Mood Disorders in HIV Infection: Prevalence and Risk Factors in a Nonepicenter of the AIDS Epidemic

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Objective: *The authors studied the lifetime, initial cross-sectional, and 6-month follow-up prevalence of mood disorders in asymptomatic HIV-infected and uninfected homosexual men who lived in an area with a low prevalence of HIV. They also determined the relationship between current major depression and potential depression risk factors.* *Method:* *Subjects included 98 asymptomatic HIV-infected and 71 uninfected homosexual men. Subjects underwent extensive clinical, psychiatric, neuropsychological, and laboratory evaluations.* *Results:* *Similar proportions of HIV-infected and uninfected subjects reported a lifetime (29% and 45%, respectively), an initial current (8% and 3%), and a 6-month follow-up (9% and 11%) history of major depressive disorder. Anxiety disorders were less common, with similar proportions of HIV-infected and uninfected subjects reporting a lifetime (7% and 13%, respectively), an initial current (3% and 7%), and a 6-month follow-up (2% and 5%) history of anxiety disorders. There were no differences in the severity of mood symptoms between HIV-infected and uninfected subjects. Current major depression at initial visit was significantly associated with lifetime history of major depression but not with neuropsychological function or vitamin B_{12} level.* *Conclusions:* *These findings are in agreement with previous studies of areas with a high prevalence of HIV. However, the proportion of subjects with mood disorders is high compared with general population studies. Both HIV-infected and uninfected homosexual men may be at high risk for major depression, especially if they have a past history of depression. Moreover, in the asymptomatic stage of HIV infection, major depression does not appear to be secondary to HIV central nervous system effects or low vitamin B_{12} levels.*

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Mood disorders have been reported to occur in similar proportions of HIV-infected and uninfected homosexual men. Several studies have shown that 4%–7% of HIV-infected and uninfected homosexual men (1, 2) and military recruits (with unspecified HIV risk factors) (3) report a major depressive episode in the month before their study evaluation. Atkinson and colleagues (4) found that 18% of their asymptomatic HIV-infected and 9% of their uninfected homosexual men met DSM-III criteria for major depression during the 6-month period before their study evaluation. In addition, it has been reported that about one-third of both asymptomatic HIV-infected and uninfected homosexual men have a lifetime history of major depression (1, 2, 4), which suggests that a significant proportion of HIV-infected homosexual men may be at high risk for development of a major depression. However, these prevalence studies have taken place in HIV epicenters. Thus, it is not known whether the results apply to other, nonurban areas, where the AIDS epidemic is spreading.

In theory, HIV may directly or indirectly cause an organic mood disorder in some infected individuals. HIV invades the central nervous system (CNS) early in the course of infection (5), and some asymptomatic HIV-infected patients may show subtle psychomotor deficits (6–8). Furthermore, Price and colleagues (9) have suggested that depressed mood is a symptom of

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HIV-related CNS impairment. Therefore, if a mood disturbance is related to the CNS effects of HIV, it is possible that a concomitant disturbance in cognition will also be present. In addition, vitamin B_{12} deficiency, previously shown to be associated with depression (10), has also been associated with HIV infection (11). Thus, major depression in HIV-infected individuals potentially may also be related to their vitamin B_{12} levels.

We studied the lifetime and initial cross-sectional prevalence of DSM-III-R mood disorders in a cohort of asymptomatic HIV-infected and uninfected homosexual men residing in a section of the Southeastern region of the United States that is not an epicenter for the AIDS epidemic. We also examined the prevalence and incidence of major depression during a 6-month follow-up period in a subsample of subjects. Finally, to better characterize disturbances in mood in HIV-infected patients, we assessed the relationship between major depression, as well as depressed or anxious mood, and neuropsychological functioning, vitamin B_{12} levels, and past history of major depression in HIV-infected men. To our knowledge, this is the first systematic report of mood disorders in HIV-infected men living in an area that is not an epicenter for the AIDS epidemic.

METHOD

Subjects

Data for the cross-sectional and longitudinal analyses were collected in North Carolina as part of an ongoing longitudinal study, the Coping in Health and Illness Project, that is investigating neuropsychiatric, psychosocial, and psychoimmune aspects of HIV infection. We studied a total of 169 subjects: 98 asymptomatic HIV-infected and 71 uninfected homosexual men. Six-month follow-up data were available for 82 HIV-infected and 64 uninfected subjects. (Fourteen HIV-infected and six uninfected subjects dropped out of the study, and two HIV-infected and one uninfected subject missed the 6-month follow-up visit but continued in the longitudinal study.) HIV status was determined by enzyme-linked immunosorbent assay, and infected status was confirmed by Western blot. Subjects were recruited from county health departments, from organizations supported by the homosexual community, by word of mouth, and by newspaper advertisements. The HIV-infected subjects had a mean age of 30 years (SD=6) and a mean of 14 years (SD=2) of education; 75% (N=73) were Caucasian. The uninfected subjects had a mean age of 31 years (SD=7) and a mean of 16 years of education (SD=2); 85% (N=60) were Caucasian.

Subjects were excluded if they 1) were less than 18 or greater than 50 years old, 2) had significant medical illness, 3) had a history of CNS disorders, including head trauma, 4) had a history of heavy alcohol or drug use, or 5) had a history of treatment with zidovudine or other antiretroviral medications. These criteria were used in order to study neuropsychiatric and psychoimmune relationships in a related project. The study was approved by the University of North Carolina School of Medicine Committee for the Protection of Human Rights, and all subjects provided written informed consent.

Procedures and Measurements

Each subject received a comprehensive assessment by specialists in psychiatry, neuropsychology, neurology, and infectious diseases on our General Clinical Research Center, including physical, neurologic, and neuropsychological examinations, and life stress and psychiatric interviews. Subjects also completed an extensive questionnaire assessing mood, psychosocial behaviors, and health habits. Current and lifetime DSM-III-R axis I diagnoses were assessed by a trained psychiatric clinician with a modified Structured Clinical Interview for DSM-III-R (SCID) (12, 13). Diagnoses were assigned at a diagnostic conference after review of all available clinical information. A videotape format was used to assess interrater reliability. Interrater reliability was good, with kappas of 0.75 for major depression and 0.72 for anxiety disorders. Trained psychiatric clinicians further evaluated symptoms of depression and anxiety with the Hamilton Depression Rating Scale (14) and the Hamilton Anxiety Rating Scale (15), respectively. Interrater reliability was excellent, with intraclass correlation coefficients of 0.99 for the Hamilton depression scale and 0.96 for the Hamilton anxiety scale. We also assessed self-report of dysphoric mood with the Profile of Mood States (POMS) (16).

We measured neuropsychological function by two 9-point summary clinical ratings that assessed global neurocognitive and motor functioning. The ratings were established independently by two experienced neuropsychologists after review of a comprehensive neuropsychological test battery. All ratings were completed without knowledge of the subjects' HIV status, psychiatric diagnoses, or mood ratings. Global functioning considered performance on measures of attention and information processing, executive function, motor function, language, visuospatial function, and learning and memory. This procedure has been previously validated and is described in detail elsewhere (6, 17). We chose to examine motor functioning separately because subtle motor slowing may be an initial indication of HIV CNS involvement (6). Vitamin B_{12} level was measured by using standard radioassay techniques.

Statistical Analyses

To compare the prevalence of mood disorders between HIV-infected and uninfected individuals, we used logistic regression (reported with a chi-square statistic), controlling for age, race, and years of education. We compared mean levels of dysphoric mood first with analysis of covariance, controlling for age, race, and years of education. Because the covariates did not alter the relationship between HIV status and mood, we report only the results of the analysis of variance. Data were analyzed by using the Statistical Analysis Software package. All reported p values are for two-tailed tests of significance.

RESULTS

Prevalence of Mood Disorders

Table 1 shows that the prevalence of mood disorders was similar between asymptomatic HIV-infected and uninfected homosexual men. Although the lifetime prevalence of anxiety disorders was low in both groups, a past history of major depressive disorder was common for both HIV-infected (29%) and uninfected (45%) men (controlling for age, race, and years of education; $\chi^2=2.6$, df=1, p=0.11). Follow-up clinical interviews were available for 82 HIV-infected and 64 uninfected men. Table 1 shows that a similar number of both HIV-infected (9%) and uninfected (11%) men met criteria for major depression during the 6-month follow-up period ($\chi^2=0.03$, df=1, p=0.86). The incidence of new cases of major depression during the 6-month follow-up period was 5% for HIV-positive and 8% for HIV-negative men.

At the initial evaluation, there were no differences in levels of dysphoric mood between HIV-infected and uninfected men, as indicated by mean scores on the Hamilton depression scale (HIV-infected mean=4.6, unin-

TABLE 1. DSM-III-R Mood Disorder Diagnoses in HIV-Positive and HIV-Negative Homosexual Men[a]

	Lifetime Prevalence				Current (past month)				6-Month Prevalence (all cases during follow-up)				6-Month Incidence (new cases during follow-up)				Epidemiologic Catchment Area Community Sample[b]	
	HIV+ (N=98)		HIV− (N=71)		HIV+ (N=98)		HIV− (N=71)		HIV+ (N=82)		HIV− (N=64)		HIV+ (N=82)		HIV− (N=64)		Current (past month)	Lifetime Prevalence
Diagnosis	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	%	%
Major depression	28	29	32	45	8	8	2	3	7	9	7	11	4	5	5	8	2.2	3.1
Bipolar disorder	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.5	0.9
Dysthmia[c]	—[d]		—[d]		0	0	2	3	0	0	1	2	0	0	0	0	2.8	—[d]
Adjustment disorder[c]	—[d]		—[d]		3	3	0	0	0	0	0	0	0	0	0	0	—[d]	—[d]
Anxiety disorder	7	7	9	13	3	3	5	7	2	2	3	5	1	1	0	0	4.7[e]	—[d]
Phobic disorder	5	5	8	11	2	2	5	7	0	0	3	5	0	0	0	0	3.5	7.6
Panic disorder	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0.3	0.9
Agoraphobia without panic disorder	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	—[d]	—[d]
Generalized anxiety disorder	—[d]		—[d]		0	0	1	1	1	1	0	0	0	0	0	0	—[d]	—[d]
Obsessive-compulsive disorder	0	0	0	0	0	0	0	0	1	1	0	0	1	1	0	0	1.2	5.0
Any mood disorder	34	35	38	54	14	14	8	11	8	10	9	14	4	5	5	8	4.5	—[d]

[a]There were no significant differences ($p<0.05$) between HIV-positive and HIV-negative subjects according to logistic regression, when age, race, and years of education were controlled for.
[b]For current (past month) disorders, prevalence is for men at three sites, aged 25–44 years, and is standardized for age, sex, and race to 1980 U.S. census (19). For lifetime disorders, prevalence is for men at three sites, all ages (20).
[c]Only current dysthymia, adjustment disorder, and generalized anxiety disorder were assessed at initial visit.
[d]Not assessed.
[e]Assessed anxiety disorders included phobic disorders, panic disorder, and obsessive-compulsive disorder (19).

fected mean=3.9) ($F=0.9$, $df=1, 163$, $p=0.34$), Hamilton anxiety scale (HIV-infected mean=4.2, uninfected mean=3.4) ($F=1.3$, $df=1, 163$, $p=0.25$), POMS Total Mood Disturbance Scale (HIV-infected mean=27.2, uninfected mean=30.9) ($F=0.6$, $df=1, 166$, $p=0.44$), or POMS Depression Scale (HIV-infected mean=11.3, uninfected mean=10.7) ($F=0.1$, $df=1, 166$, $p=0.75$).

Factors Associated with Current Major Depression

Eight of the 98 HIV-infected subjects had a current major depression at initial visit. Previous history of a major depressive episode was associated with current major depression at the initial visit ($\chi^2=7.6$, $df=1$, $p=0.006$).

In these same subjects, current major depression was not significantly associated with either global neuropsychological functioning ($\chi^2=0.11$, $df=1$, $p=0.74$) or motor functioning ($\chi^2=0.69$, $df=1$, $p=0.40$). Similarly, current major depression was not associated with vitamin B_{12} level ($\chi^2=0.24$, $df=1$, $p=0.62$). It is noteworthy that few subjects had low vitamin B_{12} levels. Only three HIV-infected subjects had vitamin B_{12} levels lower than 200 pg/ml (normal value is greater than 200 pg/ml), 11 had levels lower than 250 pg/ml, and 24 had levels lower than 300 pg/ml.

CONCLUSIONS

In our cohort of homosexual men we found that there was a high prevalence of lifetime major depression in both the HIV-infected and uninfected subjects. There were no significant differences between these two groups in the prevalence of lifetime or current axis I disorders or on any measure of dysphoric mood. Past history of major depression was common in both groups. Our finding that 29% of the HIV-infected homosexual men, residing in an area with a low prevalence of HIV (18), had had at least one episode of major depression in the past is similar to the findings of other groups in HIV epicenters (1, 2). In addition, our finding of a relatively low current and lifetime prevalence of anxiety disorders is in agreement with a previous studies that used DSM-III-R criteria (1, 2), but in contrast to an earlier study that used DSM-III criteria (4). This may be accounted for by differences in DSM-III and DSM-III-R criteria for generalized anxiety disorder (1), since DSM-III-R's requirement of both 6 months' duration and unrealistic or excessive anxiety in relation to two or more life circumstances excludes many subjects who would be included by DSM-III criteria.

Population-based estimates for the lifetime and 1-month prevalence of major depressive disorder and anxiety disorders are available from the NIMH Epidemiologic Catchment Area Study (19, 20) and are included in table 1. The lifetime and past month prevalence of major depression was substantially higher in our cohort than in population-based estimates. The reason for the frequent occurrence of major depression in our cohort cannot be determined from this study, since population-based sampling strategies are needed to determine the true prevalence of mood disorders in HIV-infected individuals with

different risk factors for HIV exposure (e.g., homosexual, heterosexual, intravenous drug use). Moreover, the frequent occurrence of mood disorders found in our study is consistent with other studies of HIV-infected men (1–4), as well as with studies of patients with medical illnesses (21), including cancer (22).

We also found that major depression at time of initial study visit was significantly associated with a past history of major depression. If a high proportion of homosexual men have a history of major depression, then this group may be at particularly high risk for development of future major depression. In support of this notion, we found that about 10% of the HIV-infected and uninfected subjects experienced a major depressive episode during the first 6-month follow-up period of this longitudinal study. Thus, homosexual men may be at high risk for development of major depression, with past history of major depression an important contributing factor.

It is important to note that we found no relationship between current major depression and neuropsychological functioning, or vitamin B_{12} level, in the asymptomatic HIV-infected men. The size of our cohort would allow for the detection of only moderate to large relationships between neuropsychological functioning or vitamin B_{12} level and current major depression. Thus, our data cannot at this time address whether a small but clinically important group of asymptomatic HIV-infected men may have mood disturbance related to HIV CNS infection or B_{12} deficiency. However, these findings are in agreement with recent findings of no association between vitamin B_{12} and neuropsychological functioning and mood in a larger, overlapping sample of HIV-infected individuals (23).

In summary, our findings from an area with a low prevalence of HIV suggest that major depression is frequent in both asymptomatic HIV-infected and uninfected homosexual men. HIV-infected homosexual men may be at high risk for the development of major depression, especially if they have a past history of major depression. In addition, we found no evidence that major depression was secondary to organic factors such as the brain effects of HIV or low serum B_{12} concentrations in the asymptomatic stage of HIV infection. Thus, comprehensive care of the patient with HIV infection should include a careful assessment for major depression. Further study will be necessary to determine optimal antidepressant treatment, as well as the role that organic factors may play in contributing to the development of depression over the course of HIV infection.

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