). Both clinician- and self-administered measures indicated significantly improved mood, energy, and quality of life among patients taking dextroamphetamine. There was no evidence of the development of tolerance of, abuse of, or dependence on the medication.

Conclusion: These results suggest that dextroamphetamine is a potentially effective, fast-acting antidepressant treatment for HIV patients with depression and debilitating fatigue.

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Standard antidepressants have been shown to be effective in treating depression in patients with the human immunodeficiency virus (HIV), including those with late-stage illness.[1–4] However, some patients report improved mood but continued low energy, which often accompanies advanced HIV illness.[5] An alternative treatment for such patients is psychostimulant medication, with its potential advantages including rapid onset of effect (2–3 days), activation properties, and absence of anticholinergic side effects. Case reports, chart reviews, and our own open-label study of depressed HIV patients treated with psychostimulants suggest that psychostimulants are well tolerated in this population and that treatment improves mood, psychomotor activity, and cognitive functioning.[6–9] However, we are not aware of any placebo-controlled trials of psychostimulants involving HIV patients.

Early placebo-controlled studies involving medically healthy patients with primary depression failed to find a difference between psychostimulants and placebo, largely because of high response rates for both.[10,11] With the advent of tricyclic antidepressants (e.g., imipramine) and selective serotonin reuptake inhibitors (e.g., fluoxetine, sertraline), psychostimulants are now primarily used as an augmentation to standard antidepressants.[10–12] However, psychostimulants have been found to be effective as the primary antidepressant treatment in subpopulations including patients with depression and apathy, depressed patients with organic impairment, and depressed medically ill patients.[11,13–15]

The primary concerns about the use of psychostimulants such as dextroamphetamine are the risks of abuse/dependence and development of tolerance. Wilbur et al.[16] reported habituation effects as efficacy declined over time; however, many studies have reported no evidence of tolerance or habituation with duration of treatment ranging from months to years.[10,17] There have been no reports of abuse or dependence on psychostimulant treatment in either HIV or non-HIV patients under medical supervision. Other adverse reactions may include increased anxiety, insomnia, and overstimulation, all of which are usually transient or reversible by dose reduction. Psychostimulants have been associated with appetite/weight loss; however, in studies of HIV patients, appetite stimulation has also been reported.[6,7,9]

We conducted a 2-week randomized, double-blind, placebo-controlled trial followed by up to 6 months of open-label treatment to assess the efficacy of dextroamphetamine in treating depression and debilitating fatigue in people with HIV. A secondary aim of the study was to study the effects of dextroamphetamine on cognitive function.

METHOD

Recruitment

Patients were recruited indirectly, having responded to general notices about ongoing treatment studies for depression or fatigue that were placed in local HIV and acquired immunodeficiency syndrome (AIDS) newsletters or posted at local AIDS organizations. It was decided not to mention the specific nature of the treatment in postings or notices to limit the risk of enrolling those who sought the treatment for recreational use. Instead, the psychologists conducting the initial evaluations for other depression treatment studies suggested this option when appropriate. Enrollment was slower than expected (the sample was recruited over a period of nearly 4 years) for other reasons as well: patients with a history of stimulant (including cocaine) abuse/dependence were excluded, which eliminated a significant proportion of the HIV community that we serve, and recent advancements in HIV treatments (i.e., protease inhibitors and combination antiretroviral therapy) led to significant improvement in the health of people with HIV, including those seeking treatment through our studies, and consequently the complaint of debilitating fatigue was much less frequent.

Eligibility Criteria

Inclusion criteria included age of 18 to 65 years, having a DSM-IV depressive disorder diagnosis, and reporting debilitating fatigue. Exclusion criteria included a history of abuse/dependence on stimulants (including cocaine) or recent (within past 6 months) abuse/dependence on any substance, psychotic symptoms, serious suicide risk, bipolar disorder, and current use of psychotropic medications. Patients were required to provide written, informed consent after study procedures and possible side effects were explained, and their primary care physicians were required to sign a statement that there were no medical contraindications to study participation.

Procedure

The study consisted of a 2-week randomized, double-blind, placebo-controlled trial, followed by up to 24 weeks of open-label treatment. For responders at week 2, the blind was maintained until week 8 or relapse in terms of mood or energy. For nonresponders at week 2, the code was broken, and those taking placebo were started on dextroamphetamine treatment, while those taking dextroamphetamine were offered standard antidepressants. Patients were instructed to follow a titrated dose schedule: b.i.d. in the morning and midafternoon with a daily dose starting at 5 mg. In the absence of clinical improvement and limiting side effects, the dose was increased every 2 days in units of 2.5 mg/day with a maximum dosage of 40 mg/day. Patients were seen weekly until response was achieved, plus patients were contacted by telephone every other day to monitor dosage and response until optimal dosage level was reached; thereafter, visits were every 2 weeks.

Measures

DSM-IV depressive diagnoses were assessed with the Structured Clinical Interview for DSM-IV (SCID).[18] The 21-item clinician-rated Hamilton Rating Scale for Depression (HAM-D)[19] was used to assess severity of depressive symptoms. Additional measures of mood included the self-report Brief Symptom Inventory (BSI)[20] and Beck Hopelessness Scale (BHS),[21] as well as a 10-point visual analog scale (VAS) from 1, "very depressed," to 10, "very happy." Fatigue was assessed with 7 items from the Chalder Fatigue Scale (CFS)[22] and a 10-point VAS with the anchors being 1, "very low energy," and 10, "very high energy."

The clinician-rated Clinical Global Impressions scale (CGI)[23] provided a global rating of severity and degree of improvement for depression and energy level separately. For ratings of improvement, a score of 1, "very much improved," or 2, "much improved," was considered a response, whereas a score of 3, "minimally improved," or greater was nonresponse. Patients were classified as responders if they responded to treatment in terms of both mood and energy.

The neuropsychological tests used to assess cognitive function included the Trail-Making Test (A and B),[24] a measure of psychomotor speed, executive function, and cognitive flexibility; and the digit symbol subscale of the Wechsler Adult Intelligence Scales-Revised (WAIS-R),[25] a measure of psychomotor speed and learning. Quality of life was assessed using the 16-item self-report Quality of Life Enjoyment and Satisfaction Questionnaire (Q-L-S-Q)[26] and the 5-item clinician-rated Quality of Life Index (QLI) by Spitzer et al.[27] Overall physical functioning was measured using the Karnofsky Performance Index.[28]

The SCID was administered at baseline; all other assessments were administered at baseline and weeks 2, 8, 16, and 26, with the exception of the side effects form, which was completed at each visit.

Statistical Analysis

Descriptive statistics were used to describe the sample. Independent t tests (2-tailed) and chi-square or Fisher exact tests were used to compare treatment groups on continuous and categorical variables, respectively. Paired t tests (2-tailed) were used to assess change following treatment.

RESULTS

Sample Characteristics

Twenty-three men entered the study between August 1995 and March 1999; women were eligible, but none enrolled. Mean ± SD age was 41 ± 8 years; most were white (N = 16; 70%), unemployed (N = 20; 87%), and had at least some college education (N = 17; 74%). As a whole, the sample had advanced HIV illness; 74% (N = 17) met criteria for an AIDS diagnosis (according to 1993 criteria from the Centers for Disease Control), including 70% (N = 16) who had a history of a major opportunistic infection. The mean CD4 cell count at baseline was 251 ± 210 cells/mm^3, with 52% (N = 12) having counts below 200. The mean number of medications used by the sample at baseline was 7 ± 5 (range, 2–23). Fifteen men (65%) were on combination antiretroviral therapy, including a protease inhibitor. Most (N = 19; 83%) of the sample scored 80 or above on the Karnofsky Performance Index, which indicates a level of functioning sufficient to "carry out normal activity with effort; some signs or symptoms of illness are present."

Baseline Symptomatology

Twelve men (52%) were diagnosed with a current major depression, 3 (13%) were diagnosed with dysthymia, and 8 (35%) had either subthreshold major depression or minor depression. The mean ± SD HAM-D score at baseline was 14.9 ± 4.2 (range, 8–23). The mean score on the BSI depression subscale was 1.88 ± 0.77, and the total score was 1.13 ± 0.45; these scores are similar to the normative means (1.80 for depression subscale, 1.32 for total score) for psychiatric outpatients. The mean score on the BHS was 9.8 ± 6.1, which is approximately equivalent to the normative mean for depressed samples; 57% (N = 13) scored above 9, which is considered a cutoff for moderate to severe levels of hopelessness.

The mean ± SD score on the CFS was 28.2 ± 4.0; 70% (N = 16) had "clinical fatigue" (defined as a score of 28 or higher; possible range of scores is 7–35). Nine men performed in the impaired range (defined as scoring more than 2 standard deviations below the normative mean) on either the Trail-Making test A or test B (N = 9; 39%), and 2 (9%) did so on the digit symbol subscale of the WAIS-R; overall, 10 subjects (44%) scored in the impaired range on at least 1 of these tests.

Outcome

All but 1 of the 23 men completed the 2-week double-blind trial. The only dropout discontinued owing to side effects (increased anxiety) from placebo. Of the 22 completers, 11 were randomly assigned to dextroamphetamine and 11 to placebo. Eight completers (73%) assigned to dextroamphetamine responded to treatment in both mood and energy, compared with 3 patients (27%) on placebo (Fisher exact test, $p < .10$). In an intent-to-treat analysis with the 1 placebo dropout included as a nonresponder, the group difference becomes statistically significant (Fisher exact test, $p < .05$). Response to energy and mood were concordant for all but 1 patient who was taking dextroamphetamine and responded in terms of energy but not mood. The mean ± SD daily dose at week 2 for those randomly assigned to dextroamphetamine was 22 ± 9 mg, with the most common daily dose being 30 mg. Once optimal dosage was obtained (usually within 2 weeks of beginning dextroamphetamine), all but 2 patients remained at that dose throughout the study. At week 26, the dose ranged from 10 mg/day to 40 mg/day with a mean daily dose of 26 ± 12 mg.

All 3 nonresponders to dextroamphetamine had major depression, compared with only 2 of the 8 responders; however, response was not associated with HAM-D score at baseline. CD4 cell count at baseline was not associated with response among those randomly assigned to dextroamphetamine, but placebo patients with higher CD4 cell counts were more likely to be responders (mean ± SD CD4 = 546 ± 141 cells/mm^3) than nonresponders (mean ± SD CD4 = 180 ± 133 cells/mm^3; $t = 4.0$, $p < .01$).

Among completers on dextroamphetamine treatment, significant improvement in depressive symptoms as measured by both the clinician-rated HAM-D and self-report BSI depression subscale as well as reduced fatigue and improved quality of life and physical functioning were found at week 2 compared with baseline (Table 1). There were indicators of mild improvement (trend level of significance) in cognitive functioning. Among patients on placebo, fewer parameters showed improvement; there were indications of improved mood and fatigue, but not quality of life and physical functioning (Table 2).

Eleven patients were taking dextroamphetamine at week 8, including 5 dextroamphetamine responders, 5 placebo nonresponders, and 1 placebo responder who later relapsed; an additional 4 patients (2 dextroamphetamine responders and 2 placebo responders at week 2) discontinued treatment prior to week 8 because of side effects. Among these 11, significant improvement in depressive symptoms, energy level, and quality of life were found at week 8 compared with baseline (or week 2 for placebo responders who started dextroamphetamine; data not shown). Nine of these 11 men went on to complete the 6-month trial; of the remaining 2, 1 died shortly after week 8 from leukemia and the other discontinued treatment at week 16 because of a relapse in depression.

Side effects. Although none of the patients randomly assigned to dextroamphetamine discontinued treatment prior to week 2, 4 patients (including 2 placebo nonresponders who started dextroamphetamine) later discontinued dextroamphetamine because of side effects (overstimulation, heart palpitations, sleep deprivation). The most common treatment-emergent side effects were

Table 1. Change in Symptom Domains Following 2 Weeks of Dextroamphetamine Treatment Among Completers (N = 11)[a]

	Baseline		Week 2			
Symptom Domain	Mean	SD	Mean	SD	t	p Value
Mood						
HAM-D	15.1	3.6	7.5	3.9	5.3	.000
BSI total score	1.18	0.49	0.73	0.60	2.0	.077
BSI depression subscale	2.00	0.85	0.98	1.04	3.1	.015
BHS	8.4	5.9	8.2	6.9	0.2	.810
VAS item	3.9	0.9	6.0	1.9	2.8	.018
Energy						
CFS	26.8	4.9	18.3	3.9	5.5	.000
VAS item	3.3	1.3	6.7	2.3	8.4	.000
Quality of life						
Q-LES-Q	39.6	6.2	52.2	12.1	4.2	.002
QLI	5.3	1.3	7.0	2.4	2.3	.042
Karnofsky Performance Index	82.7	7.9	92.7	7.9	3.3	.008
Cognitive functioning						
Trail-Making Test A (percentile)	50.3	30.1	64.2	20.2	1.3	.216
Trail Making Test B (percentile)	45.6	20.7	65.3	21.1	2.2	.063
WAIS-R, digit symbol subscale (age-adjusted mean)	10.2	1.9	11.5	1.8	1.9	.090

[a]Abbreviations: BHS = Beck Hopelessness Scale, BSI = Brief Symptom Inventory, CFS = Chalder Fatigue Scale, HAM-D = Hamilton Rating Scale for Depression, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, QLI = Quality of Life Index, VAS = visual analog scale, WAIS-R = Wechsler Adult Intelligence Scales-Revised.

Table 2. Change in Symptom Domains Following 2 Weeks of Placebo Among Completers (N = 11)[a]

	Baseline		Week 2			
Symptom Domain	Mean	SD	Mean	SD	t	p Value
Mood						
HAM-D	14.4	4.8	9.4	6.1	2.5	.033
BSI total score	1.03	0.46	0.71	0.27	2.4	.036
BSI depression subscale	1.77	0.75	1.29	0.72	1.7	.120
BHS	10.1	6.7	9.5	6.6	0.6	.572
VAS item	4.1	1.9	4.9	2.3	1.6	.146
Energy						
CFS	29.2	3.1	25.4	4.4	2.6	.026
VAS item	3.2	1.2	4.3	2.1	1.7	.126
Quality of life						
Q-LES-Q	40.3	7.9	42.6	12.1	0.8	.424
QLI	4.7	2.0	6.0	2.4	1.7	.116
Karnofsky Performance Index	80.9	11.4	81.8	15.4	0.6	.588
Cognitive functioning						
Trail-Making Test A (percentile)	44.6	31.6	61.2	32.5	2.3	.048
Trail-Making Test B (percentile)	55.9	31.4	59.2	34.7	0.3	.736
WAIS-R, digit symbol subscale (age-adjusted mean)	10.5	2.4	10.9	1.8	0.6	.563

[a]Abbreviations are explained in the footnote to Table 1.

overstimulation, insomnia, and loss of appetite and/or weight, with each reported by 5 patients (22%) at some point during the study. Other less common side effects included heart palpitations and headaches, with each reported by 3 patients. In general, side effects were transient, reversible, and well managed with dose reduction; no serious medical side effects were reported.

DISCUSSION

Results suggest that dextroamphetamine is a potentially effective, fast-acting antidepressant treatment for HIV patients with depression and debilitating fatigue. Although the numbers are small, the data suggest that treatment may be less likely to be effective for patients with more severe depression (major depression). Among those randomly assigned to dextroamphetamine, less than half (2/5) of the patients diagnosed with major depression were responders, compared with all 6 of the patients with more mild depression (i.e., dysthymia, subthreshold depression, or minor depression). Since improvement in mood nearly always coincided with improved energy, we were unable to assess whether dextroamphetamine has an antidepressant effect independent of its activation properties. Measures of cognitive function suggested a mild treatment effect; the trends we found may have been statistically significant with a larger sample size.

Although psychostimulants are not a first-line standard antidepressant to be used with most patients, for depressed patients with fatigue and medical illness the potential for the treatment to enhance overall functioning and quality of life makes it a viable treatment option. Patients described being able to resume activities of daily living including grocery shopping, cleaning the house, and visiting with friends, and at least 2 patients credited the treatment for their ability to return to work. Since return to work is more widely discussed as HIV becomes more of a chronic illness, treatments such as psychostimulants that can reduce the barriers of fatigue and depression become relevant to a broader range of people living with HIV.

Psychostimulant use is controversial and often not considered a treatment option for several reasons including the potential for abuse and dependence, development of tolerance and withdrawal reactions, and restrictive regulations regarding its prescription since it is a controlled substance. It is our clinical impression that these concerns, along with the illicit "street drug" use of amphetamines, have resulted in a stigma attached to psychostimulants that has both patients and clinicians skeptical about their value and appropriateness; a number of patients in our trial who benefited from treatment found it difficult to convince their doctors to continue the dextroamphetamine prescriptions following the completion of their study participation. Results from this study did not support these concerns; 10 of 15 responders to dextroamphetamine (includes nonresponders to placebo

who switched to dextroamphetamine) maintained their response throughout their participation in the 6-month trial. Although an additional 4 patients discontinued treatment due to side effects, only 1 patient experienced a relapse in depression after having been a responder, and improvement in energy level was consistently maintained. At least in the short term, there was little evidence of tolerance development in the study; although 2 patients required a 40--g/day dose to obtain a therapeutic effect, patients did not require ever increasing doses to maintain response. Some patients who had reached a dose of 30 or 40 mg/day reduced the dose slightly over time without a loss of effect. Alternatives to psychostimulants for use in treating patients with histories of drug addiction include hormonal therapies such as testosterone[29] for men and dehydroepiandrosterone (DHEA)[30] for men and women, both of which we have found to have positive effects on mood and energy in open-label trials with HIV patients.

Overall, the treatment was tolerated well by the sample. The efficacy and well-tolerated nature of the treatment are exemplified by the intention of all but one of the patients who completed the entire 26-week trial to continue the treatment with their primary care physician. The one patient who chose not to continue successfully weaned himself off treatment without a significant loss of effect in terms of energy or mood. This patient's experience highlights the possibility that long-term treatment may not be necessary for some patients, particularly as HIV treatments continue to improve. Extended follow-up assessments are needed in future research to address issues related to safety, especially concerning tolerance and abuse/dependence.

In closing, a larger controlled trial that includes women is needed to assess treatment efficacy for severe as well as moderate and mild depression and whether dextroamphetamine can improve mood independent of energy level.

Drug names: dextroamphetamine (Dexedrine and others), fluoxetine (Prozac), sertraline (Zoloft).

REFERENCES

1. Rabkin JG, Wagner G, Rabkin R. Sertraline effects on mood and immune status in patients with major depression and HIV illness: an open trial. J Clin Psychiatry 1994;55:433–439
2. Rabkin JG, Wagner GJ, Rabkin R. Fluoxetine treatment for depression in patients with HIV/AIDS: a randomized placebo-controlled trial. Am J Psychiatry 1999;156:101–107
3. Rabkin JG, Rabkin R, Harrison W, et al. Effects of imipramine on mood and immune status in depressed patients with HIV illness. Am J Psychiatry 1994;151:516–523
4. Levine S, Anderson D, Bystritsky A, et al. A report of eight HIV-seropositive patients with major depression responding to fluoxetine. J AIDS 1990;3:1074–1077
5. Darko DF, McCutchan JA, Kripke DF, et al. Fatigue, sleep disturbance, disability and indices of progression of HIV infection. Am J Psychiatry 1992;149:514–520
6. Holmes VF, Fernandez F, Levy JK. Psychostimulant response in AIDS-related complex patients. J Clin Psychiatry 1989;50:5–8
7. Fernandez F, Levy JL, Galizzi H. Response of HIV-related depression to psychostimulants: case reports. Hosp Community Psychiatry 1988;39:628–631
8. Angrist B, d'Hollosy M, Sanfilipo M. Central nervous system stimulants as symptomatic treatments for AIDS-related neuropsychiatric impairment. J Clin Psychopharmacol 1992;2:268–272
9. Wagner G, Rabkin JG, Rabkin R. Dextroamphetamine as a treatment for depression and low energy in AIDS patients: a pilot study. J Psychosom Res 1997;42:113–116
10. Satel SL, Nelson JC. Stimulants in the treatment of depression: a critical overview. J Clin Psychiatry 1989;50:241–249
11. Nelson JC. Psychostimulants in the treatment of depression. Prim Psychiatry 1995;2:26–27
12. Stoll AL, Pillay SS, Diamond L, et al. Methylphenidate augmentation of serotonin selective reuptake inhibitors: a case series. J Clin Psychiatry 1996;57:72–76
13. Wallace AE, Kofoed LL, West AN. Double-blind, placebo-controlled trial of methylphenidate in older, depressed, medically ill patients. Am J Psychiatry 1995;152:929–931
14. Frierson RL, Wey JJ, Tabler JB. Psychostimulants for depression in medically ill. Am Fam Physician 1991;43:163–170
15. Masand P, Pickett P, Murray GB. Psychostimulants for secondary depression in medical illness. Psychosomatics 1991;32:203–208
16. Wilbur DL, MacLean AR, Allen EV. Clinical observations on the effect of benzedrine sulfate. JAMA 1937;109:549–554
17. Fernandez F, Adams F, Holmes VF. Methylphenidate for depressive disorders in cancer patients. Psychosomatics 1987;28:455–462
18. Spitzer RL, Williams JBW, Gibbon M, et al. Structured Clinical Interview for DSM-IV (SCID). New York, NY: Biometric Research, New York State Psychiatric Institute; 1994
19. Hamilton M. Development of a rating scale for primary depressive illness. Br J Soc Clin Psychol 1967;6:278–296
20. Derogatis LR, Melisaratos M. The Brief Symptom Inventory: an introductory report. Psychol Med 1983;13:595–605
21. Beck AT, Weissman A, Lester D, et al. The measurement of pessimism: the hopelessness scale. J Consult Clin Psychol 1974;42:861–865
22. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. J Psychosom Res 1993;37:147–153
23. Guy W. ECDEU Assessment Manual for Psychopharmacology. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976:218–222
24. Army Individual Test Battery. Manual of Directions and Scoring. Washington, DC: War Department, Adjutant General's Office; 1944
25. Wechsler D. Wechsler Adult Intelligence Scales-Revised. New York, NY: Psychological Corp; 1981
26. Endicott J, Nee J, Harrison W, et al. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmacol Bull 1993;29:321–326
27. Spitzer WO, Dobson AJ, Hall J, et al. Measuring the quality of life of cancer patients: a concise QL-Index for use by physicians. J Chronic Dis 1981;34:585–597
28. Schag CC, Heinrich RL, Ganz PA. Karnofsky Performance Status revisited: reliability, validity, and guidelines. J Clin Oncol 1984;2:187–193
29. Rabkin JG, Wagner G, Rabkin R. Testosterone therapy for HIV+ men with and without hypogonadism. J Clin Psychopharmacol 1999;19:19–27
30. Rabkin JG, Ferrando SJ, Wagner GJ, et al. DHEA treatment for HIV+ patients: effects on mood, androgenic and anabolic parameters. Psychoneuroendocrinology 2000;25:53–68