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Trauma, stressful life events and depression predict HIV-related fatigue

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Abstract

Despite the fact that fatigue is a common and debilitating symptom among HIV-infected persons, we know little about the predictors of fatigue in this population. The goal of this cross-sectional study was to examine the effects of early childhood trauma, recent stressful life events and depression on intensity and impairment of fatigue in HIV, over and above demographic factors and clinical characteristics. We studied 128 HIV-infected men and women from one southern state. The median number of childhood traumatic events was two and participants tended to have at least one moderate recent stressful event. Multiple regression findings showed that patients with less income, more childhood trauma, more recent stressful events and more depressive symptoms had greater fatigue intensity and fatigue-related impairment in daily functioning. Recent stresses were a more powerful predictor of fatigue than childhood trauma. None of the disease-related measures (e.g. CD4, viral load, antiretroviral medication) predicted fatigue. Although stress and trauma have been related to fatigue in other populations, this is the first study to examine the effects of traumatic and recent stressful life events on fatigue in an HIV-infected sample.

Keywords

trauma; depression; stressful life events; HIV-related fatigue

Introduction

Now that people are living with HIV as a chronic disease, it behooves us to focus on medical symptoms that are both prevalent and interfere with daily functioning. Fatigue is both widespread, with estimates generally ranging from 55 to 65% (Breitbart, McDonald, Rosenfeld, Monkman, & Passik, 1998; Duran et al., 2001; Fontaine, Larue, & Lassauniere, 1999; Henderson, Safa, Easterbrook, & Hotopf, 2005; Sullivan et al., 2003; Voss, 2005) and debilitating (Barroso, 2001; Jenkin, Koch, & Kralik, 2006; Sullivan et al., 2003).

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Studies have shown that depressed mood is highly associated with symptoms of HIV-related fatigue (Barroso, 2001; Barroso et al., 2002; Barroso, Carlson, & Meynell, 2003; Breitbart, McDonald, Rosenfeld, Monkman, & Passik, 1998; Henderson, Safa, Easterbrook, & Hotopf, 2005; Millikin, Rourke, Halman, & Power, 2003; Phillips et al., 2004; Voss, 2005). This is not surprising given that fatigue is part of the symptom complex of major depression and mood disturbance. The timing of depression relative to fatigue is unclear, given that depression can lead to fatigue and vice versa.

The role of psychosocial factors in the development of fatigue would be better demonstrated by examining the predictive effects of past trauma and recent stressful events. Traumatic events (e.g. sexual abuse, physical abuse, neglect) occurring in childhood would most likely occur before development of fatigue. In fact, large population-based studies have shown that childhood sexual abuse and other trauma and neglect during the first 18 years of life predict greater fatigue in adulthood (Anda et al., 2006; Hulme, 2000; McCauley et al., 1997; Walker et al., 1999). We could find no such studies documenting the role of trauma on fatigue in an HIV-infected sample. In addition to childhood trauma, recent stressful life events would provide further evidence of a relationship between psychosocial factors and fatigue development. One study showed that perceived stress was associated with HIV-related fatigue (Phillips et al., 2004); however, no studies have examined the impact of stressful life events on HIV-related fatigue. Stressful events have been associated with fatigue in other diseases (Mancuso, Rincon, Sayles, & Paget, 2005; Van, Egle, & Luyten, 2005).

Thus, the goal of the current study is to examine the effects of early childhood trauma, recent stressful life events and depression on fatigue intensity and the impact of fatigue on daily functioning in a sample of HIV-positive men and women. Specifically, we hypothesize that more trauma, stressful events and depression will predict greater fatigue over and above demographic and clinical characteristics such as CD4 count, HIV RNA viral load and antiretroviral therapy.

Methods

Sample and procedure

We studied 128 HIV-positive men and women. Eligibility for the study was based on being HIV-positive, 21 years and older, able to read and speak English and judged mentally competent by our principal investigator (JB). Excluded from the study were those with a comorbid condition marked by fatigue (e.g. renal disease, cancer) and women who were pregnant or less than 12 months post-partum. Flyers advertising the study were distributed at several HIV/AIDS treatment centers that typically see a referral population and at service organizations within one southern state. While fatigue was prominent on the flyer, we stated that we were searching for both fatigued and non-fatigued people. The study was approved by our Institutional Review Board and all participants read and signed an informed consent.

The principal investigator (JB) screened all potential participants by telephone. From March, 2005 until May, 2006, we enrolled 128 participants in a longitudinal study. This paper focuses on baseline data. The study visits were conducted at the General Clinical Research Center of an academic medical center. Baseline demographic/background data (e.g. income, years since HIV diagnosis and use of antiretroviral therapy) and information on stressful life events were collected by interviews with one of the two research assistants. Baseline data on trauma, fatigue and depression were gathered from self-report instruments (which were reviewed with participants by one of the research assistants). A blood draw to collect CD4 T lymphocyte count and HIV viral load was performed after the interview and questionnaire administration.

Measures

Fatigue was measured with the HIV-Related Fatigue Scale (HRFS) (Barroso & Lynn, 2002), a Likert-type 56-item self-report measure assessing several aspects of fatigue. We focused on the two summary measures: fatigue intensity (8 items; Cronbach's alpha 0.93) and impact of fatigue on daily functioning (e.g. activities of daily living, socializing and mental functioning) (22 items; Cronbach's alpha 0.98). Responses range from 1–10. A higher score on scales indicates more intense fatigue or greater impact of fatigue during the prior week. Subjects whose intensity of fatigue was low (1 or 2) on all of the first seven HRFS items (e.g. my level of fatigue today; my level of fatigue on most days; how severe is the fatigue) were told to skip the rest of the instrument, since all of the remaining items were dependent on the subjects being fatigued. The few subjects with virtually no fatigue ($n=15$) were given a 1 on all scales.

Number of categories of traumatic events was adapted from previous research (Felitti et al., 1998; Kilpatrick & Resnick, 1993; Leserman et al., 1996, 2005) and was assessed with a detailed questionnaire, particularly in assessing sexual and physical abuse. Each trauma component has been described previously (Leserman et al., 2005). Number of categories or types of traumatic events has been widely used in research; experiencing more types of trauma has been shown to predict higher rates of life-threatening medical conditions among health maintenance organization patients (Felitti et al., 1998) and higher risk for mortality in HIV (Leserman et al., 2007).

In this study we examined the number of categories of childhood and adult trauma separately. Childhood trauma was constructed by assigning one-point for each of 14 traumas occurring at or before age 18. These included: sexual abuse; physical abuse; growing up without enough to eat; primary caretakers with substance abuse, mental illness or suicidality; primary caretaker in prison; violence between primary caretakers; subject in foster care, orphanage or reform school; murder of close family members or friends; other deaths of immediate family members; death of a child; child with life threatening illness but not death; death of spouse or committed partner; and a life-threatening illness or injury (not HIV). The number of categories of adult trauma included seven types of trauma occurring after age 18: sexual abuse, physical abuse, murder of close family members or friends, death of a child, child with life threatening illness but not death, death of spouse or committed partner and a life-threatening illness or injury (not HIV).

Recent stressful life events were measured via a methodology developed in a previous nine-year HIV study showing that cumulative stressors predicted faster HIV disease progression (Leserman et al., 1999, 2000, 2002). Subjects completed a checklist of possible stressful life events and difficulties experienced during the previous six months (list originally modified from the Psychiatric Epidemiology Research Interview [Dohrenwend, Krasnoff, Askenasy, & Dohrenwend, 1978]). Subjects were then interviewed concerning the nature and context of each of the endorsed stresses. Interviewers objectively rated each stress from zero (no threat) to four (severe threat) using a manual of norms and vignettes, a methodology similar to that developed by Brown and Harris (1978). Norms for each stressful event were based on the degree of threat that most people would experience given the particular circumstances (e.g. financial impact, life threat, personal involvement). The objective threat rating was made independently from the subject's appraisal, in order to reduce the possibility that worsening disease or fatigue might lead to higher stressful event scores. Two interviewers were trained by one of the investigators (JL). They were allowed to rate stresses independently, once they achieved reliability with the investigator's ratings (89–90% agreement, Kappa > 0.83). Periodic reliability checks and retraining were done to insure that the interviewers maintain their consistency. All stresses rated above one were summed, except that we removed stressors that were likely to be caused by disease progression (e.g. CD4 count decline, retirement due to HIV

worsening). We did not count stresses rated one, as these were typically positive stresses or daily hassles (e.g. job promotion).

Depressive symptoms were measured with the Beck Depression Inventory, a 21-item instrument that assesses cognitive, affective and somatic symptoms of depression (Beck, Steer, & Garbin, 1988). This widely used inventory has acceptable test-retest reliability ($r=0.79$) in a non-clinical population. We omitted somatic symptom items that might overlap with HIV-related medical symptoms.

Statistical analyses

We standardized our two dependent variables (the fatigue intensity scale and the impact of fatigue on daily functioning scale) to have a mean of zero and a standard deviation of one, and then fit multiple linear regression models to assess predictors of each scale. All independent variables were also standardized so that regression coefficients have the interpretation of the change in standard deviation units in the dependent variable that is associated with a one-standard deviation change in the relevant independent variable. To develop models, we first entered all socio-demographic (gender, race, employment and log-transformed income) and clinical variables (other chronic illnesses; current antidepressant use; years since HIV diagnosis; and, for functioning scale only, current alcohol problems) that had a p -value <0.20 in bivariate analyses. We retained only those predictors that remained associated with the relevant scale at $p <0.10$ in the multivariable model. We further forced into the model three HIV-related clinical variables deemed substantively important: CD4 count, HIV RNA viral load (log-transformed), and being on antiretroviral therapy (dichotomous variable). In a second stage, we added two variables for the number of categories of childhood and adulthood traumatic experiences. In stage three, we added the recent stressful life events score and in stage four, the depressive symptoms score was entered. We confirmed key model assumptions, including normal distribution and homoskedasticity of the dependent variables as well as the appropriateness of linear specifications for continuous independent variables.

Results

Table 1 shows descriptive information about the sample. The majority of subjects were African American (66%), followed by Caucasian (30%). Sixty-six percent of the subjects were male and the median age was 44 years old. The sample was predominantly made up of people who had lived with HIV infection for a long time (median 10 years since diagnosis). Seventeen percent had experienced a CDC Category C illness. Most (82%) were on antiretroviral therapy at baseline. The mean score for fatigue intensity was 4.9 and the mean score for fatigue-related impairment was 5.6.

The mean number of childhood traumas in our sample was 2.01 ($SD=1.70$), with 53% having at least two or more traumas. The mean number of adulthood traumas was 1.12 ($SD=1.06$), with 34% having two or more traumas. Thirty-two per cent of the sample had been sexually abused and 8% had been physically abused in childhood. As adults, 23% were sexually abused and 38% were physically abused; 57% had been sexual and/or physical abused during their lifetime. The mean of stressful life events in the past six months was 3.36 ($SD=3.87$), with a median of two (one moderate stress). The average score on the BDI (without somatic symptoms) was 14.72 ($SD=9.48$); the suggested cutoff score for clinical depression when somatic items are removed is 10 (Kalichman, Rompa, & Cage, 2000). Fully 49% scored 15 or greater, the cutoff for moderate depression when using the total scale (Beck, Steer, & Brown, 1996).

Table 2 shows the correlations among psychosocial and fatigue variables. Those with childhood trauma tend to have more adult trauma ($r=0.31$, $p <0.001$). The number of childhood

or adult types of trauma was not related to recent stressful events or depressive symptoms. Recent stress was somewhat associated with higher depression scores ($r=0.20$, $p < 0.05$). Note that all variables except adulthood trauma are significantly correlated with fatigue variables and that the fatigue variables are highly interrelated ($r=0.86$, $p < 0.0001$).

Table 3 shows the multivariate analysis with demographic and illness-related variables, number of types of trauma, recent stresses and depressive symptoms predicting fatigue intensity and fatigue-related impairment in functioning, respectively. Note that the findings are nearly identical for these two fatigue measures. Patients who had lower monthly income had significantly more fatigue intensity and impairment due to fatigue. There was a trend for those with more recent diagnoses to have more fatigue. None of the other demographic or illness-related variables (e.g. age, CD4, viral load) was significant in predicting either of the fatigue variables.

Patients with more childhood trauma had more fatigue intensity and impairment of functioning (explaining 4% of the variance on fatigue); number of adulthood traumas was unrelated to fatigue. A one standard deviation increase in childhood trauma count was associated with a 0.18 standard deviation increase in both fatigue measures, after adjusting for controls. This corresponds to about a fifth of a standard deviation in fatigue (0.21) for every two childhood traumas (the median number in this sample).

Patients who had more stressful life events scored considerably higher on both fatigue intensity and impairment, with a one standard deviation change in stressful life events (equivalent to one severe stress or two moderate stresses) associated with about onequarter of a standard deviation increase in fatigue (0.25 and 0.27, respectively). Number of recent stresses explained 5% of the variance in fatigue intensity and 6% of the variance in fatigue-related impairment of functioning. To aid the interpretation of findings in Table 3, we performed a median split on stress and fatigue measures. For those above the median in recent stressful events, 61% scored high in fatigue intensity compared to 41% at or below the median in stress (Pearson chi square = 5.41, $p = 0.02$). Likewise, 67% of those scoring above the median in stressful events had high fatigue related impairment compared to 36% of those scoring at or below the median on stress (Pearson chi square = 11.57, $p = 0.001$).

Depressive symptoms was highly predictive of both measures of fatigue, explaining 20% of the variance in intensity and 23% of the variance in impairment over and above all of the other variables in the model. Depressive symptoms reduced the effect of both childhood trauma and number of stressful events; about 1/3 of the effect of stressful events is explained by the depression measure. However, recent stress remained significant in both models even after the inclusion of depressive symptoms. The four variables – monthly income, childhood trauma, stressful events and depressive symptoms – accounted for 38% of the variance in fatigue intensity and 48% of the variance in fatigue impairment.

Discussion

Our study showed that patients with less income, more childhood trauma, more recent stressful events and more depressive symptoms were more likely to rate high on fatigue intensity and impairment in daily functioning. Although childhood trauma accounted for some of the variance in current fatigue, recent stresses were a more powerful predictor of fatigue. It is apparent that some of the effects of childhood trauma and recent stress on fatigue are due to more depressive symptoms in patients with more trauma and stress. It is not surprising that depressive symptoms would be related to fatigue, given that fatigue is a component of depression. We did, however, remove somatic symptoms from our depression measure. It was

notable that none of the disease-related measures (e.g. CD4, viral load, antiretroviral medication) predicted fatigue.

Some limitations of the current study include lack of a representative sample, possible recall bias in remembering trauma and stress and inability to determine causality. The rates of trauma in our sample were similar to those seen in a consecutive sample of clinic patients in the rural southeast (Leserman et al., 2005), although it is possible that current stress or depression affected trauma recall. We do not know whether depressed mood leads to fatigue or whether people who are fatigued rate themselves as more depressed. Perhaps a better indicator of the relationship between psychosocial factors and fatigue is the relationship of fatigue with number of stressful life events. Because the stressful life events measure is objectively rated by interview and independent of the subject's way of coping, it provides stronger evidence than depression of a relationship between psychosocial factors and fatigue. It is more plausible that recent stressful life events contributed to fatigue than greater fatigue led to higher event scores. This is especially the case since stresses related to HIV disease progression were removed.

It is unclear why only childhood trauma, and not adult trauma, was associated with fatigue. The adult trauma measure included rather limited events and may not have reflected the full scope of trauma experienced. People who were recently diagnosed with HIV tended to have more fatigue; perhaps those surviving a longer time with the diagnosis have adjusted better to their condition. Although lower income was related to fatigue, it was rather surprising that older age and HIV-related clinical indicators (e.g. low CD4 and high viral load) were unrelated to the fatigue measures.

Although stress and trauma have been related to fatigue in other populations (e.g. Anda et al., 2006; Hulme, 2000; McCauley et al., 1997; Walker et al., 1999), this is the first study to examine the effects of traumatic and recent life events on fatigue in an HIV-infected sample. Psychosocial variables were more predictive of fatigue than physiological factors. When patients present to their physicians with fatigue, a thorough history should include psychosocial evaluation of patients' past stresses and current depression and not just a search for physiological causes.

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Table 1
Demographic and clinical characteristics of sample ($n = 128$).

Characteristic	<i>n</i> (%) or Median (IQR)
Age, years (range: 26–66)	44 (38–48)
Female	44 (34.4)
Race:	
African-American	84 (65.6)
Caucasian	39 (30.5)
Other	5 (3.9)
HIV risk factor:	
MSM	50 (39.1)
Heterosexual sex	42 (32.8)
IDU	12 (9.4)
Other/multiple/don't know	24 (18.8)
Years of schooling (range: 4–20)	12 (12–14)
Monthly income (range: \$0–\$6,000)	\$686 (\$504–\$1,300)
Employed part/full time	42 (32.8)
Primary caregiver for another	19 (14.8)
Number of household members	2 (1–3)
Years since HIV diagnosis (range: 0–25)	10 (6–15)
On any antiretroviral therapy	105 (82.0)
Any HIV-related illness	
CDC Category B	12 (9.4)
CDC Category C	22 (17.2)
Any other chronic illnesses	83 (64.8)
Current psychotropic medication use	53 (41.4)
Antidepressant	50 (39.1)
Anxiolytic	19 (14.8)
Ever used street drugs	98 (76.6)
Ever used non-marijuana drugs	84 (65.6)
Currently using street drugs	28 (21.9)
Ever injected street drugs	26 (20.3)
Current alcohol problem	12 (9.4)
Currently in pain	58 (45.3)
Pain on 1–10 scale	7 (5–8)

Notes: IQR: Interquartile range (25th–75th percentile); MSM: Men who have sex with men; IDU: Injection drug use.

Table 2

Correlations among fatigue and psychosocial variables.

	Fatigue intensity	Fatigue-related impairment of functioning	Number of childhood traumas	Number of adulthood traumas	Recent stressful events	Depressive symptoms
Fatigue intensity	1.00					
Fatigue-related impairment of functioning	0.86***	1.00				
Number of childhood traumas	0.21*	0.20*	1.00			
Number of adulthood traumas	0.03	0.08	0.31**	1.00		
Recent stressful events	0.31**	0.32**	0.13	0.12	1.00	
Depressive symptoms	0.55***	0.61***	0.11	-0.04	0.20*	1.00

* Notes: $p < 0.05$;** $p < 0.001$;*** $p < 0.0001$; $n = 128$ for all correlations except $n = 126$ for correlations with fatigue variables due to missing data.

Table 3 Psychosocial predictors of fatigue intensity and fatigue-related impairment of functioning.*

	Model 1			Model 2			Model 3			Model 4		
Predictors: Fatigue intensity												
Predictors	ST Beta	95% CI	p	ST Beta	95% CI	p	ST Beta	95% CI	p	ST Beta	95% CI	p
Monthly income (log-10)	-0.26	(-0.44, -0.09)	0.003	-0.25	(-0.42, -0.08)	0.005	-0.23	(-0.40, -0.07)	0.007	-0.13	(-0.27, 0.02)	0.094
Years since HIV diagnosis	-0.17	(-0.34, 0.01)	0.064	-0.16	(-0.33, 0.02)	0.076	-0.12	(-0.29, 0.05)	0.159	-0.06	(-0.21, 0.08)	0.390
CD4 count (per 100 cells)	-0.11	(-0.30, 0.08)	0.251	-0.11	(-0.29, 0.08)	0.253	-0.12	(-0.30, 0.06)	0.180	-0.08	(-0.23, 0.08)	0.336
HIV viral load (log-10)	0.00	(-0.21, 0.21)	0.968	-0.03	(-0.24, 0.18)	0.800	-0.02	(-0.23, 0.18)	0.810	0.00	(-0.17, 0.18)	0.964
On antiretroviral therapy	-0.13	(-0.32, 0.06)	0.188	-0.14	(-0.33, 0.06)	0.163	-0.11	(-0.30, 0.07)	0.226	-0.10	(-0.26, 0.06)	0.236
Number of childhood traumas				0.18	(0.00, 0.36)	0.047	0.16	(-0.02, 0.34)	0.073	0.11	(-0.05, 0.26)	0.171
Number of adulthood traumas				-0.03	(-0.21, 0.15)	0.727	-0.05	(-0.23, 0.12)	0.543	-0.02	(-0.17, 0.13)	0.817
Recent stressful events							0.25	(0.08, 0.42)	0.004	0.17	(0.02, 0.31)	0.028
Depressive symptoms							-0.01	(-0.18, 0.16)	0.918	0.49	(0.33, 0.65)	0.000
R ²			0.948						0.908			0.863
F statistic (df); p-value			4.34 (5, 112); <0.01						4.60 (8, 109); <0.01			9.64 (9, 108); <0.01
Predictors: Fatigue-related impairment of functioning												
Predictors	ST Beta	95% CI	p	ST Beta	95% CI	p	ST Beta	95% CI	p	ST Beta	95% CI	p
Monthly income (log-10)	-0.37	(-0.54, -0.20)	0.000	-0.35	(-0.52, -0.19)	0.000	-0.34	(-0.50, -0.18)	0.000	-0.22	(-0.35, -0.09)	0.001
Years since HIV diagnosis	-0.16	(-0.33, 0.01)	0.067	-0.15	(-0.32, 0.01)	0.074	-0.12	(-0.28, 0.05)	0.163	-0.05	(-0.19, 0.08)	0.437
CD4 count (per 100 cells)	-0.01	(-0.19, 0.17)	0.880	-0.01	(-0.19, 0.17)	0.904	-0.03	(-0.20, 0.15)	0.762	0.02	(-0.12, 0.16)	0.733
HIV viral load (log-10)	0.01	(-0.20, 0.21)	0.945	-0.01	(-0.21, 0.19)	0.913	-0.01	(-0.20, 0.19)	0.929	0.02	(-0.14, 0.18)	0.777
On antiretroviral therapy	-0.06	(-0.25, 0.12)	0.506	-0.06	(-0.25, 0.12)	0.495	-0.04	(-0.22, 0.14)	0.648	-0.02	(-0.17, 0.12)	0.765
Number of childhood traumas				0.18	(0.01, 0.35)	0.044	0.15	(-0.01, 0.32)	0.070	0.10	(-0.04, 0.23)	0.173
Number of adulthood traumas				0.03	(-0.14, 0.20)	0.724	0.01	(-0.16, 0.17)	0.926	0.05	(-0.09, 0.18)	0.494
Recent stressful events							0.27	(0.10, 0.43)	0.001	0.17	(0.04, 0.31)	0.012
Depressive symptoms							-0.03	(-0.19, 0.13)	0.693	0.54	(0.39, 0.68)	0.000
R ²			0.762			0.713			0.693			0.912
F statistic (df); p-value			5.78 (5, 112); <0.01			5.20 (7, 110); <0.01			6.08 (8, 109); <0.01			14.28 (9, 108); <0.01

* Notes: Results from multiple linear regression are presented as standardized (ST) beta (95% confidence interval) and p value. The standardized beta coefficient should be interpreted as the change in standard deviation units in the dependent variable that is associated with a one-standard deviation change in the relevant independent variable, controlling for the other included covariates. Model 1 tests sociodemographic and clinical variables, retaining those with $p < 0.10$ and CD4, viral load, and antiretroviral therapy. Model 2 adds number of childhood traumas and number of adult traumas. Model 3 adds number of recent stressful life events and Model 4 adds depressive symptoms. $n = 118$ for all models due to missing data.