

Interrelation between Psychiatric Disorders and the Prevention and Treatment of HIV Infection

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Psychiatric disorders, particularly major depression, have a profound affect on the use of and adherence to highly active antiretroviral therapy (HAART) among patients with human immunodeficiency virus (HIV) infection. Because some of the symptoms of HIV infection are similar to those of major depression, efforts to diagnose and treat major depression are further complicated. Moreover, major depression increases vulnerability to HIV infection by provoking high-risk behaviors, and it interferes with a patient's ability to comply with protocols for the prevention and treatment of HIV infection. HIV infection itself can disguise, help initiate, or exacerbate major depression. In this report, the interrelation between major depression and HIV infection is evaluated, the impact of this interrelation on adherence to HAART is described, and methods for effective treatment of psychiatric conditions in HIV-infected persons are discussed.

HIV infection and psychiatric illness have features in common, and each is a significant risk factor for the other. Among individuals who are HIV positive, the prevalence of major depression is ~30% [1, 2], and the prevalence of HIV infection among people with severe mental illness is 4.0%–22.9% [3]. HIV infection can damage the subcortical structures of the brain and provokes a sense of hopelessness and demoralization. At the same time, it magnifies the risk of iatrogenic addictions and potentiates psychiatric disorders. Moreover, in HIV-infected patients, psychiatric disorders increase the risk of nonadherence to HIV therapy and for transmitting HIV infection. The cumulative impact of a number of educational programs is evidenced by increased awareness of risk factors for HIV infection, enhanced compliance with infection-prevention practices, and, ultimately, a decreased rate of HIV transmission. Yet there are persons whose vulnerability to infection is higher than normal because they cannot or

will not make reasonable risk assessments or practice safe sex. Many of these individuals may have psychiatric disorders that are barriers to initiating appropriate changes to behavior [4].

PSYCHIATRIC DISORDERS IN PERSONS WITH HIV/AIDS

In examining the records of new patients admitted to the Moore HIV clinic at John Hopkins Hospital (Baltimore, MD), we found that a large percentage of patients who presented for medical care (54%) had a psychiatric diagnosis (table 1) [5–7]. It should be noted that the Moore clinic is an inner city clinic and that there is a high prevalence of drug use in our patient population. Approximately 75% of new patients had had a needle- or nonneedle-associated substance-abuse disorder diagnosed that was either ongoing or in remission. These data suggest that a significantly large percentage of patients with psychiatric illness, including major depression, also had a substance-abuse disorder, further complicating treatment. Eighteen percent of new patients had cognitive impairment consistent with an intelligence-quotient function of <70, a substantial barrier to understanding the importance of safe-sex behavior and clean-needle use.

According to an outcome study at the Moore clinic, aggressive treatment of major depression with psycho-

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Table 1. Psychiatric disorders diagnosed in new patients who presented to the Moore clinic at Johns Hopkins Hospital (Baltimore, MD).

Diagnosis	Percentage of new patients
Axis I	
Overall	54
Major depression	20
Demoralization (i.e., adjustment disorder)	18
Substance abuse	74
Cognitive impairment	18
Axis II	
Personality disorder	26 ^a

NOTE. Data are from [6], unless otherwise indicated.

^a Unpublished observation.

therapy and psychotropic medication was beneficial for ~85% of patients, and the condition of half of those who responded to therapy returned to baseline [7]. Although major depression is readily diagnosed and treated, it remains the most under-recognized and undertreated psychiatric disorder in patients with chronic illness. These data strongly suggest that access to psychiatric care is essential for HIV-infected persons and that it should be accessible within the HIV clinic [5, 6].

In general, the cascade of problems that originate from major depression lead to decreased rates of compliance with standard protocols for the prevention and treatment of HIV infection and to increased rates of high-risk behavior. This interrelation between major depression and HIV infection results in an increased rate of HIV infection among vulnerable depressed patients and accounts in part for the high rate of major depression among patients who visit HIV clinics.

MAJOR DEPRESSION, DEMORALIZATION, AND PERSONALITY DISORDER

The term “depression” is often used without a clear definition. For the purpose of this discussion, we draw a distinction between “major depression” and “demoralization.” Major depression is a psychiatric disease presumably caused by a structural or functional brain lesion and is the most common mental disorder among patients who present to the Moore clinic [7]. Demoralization (also known as “adjustment disorder”) is characterized as a state of exaggerated grief, persistent sadness, disillusionment, and despondency that arises in response to a difficult event in a person’s life. At the Moore clinic, ~50% of the patients present with major depression, and ~50% present with demoralization, but there is considerable overlap between the 2 conditions. There are also patients with AIDS-associated dementia and delirium. Unfortunately, these conditions are often hard to distinguish in a clinical situation. The diagnosis of major depression is further complicated among patients with

bipolar disorder, a condition in which the depressive phase is very hard to distinguish from major depression. Patients with bipolar disorder experience episodes of mania, excitation, euphoria, grandiosity, irritability, and dramatically increased energy, as well as episodes of major depression. Patients with bipolar disorder need evaluation by a clinician with expertise in the treatment of mood disorders.

The classic symptoms of major depression—a diminution in mood, sense of well-being, and self-attitude—may not be identifiable for HIV-infected patients because these symptoms may be a manifestation of the infection or other factors, rather than an indication of major depression. Because patients with HIV/AIDS have valid reasons for being demoralized and because patients can present with both demoralization and major depression, it is important to differentiate the 2 conditions so that interventions with the greatest benefit can be chosen. Major depression can be treated by a variety of antidepressants, many of which have been shown to be effective in patients infected with HIV. A variety of drug-drug interactions—both theoretical and demonstrated—have been discussed [8], but they seem to have a very limited clinical impact.

Individuals who are clinically depressed will benefit from antidepressant medication and possibly from cognitive behavioral and interpersonal therapies. In contrast, for demoralized patients, the greatest benefit will be derived from supportive psychotherapy, encouragement, coaching, and rehabilitation.

A hallmark of major depression is anhedonia, which is characterized by the loss of a sense of reward with regard to particular behaviors (table 2). It is a useful tool in differentiating major depression from the demoralization common in persons with HIV disease. Patients with major depression will report that the reward that used to be associated with the activities they enjoyed are gone or diminished. Early morning awakening—a neurophysiologic disturbance—is a significant feature of major depression, and should be ascertained with a comprehensive history and clinical examination.

The presence of personality disorder increases the risk of missing the diagnosis of major depression. Personality influences the presentation or manifestation of major depression. Consider the differences between introverted persons and ex-

Table 2. Behaviors associated with the loss of reward in persons with anhedonia.

Appetite-directed behaviors	
	Sleeping
	Eating
	Having sex
Function-directed behaviors	
	Working
	Engaging in hobbies
	Exercising

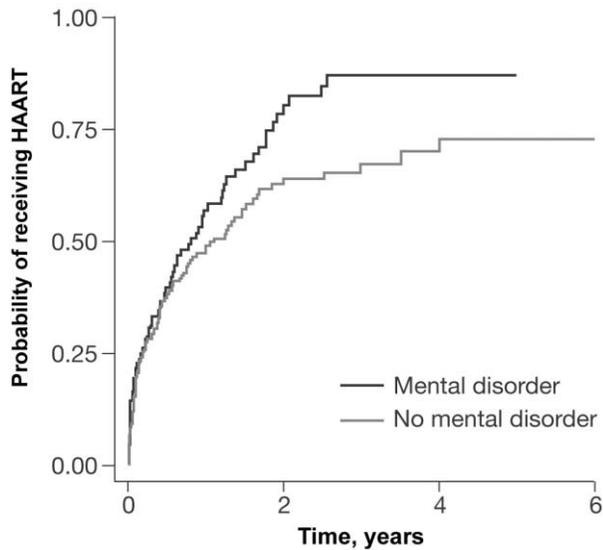


Figure 1. Probability of receiving HAART among patients with AIDS who did or did not have a concomitant mental disorder, Moore HIV clinic, Johns Hopkins Hospital (Baltimore, MD). Data are from [20].

troverted persons: the former are consequence averse, punishment averse, future directed, and function directed, whereas the latter are reward directed, present directed, and feeling directed. These features can adversely impact the decision whether to diagnose major depression. For example, depressed individuals with extroverted personalities tend to report how they currently feel; if they are having a good day, they may deny that they are depressed.

Personality differences are relevant to the implementation of programs to prevent HIV infection. Individuals who are averse to punishment and consequence are more likely to comply with prevention procedures. In contrast, because some persons with extroverted personalities are not likely to recognize the consequences of their actions and are more likely to continue their present behavior, they must be presented with reward-directed and feeling-directed interventions on a long-term basis to achieve prevention success. These differences also affect the treatment of major depression. A person with an extroverted personality is at risk of discontinuing therapy as soon as they feel better and may discontinue coming to the clinic.

IMPACT ON BEHAVIOR AND OUTCOMES

HIV-infected individuals with mental illness are marginalized, impoverished, and hopeless, and their illness increases the likelihood that they will engage in high-risk behavior and be in close proximity to other HIV-infected persons [9]. Major depression has been shown to alter the function of killer lymphocytes in HIV-infected women, resulting in increased levels of CD8 T lymphocytes and HIV, and may be associated with the progression of HIV disease [10, 11].

In both HIV-infected men and women, major depression is associated with a decrease in CD4 cell count and the progression of HIV disease; in HIV-infected women, major depression is associated with an increased mortality rate [12, 13]. Finally, HIV-positive patients with mental disorders are less likely to receive and adhere to HAART [9, 14–17]. Of particular interest, Turner and Fleishman [18] found that minority women were associated with a high prevalence of dysthymia and a 50% reduction in the odds of receiving HAART, suggesting that dysthymia may be more important than major depression in explaining why HIV-infected men were more likely than HIV-infected women to use HAART.

The effect of psychiatric treatment on access to and outcome of antiretroviral therapy was evaluated in a retrospective study conducted at the Moore clinic [19, 20]. The study involved a cohort of patients with AIDS who did or did not have a concomitant psychiatric disorder. All patients with a psychiatric disorder had a history of psychiatric illness, were currently receiving psychotropic medication, and underwent a psychiatric evaluation by on-site consultants. The goals of the investigation were to determine whether the presence of psychiatric disorder affected the interval between study enrollment and the initiation of HAART, predicted the likelihood of receiving HAART for ≥ 6 months, or affected survival. Our results contradicted results of some of the studies cited above, as well as our original hypothesis that patients who had AIDS and psychiatric illness would be less likely to receive HAART and would have a greater risk of mortality, compared with patients who had AIDS but no mental disorder. On the contrary, patients with a mental disorder were 2.7 times as likely to receive HAART ($P = .05$)

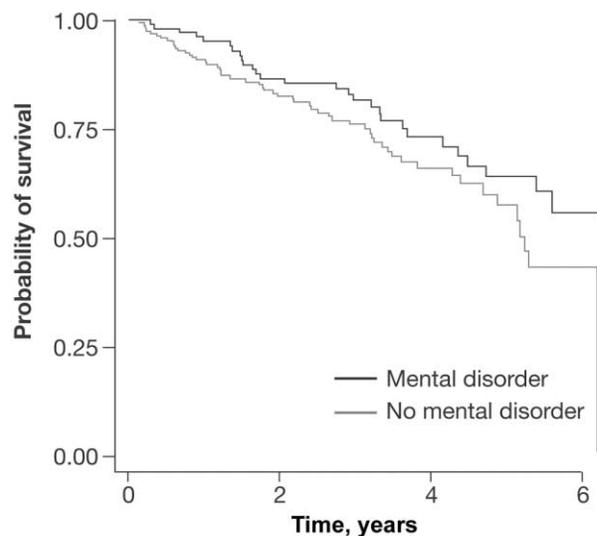


Figure 2. Probability of survival among patients with AIDS who did or did not have a concomitant mental disorder, Moore clinic, Johns Hopkins Hospital (Baltimore, MD). Data are from [20].

(figure 1), 2.5 times as likely to receive HAART for at least 6 months, and had a trend toward being more likely to be alive at the end of the study (figure 2), compared with patients with no mental disorder [20].

The superior response to HAART by patients with psychiatric disorders warrants further study to determine the reasons for this outcome. For example, communication between HIV medicine and psychiatric teams may have enhanced the efficacy of treatment specific to each condition; patients treated with psychiatric medication may have been more amenable to taking other medications, such as HAART; and health care professionals may have been more confident about initiating HAART to patients who had received adequate psychiatric care. This study demonstrated that, among patients with AIDS and a psychiatric disorder, appropriate psychiatric intervention may increase access to HAART, increase adherence to HAART, and decrease mortality. These findings were in agreement with those of a retrospective study of >1700 HIV-infected patients, 57% of whom were depressed [21]. In their study, Yun et al. [21] found that patients who were adherent to antidepressant therapy had a significantly greater rate of adherence to antiretroviral therapy, compared with patients who were not adherent to or were not prescribed antidepressant therapy.

CONCLUSION

Optimizing prevention and treatment of HIV infection in patients with psychiatric disorders can be achieved by giving these patients appropriate psychiatric treatment that can decrease risk behaviors, improve treatment adherence, improve quality of life, and help decrease mortality. Therefore, patients with HIV/AIDS and psychiatric comorbidities should not be automatically excluded from receiving HAART, especially when they have demonstrated their ability to adhere to psychiatric therapy. The primary requisite for implementing effective psychiatric treatment, however, is the ability to recognize the signs and symptoms of major depression that are often masked by those associated with other comorbidities commonly found in HIV-infected patients. This is a particularly critical requirement, given that psychiatric illness is present in almost half of HIV-positive patients and that, of these patients, ~50% do not receive psychotropic medication [22, 23].

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