

Depression is inversely associated with sexual satisfaction and physical function in men living with HIV/AIDS

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OBJECTIVE: To assess the associations between depression and physical fitness and function in men living with HIV/AIDS and the role of sexual satisfaction in these associations.

DESIGN: Cross-sectional study conducted with 40 males living with HIV/AIDS (40.75 ± 8.68 years [25-66 yrs. old]) divided in two groups based on CD4⁺ nadir (low nadir < 200 cells/mm³; high nadir ≥ 200 cells/mm³).

METHODS: Depression was determined by the Beck Depression Inventory. Participants were asked to evaluate their satisfaction with sexual life and their physical fitness was assessed by flexibility, muscle strength and peak oxygen uptake (VO_{2peak}). Physical function was measured by time taken to move from seated to standing position (TSSP), time to tie sneakers, and time to walk 3.33 m.

RESULTS: Depression was inversely associated with sexual satisfaction (for low and high CD4⁺ nadir) and flexibility (for low CD4⁺ nadir), and positively associated with walking time (for low CD4⁺ nadir and total sample), and time to tie sneakers (for the total sample). Sexual satisfaction was positively associated with muscle strength (for low CD4⁺ nadir and total sample), but inversely with TSSP (for low CD4⁺ nadir and total sample), walking time (for low CD4⁺ nadir and total sample), and time to tie sneakers (for high CD4⁺ nadir and total sample).

CONCLUSION: Findings suggest a negative association between depression and physical function regardless of retrospective clinical status of men living with HIV/AIDS and a potential role for sexual satisfaction in explaining this association.

KEYWORDS: AIDS; Lymphocytes; Depression; Physical function; Physical fitness; Sexual behavior.

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INTRODUCTION

HIV infection per se causes a profound deleterious impact on phenotype, function and number of CD4⁺ cells,¹ which represent some of the most important indicators to guide therapeutic strategies in individuals living with HIV/AIDS.² The lowest CD4⁺ cell count, or CD4⁺ nadir, disrupts the

balance among functional subsets of peripheral CD4⁺ cells.¹ A count lower than 200 cells·mm³ has been independently associated with negative health outcomes including more aggressive viral hepatitis C in co-infected individuals,³ carotid atherosclerosis,⁴ neurocognitive impairment⁵ and disease progression⁶ although mainly in pregnant women.⁷ Moreover, it has also been observed that an incomplete immunological reconstitution, i.e., the inability to restore CD4⁺ count to more than 200 cells·mm³ substantially increases mortality risk.⁸

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In parallel, depression may occur following the diagnosis of HIV and commonly persists throughout HIV/AIDS therapy.⁹ Generally, depressive symptoms have been associated with lipodystrophy syndrome,¹⁰ disability,¹¹ and tend to become more prevalent as the disease progresses,¹² especially among those individuals with low nadir (i.e., CD4⁺ < 200 cells).^{9,13} Health-related quality of life¹⁴ as well as sexual disturbances^{15,16} are also negatively influenced by psychological factors, which seem to represent the most important contributors to feelings of unattractiveness as well as to diminished interest, sexual desire or satisfaction in individuals living with HIV/AIDS.^{15,16}

Depression per se¹⁷ or associated with fatigue¹⁸ is related to physical limitations to perform activities of daily living. A significant proportion of individuals living with HIV/AIDS experiences impairments with self-care (65%)¹⁹ and mobility (40%).²⁰ Sensorimotor abnormalities have been shown to contribute to impaired mobility²¹ and neuromuscular function²⁰ as well as reduced aerobic power²² and may therefore be responsible for mobility limitations in individuals living with HIV/AIDS. Nevertheless, it is possible that a co-dependent bidirectional association exists between HIV and mobility dysfunction especially with disease progression (i.e., CD4⁺ < 200 cells).^{23,24} Although the importance of sexual disturbances in this process is unclear, a low level of sexual satisfaction is associated with depression risk, fatigue, poor diet and insufficient physical activity in people with multiple sclerosis.²⁵ Major depressive disorder has been associated with decreased sexual interest and arousal; in addition, individuals without sexual satisfaction, also had a poor quality of life.²⁶ This suggests that sexual satisfaction mediates some effects on health outcomes. Therefore, the purpose of this study was to investigate associations between depression and physical fitness and physical function in men living with HIV/AIDS according to CD4⁺ nadir and the role that sexual satisfaction might play in these associations.

METHOD

Volunteers

Male volunteers living with HIV/AIDS were recruited from an outpatient ambulatory clinic. Fifty-six interested volunteers were contacted by telephone for a preliminary screening focused on their current health status, drugs and cigarette use, and current physical activity level. They were then invited to the hospital for tests including a standard history and physical examination that considered current and past detailed health status, a 12-lead electrocardiogram, depression symptoms, self-reported capability to perform basic and instrumental activities of daily living, body composition, and general laboratory blood and urine tests. Volunteers were excluded if they had: (1) acute or chronic neurological or psychological disturbances; (2) central or

peripheral nervous system disorders; (3) musculoskeletal problems; or (4) cardiopulmonary or metabolic disorders. Other exclusions included cigarette smoking, surgery or bed rest in the previous three months, and any orthopedic conditions that could limit or which could be exacerbated with exercise testing. Forty volunteers aged 25 to 66 were selected for inclusion. All volunteers were informed about the procedures and risks before giving written consent. This study was approved by the research ethics committee of the institution.

Depression

The Beck depression inventory was used to measure level of depressive symptomatology.²⁷ The instrument is a 21-item, self-reported questionnaire designed to detect and quantify depression symptoms. Each item lists four statements arranged in increasing severity about a particular symptom of depression, and the continuous scores were used in the analysis.

Sexual satisfaction

Sexual satisfaction was determined by asking participants to evaluate their level of satisfaction with their sexual life.²⁸ Answers were measured on a five-point Likert scale scoring from very unsatisfied (1) to very satisfied (5).

Cardiopulmonary parameters

Peak oxygen uptake (VO_{2peak}) was directly measured breath-to-breath through a modified Heck protocol during cardiopulmonary exercise testing on a treadmill using an automated gas analyzer (CPX/D, Medgraphics, Saint Paul, MN, USA). During cardiopulmonary testing, the subjects' respiratory exchange ratio (RER), blood pressure, and cardiac function (by a 12-lead electrocardiogram) were constantly monitored. The incremental protocol consisted of an initial walking velocity of 3.6 km·h⁻¹ with treadmill gradient at 1%. At every minute velocity was increased by 1.2 km·h⁻¹ until volitional exhaustion was reached. The gas exchange data were obtained every 30 seconds, and gas analyzers were calibrated before each stress test in relation to room air and medically-certified calibration gases (11.9% and 20.9% O₂ and 5.12% CO₂, respectively), balanced with nitrogen according to the manufacturer's instructions. VO_{2peak} was achieved when the following criteria were satisfied: 1) respiratory exchange ratio \geq 1.10; 2) age-specific maximum predicted heart rate; 3) volitional fatigue; and 4) subjective signs of exhaustion toward the end test (unsteady gait, hyperpnea, sweating, facial flushing, and grimacing).²⁹

Muscle strength

Muscle strength was determined by isokinetic dynamometer (Biodex Multi-Joint System3, Shirley, NY). Participants performed a 5-minute walking warm-up on a

treadmill at a velocity ranging from 3.6 to 5.0 km·h⁻¹ with a fixed 1% inclination. Three sub-maximal warm-up trials preceded maximal muscle actions at each velocity, and a 2-minute rest period was allowed between tests at each velocity. After the instruction and familiarization trials, the test protocol began with each volunteer performing knee flexion and extension in the velocities of 60°·s⁻¹ (five repetitions) with each lower extremity, and the highest level of torque reached by the dominant leg in the five repetitions was considered (peak torque). We initially instructed participants to push and pull as hard and fast as possible and provided verbal encouragement during testing for motivation.³⁰

Flexibility

Flexibility was measured by a sit-and-reach test. Subjects were asked to sit on the floor, with their legs straight and their feet against a Wells-type sit-and-reach box, and then reach forward with their arms as far as possible along a measuring tape running across the box. They were then asked to bend forward slowly and reach as far forward as possible. The best of two trials was considered in the analysis.²⁹

Physical function

Physical function was determined using three tests. Participants were asked to stand up from a seated position three times and time to stand in each trial was considered (chair stand time). The time needed to tie shoes was also recorded. Participants were asked to tie their shoes from a seated position, i.e., each participant sat on a chair with the knees and ankles laterally away according to the width shoulders, and each shoe beside of the respective foot. Lastly, the time to walk 3.33 meters in a usual speed was measured (walking time) in two trials. Briefly, volunteers were instructed to perform each test as fast as possible (except for walking time), and the best result was used in the analysis.

Blood collection

Volunteers were instructed not to ingest solid or liquid food containing caffeine, chocolate, or cola-based products 48 hours prior to the blood collection. They were also informed not to participate in any exercise sessions and not to perform any moderate or vigorous physical activity 48 h before blood sampling. Participants were asked to report to the laboratory at 7:00 a.m. after having fasted overnight. After a 30-min rest period in the sitting position, antecubital venous blood samples were obtained. Blood samples were analyzed on a Cell-Dyn 3500 cell analysis system (Coulter Corp., Miami, FL).

Flow cytometry

Two hundred microliters of whole blood were incubated with five microliters of monoclonal antibodies

(CD4⁺, CD8⁺ [Becton-Dickinson, Miami, FL]). Whole-blood aliquots with appropriate MABs were incubated at room temperature in the dark for 20 minutes. Samples with isotypic control antibodies (IgG1[FITC]/IgG1[PE]/IgG1[PCy-5]) were run in parallel with each sample. A minimum of 5000 cells were analyzed on a Coulter XL-MCL (Coulter Corp., Miami, FL), and data analyses were performed using XL System II software. CD4⁺ lymphocytes nadir was considered as the lowest count of CD4⁺ showed by each volunteer during whole infection history according to their medical records. Subsequently, and on the basis of their history, participants were separated in CD4⁺ nadir < 200 cells/mm³ (n=18) or CD4⁺ nadir ≥ 200 cells/mm³ (n=22). This cutoff point (CD4⁺ nadir of < 200 cells/mm³) has been associated with a higher risk for disease progression.⁶ From here onwards the 18 participants with CD4⁺ nadir < 200 cells/mm³ will be called as low nadir; the 22 participants with CD4⁺ nadir ≥ 200 cells/mm³ will be called as high nadir.

Statistical Analysis

The Kolmogorov-Smirnov test was used to analyze data normality. Unpaired Student t-test was employed to compare low nadir vs high nadir participants on different variables (age [chronological age], body weight [total body mass], body height [total height in standing position], body mass index [body weight / body height²], depression symptoms, sexual satisfaction, physical fitness, physical function and immunological parameters). Stepwise multiple regression analysis was employed to investigate associations between depression and sexual satisfaction, and different measures of physical fitness and physical function. All analyses were performed using the Predictive Analytics Software 17.0 for Windows package (PASW, Inc., Chicago, IL). Statistical significance was determined using the standard p level of < 0.05.

■ RESULTS

Homosexual (N=15 [37%]), heterosexual (N=17 [43%]) and bisexual (N=8 [20%]) represent the categories of HIV infection risk. The average time since infection diagnosis was 6.1 ± 0.8 years, while the average time since the volunteers developed AIDS was 6.0 ± 0.9 years. Eighteen volunteers received highly active antiretroviral therapy (HAART). Mean time of HAART was 4.5 ± 0.7 years (range: 2 to 16 years). Mean adherence to HAART was 9.2 ± 0.3 (0 to 10 scale). CD4⁺ cell count was significantly higher in high nadir versus low nadir (Table 1), but no other significant differences were found between the two groups.

The associations of depression and sexual satisfaction with the various measured parameters are displayed in Table 2. Significant associations are indicated. Depression was significantly associated with (a)

Table 1 - General characteristics, physical fitness, physical function, and immunological parameters according to the CD4⁺ nadir¹.

	CD4 ⁺ nadir (cells/mm ³)		
	< 200 (n=18)	≥ 200 (n=22)	Total
Age (years-old)	40.3 ± 1.6	41.0 ± 2.1	40.7 ± 1.3
Body weight (kg)	75.7 ± 2.3	70.3 ± 2.7	72.2 ± 1.9
Body height (cm)	173.2 ± 1.4	169.7 ± 1.7	171.6 ± 1.2
Body mass index (kg·m ⁻²)	25.2 ± 0.7	24.4 ± 0.9	24.5 ± 1.0
Depression symptoms	15.7 ± 2.6	10.5 ± 2.0	13.3 ± 1.6
Sexual satisfaction	3.2 ± 0.3	3.3 ± 0.2	3.2 ± 0.2
Physical fitness			
Flexibility (cm)	19.8 ± 2.5	17.0 ± 2.0	18.5 ± 1.5
Muscle strength (N·m ⁻¹)	181.0 ± 9.6	175.0 ± 7.8	177.6 ± 6.0
VO _{2peak} (ml·kg ⁻¹ ·min ⁻¹)	34.8 ± 1.4	33.9 ± 1.1	34.1 ± 0.9
Physical function			
Chair stand time (s)	1.9 ± 0.2	1.9 ± 0.1	1.9 ± 0.1
Walking time (s)	3.1 ± 0.1	3.1 ± 0.1	3.1 ± 0.1
Time to wear sneakers (s)	20.5 ± 0.9	22.7 ± 0.8	21.7 ± 0.6
Immunological parameters			
CD4 ⁺ (cells/mm ³)	414.6 ± 65.8	588.2 ± 89.7*	510.1 ± 58.5
CD8 ⁺ (cells/mm ³)	1036.0 ± 117.8	1085.6 ± 167.0	1061.0 ± 104.8
Viral load (log)	4.2 ± 0.3	4.5 ± 0.2	4.4 ± 0.2

¹ Data are presented as mean ± SD with differences between the two CD4⁺ nadir groups tested with unpaired T test (*p<0.05); VO_{2peak}: peak oxygen consumption.

Table 2 - Association of depressive symptoms and sexual satisfaction with physical fitness and function according to CD4⁺ nadir.

	Depression symptoms			Sexual satisfaction		
	CD4 ⁺ nadir (cells/mm ³)			CD4 ⁺ nadir (cells/mm ³)		
	< 200	≥ 200	Total	< 200	≥ 200	Total
Sexual satisfaction	-0.080 (0.024)*	-0.059 (0.024)*	-0.069 (0.015)*	—	—	—
Flexibility	-0.583 (0.207)*	0.024 (0.266)	-0.197 (0.165)	2.789 (1.910)	-1.140 (2.117)	0.800 (1.400)
Muscle strength	-0.378 (1.112)	-1.205 (1.432)	-0.135 (0.093)	5.461 (8.881)	25.316 (10.300)*	13.459 (6.577)*
VO _{2peak}	-0.224 (0.135)	-0.022 (0.152)	-0.789 (0.811)	0.638 (1.263)	0.961 (1.199)	0.938 (0.828)
TSSP	0.027 (0.022)	0.012 (0.013)	0.017 (0.012)	-0.447 (0.143)*	-0.156 (0.104)	-0.301 (0.090)*
Walking time	0.021 (0.009)*	-0.0001 (0.009)	0.016 (0.007)*	-0.215 (0.063)*	-0.105 (0.071)	-0.180 (0.052)*
Time to tie sneakers	0.124 (0.099)	0.177 (0.104)	0.145 (0.065)*	-0.592 (0.808)	-1.867 (0.819)*	-1.213 (0.554)*

*p<0.05; Results are presented as beta (standard error); TSSP: time taken to move from seated to standing position

lower sexual satisfaction ($\beta=-0.069$ [SE=0.015; p<0.05]) regardless of CD4⁺ nadir status; (b) lower flexibility and higher walking time in the low nadir group; and (c) with higher time to tie sneakers only when the association was assessed in the larger sample. Table 2 also shows the associations of sexual satisfaction with the same outcome parameters. This was associated with higher muscle strength and lower time to tie sneakers among the high nadir subjects and with poorer TSSP and walking time in the low nadir group.

DISCUSSION

Our study provides evidence that the association between depression and physical function observed in the general population³²⁻³⁶ is also present in HIV/AIDS patients. Depressed males living with this chronic condition are more likely to present a poor physical function profile. Moreover, although a more formal mediation analysis is needed before sexual satisfaction is identified as an adequate mediator, our findings suggest that sexual satisfaction may play a role in the association observed between depression and

physical function indicators (e.g. walking time, time to tie sneakers) in men living with HIV/AIDS. This possible mediating effect of sexual satisfaction on the association between depression and physical function in this select group should be examined more formally in future studies. Confirmation of this pathway would suggest that interventions to maintain physical function in men living with HIV/AIDS might benefit from incorporating strategies to treat depression, particularly those that address sexual satisfaction in this patient group. Furthermore, although the nadir level appears to moderate the associations between depression, sexual satisfaction and walking time, this trend was not consistent across all measures of physical function/fitness. Further investigation is needed before an interaction between retrospective clinical status and depression in relation to physical function in HIV/AIDS patients may be suggested.

Moreover, the results observed for flexibility, muscle strength, and VO_{2peak} , as well as for time to move from seated to standing position, walking time, and time to tie sneakers were similar for volunteers with low and high nadir; this suggests that retrospective clinical status *per se* does not seem to represent an important factor that negatively influences physical fitness or physical function over a long-term period. Nevertheless, although it appears that nadir level may not play a role in the studied associations, the patterns are not consistent enough to make a clear statement. Further investigation is needed.

Presence of physical impairments has been shown to restrict engagement in activities of daily living.³⁶⁻⁴⁰ This seems to apply more to instrumental activities of daily living (IADL) than to basic ADL, but both of them are associated with CD4⁺ cells counts.³⁹ Our results show that those activities which require an elevated metabolic demand (i.e., chair stand time and walking time) were related to depression and sexual satisfaction especially in volunteers with low nadir. Nevertheless, an association with time to tie sneakers, an activity with a low metabolic demand was also noted. It is possible that lifestyle changes promote a cascade of events characterized by psychosocial, cognitive, and physical disturbances that mentally and physically disable the individuals to perform ADL, which associated to isolation and depression, could diminish the opportunities for social interaction and independent living, and may contribute to disease progression.¹¹ For example, presence of limitations in performing ADL is significantly associated with lower quality of life and higher risk of death, particularly in patients with advanced HIV disease.³⁸ Moreover, ADL limitations have been shown to predict mortality better than CD4⁺.⁴⁰

Sexual disturbances seem to be differently influenced by biological and psychological factors. The biological causes have been suggested to be responsible for 80% of erectile dysfunction, while the other 20% is represented by psychological factors in elderly people.⁴¹ Anomalies

of visceral adipose tissue (e.g., inducing aromatization of testosterone on estrogen), and peripheral and autonomic neuropathy (e.g., inducing disturbances of neural pathway on tissue stimulation and sensitivity, as well as local circulation) generally caused by HAART, may have a significant impact on sexual satisfaction.⁴¹⁻⁴⁴ On the other hand, it has been demonstrated that there is no significant relationship between diminished sexual desire and deficient levels of testosterone, *dehydroepiandrosterone* or mood disorders, but sexual desire disturbances have been significantly associated with depressive symptoms.¹⁶ It follows that psychological factors as well as route of infection might be more important than disease related factors (e.g., CD4⁺ cell counts, disease stage).^{15,16} Our study findings support this hypothesis as we did not find any statistically significant differences in sexual satisfaction when volunteers were analyzed by the presence of lipodystrophy syndrome regardless of CD4⁺ nadir (data not shown).

However, although it could also be possible that the knowledge of HIV infection has an important effect on the psyche, and long-term HAART might additionally have negative psychological effects on sexual health⁴¹, the relationship between depression and sexual satisfaction is a complex process.⁴⁵ It has been suggested that depressive symptoms could induce a pronounced sexual inhibition in some men, but others with elevated excitatory tone could respond with a heightened sexual responsiveness, suggesting a dual control mechanism constituted by different degrees of sexual excitation and inhibition⁴⁶ that appear to occur regardless of HAART,⁴⁷ and also, most possibly, independently of CD4⁺ nadir.

In the same way, our findings regarding the associations between depression, sexual satisfaction disturbances, and physical fitness and physical function could be interpreted to suggest complex interactions among behavioral, psychological and biological factors mediated by mood states changes and social support,^{11,48} chronic activation of hypothalamic-pituitary-adrenal axis,⁴⁹ and synthesis and concentration imbalance of pro-inflammatory cytokines.⁵⁰ Therefore, depression is inversely associated with sexual satisfaction, and either depression or sexual satisfaction also has a negative impact on physical fitness and physical function regardless of retrospective clinical status of men living with HIV/AIDS. Most possibly, these findings suggest that programs for detection and treatment of depression, as well as those addressing issues of sexual satisfaction may have the potential to improve the physical function of men living with HIV/AIDS regardless of the stage in the disease process.

The small sample size, inclusion of men only, and the lack of control for potential confounders represent limitations of this study and, consequently, should be considered when replicating this study design.

■ CONCLUSION

In conclusion, our findings suggest a negative association between depression and physical function regardless of retrospective clinical status of men living with HIV/AIDS and a potential role for sexual satisfaction in explaining this association.

■ CONFLICT OF INTEREST

The authors declare that they have no conflict of interest with respect to this project.

■ AUTHOR CONTRIBUTION

Study concept and design: Raso V. Acquisition of data: Raso V. Analysis and interpretation of data: Raso V and Tolea M. Drafting of the manuscript: Raso V and Tolea M. Critical revision of the manuscript for important intellectual content: Casseb JSR, Greve JMD, Raso V and Tolea M. Statistical analysis: Raso V. Administrative, technical, or material support: Casseb JSR, Duarte AJS and Greve JMD. Study supervision: Casseb JSR, Duarte AJS and Greve JMD.

A DEPRESSÃO ASSOCIA-SE INVERSAMENTE COM SATISFAÇÃO O SEXUAL E FUNÇÃO FÍSICA EM HOMENS POSITIVOS PARA HIV/AIDS

OBJETIVO: Analisar as associações entre depressão e aptidão e função físicas em homens vivendo com HIV/AIDS, e o papel da satisfação sexual nessas associações.

MÉTODOS: Estudo transversal conduzido com 40 homens vivendo com HIV/AIDS (40,75 ± 8,68 anos [25-66 anos de idade]) divididos em dois grupos de acordo com o nadir de CD4⁺ (nadir baixo < 200 células/mm³; nadir alto ≥ 200 células/mm³). A depressão foi estimada pelo inventário de depressão de Beck. Os participantes auto-classificaram sua satisfação sexual. A aptidão física foi avaliada por meio da flexibilidade, força muscular e consumo de oxigênio de pico (VO_{2pico}). A função física foi mensurada pelo tempo para levantar-se de uma posição sentada (TLPS), tempo para amarrar o tênis, e tempo para caminhar 3,33 m.

RESULTADOS: A depressão foi inversamente associada com satisfação sexual (para nadir baixo e alto) e flexibilidade (para nadir baixo), e positivamente associada com tempo de caminhada (para nadir baixo e amostra total), e tempo para calçar e amarrar o tênis (amostra total). A satisfação sexual foi positivamente associada com força muscular (para nadir alto e amostra total), mas inversamente com TLPS (para nadir baixo e amostra total), tempo de caminhada (para nadir baixo e amostra total), e tempo para calçar e amarrar o tênis (para nadir alto e amostra total).

CONCLUSÃO: Os dados sugerem que existe associação negativa entre depressão e função física independente do quadro clínico retrospectivo de homens vivendo com HIV/AIDS, e que parece existir, potencialmente, um papel para a satisfação sexual como explicação para essa associação.

PALAVRAS-CHAVE: AIDS; Aptidão física; Depressão; Função física; Linfócitos; Comportamento sexual.

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