



RESEARCH ARTICLE

Autonomic nervous system assessment in people with HIV: A cross-sectional study [version 1; referees: awaiting peer review]

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Abstract

Background: People diagnosed with HIV may exhibit orthostatic hypotension (OH) as a result of the infection and of secondary effects of medications. Such impairments are attributed to autonomic nervous system (ANS) deficits. The purpose of this study was to assess OH during a balance sensory condition test (SCT) and evaluate the role of the cardiac autonomic system, regarding blood pressure (BP) and heart rate (HR), during this balancing task. We hypothesized that BP and heart rate would rise with an increase in postural instability, thus revealing OH.

Methods: Eight individuals diagnosed with HIV were recruited from a community health center in the area of San Juan, Puerto Rico. BP and HR were measured after 5 minutes of sitting, immediately after standing up and 1 minute after this, during the SCT. A t-test was used to assess the difference between BP in sitting, BP in standing, and BP while performing the SCT. HR was also evaluated the same way.

Results: There was an increase of more than 10 mmHg in systolic BP (SBP) from sitting compared to standing while performing the SCT ($p \leq 0.01$). Likewise, HR and SBP standing versus standing during the SCT increased significantly ($p \leq 0.01$).

Conclusion: The results of this study show that the ANS may be impaired in people with HIV.

Keywords

HIV, orthostatic hypotension, ANS impairments, blood pressure, postural instability, heart rate

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REVIEW

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Introduction

HIV can destroy or substantially affect essential cells (CD4+ T cells or T helper cells) of the immune system, which ordinarily help combat diseases. The virus spreads through the exchange of certain bodily fluids such as blood or as a result of unprotected sex. HIV affects more than 34 million people in the world according to [WHO statistics](#), and more than 3.3 million North Americans aged 13 years and older, according to CDC statistics ([Centers for Disease Control and Prevention, 2015](#)). There is no cure for this disease, and if left untreated, it can progress to AIDS (acquired immune deficiency syndrome, defined as 200 or fewer CD4+ cells/ μ l); however, medication to control HIV exists (antiretroviral therapy) which can prolong the lives of patients ([Song *et al.*, 2017](#); [WHO, 2011](#)).

Patients with HIV can develop symptoms that vary depending on the disease stage. The most common symptoms are fever, fatigue, weight loss, swollen lymph nodes and shingles, amongst others. Typically, neurological complications, such as difficulty walking, are often seen in patients with advanced stages of HIV or AIDS. Nevertheless, there is one symptom that is not often mentioned, which it is known to affect HIV patients: orthostatic hypotension (OH) ([Cohen *et al.*, 1991](#); [Robinson-Papp *et al.*, 2013](#); [Song *et al.*, 2017](#); [WHO, 2011](#)).

By definition, OH is a reduction in blood pressure (BP) of at least 20 mmHg systolic or 10 mmHg diastolic after either 1 or 3 minutes of standing when the patient moves from supine or to the upright position. Symptoms of OH are often associated with medications, dehydration, and infections, as explained by [Cohen *et al.*, 1991](#). One theory of why OH may affect patients with HIV is due to impairments in the autonomic nervous system (ANS), which is typically responsible for the modulation of numerous functions, including heart rate and vasomotor tone ([Robinson-Papp *et al.*, 2013](#)).

Although neurologic complications due to HIV are well characterized in the central and peripheral nervous systems, it is not entirely understood in the ANS due to its complexity. However, studies show that autonomic dysfunctions ([Cohen *et al.*, 1991](#)) and autonomic neuropathy ([Robinson-Papp *et al.*, 2013](#)) are common in patients with HIV. The symptoms of autonomic neuropathy, therefore, could include orthostatic dizziness or fainting, among others ([Robinson-Papp *et al.*, 2013](#)).

Although there is some evidence of a connection between OH and impairments to the ANS, this connection is unclear and poorly understood. Therefore, the objective of this study is to evaluate OH during balance sensory condition tests (SCTs) and to assess the function of the cardiac autonomic system, such as BP and heart rate (HR), during a balance task. We hypothesized that BP and HR would rise with a change in postural positioning, thus revealing ANS dysfunction.

Methods

Ethical statement

The study protocol was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus (Protocol A2540114). Authorization was given by the Executive

Director of the Institution. Every participant read and signed an informed consent document after being informed of all risks and discomforts related to their participation in this investigation.

Participants

We recruited eight Puerto Rican participants with a diagnosis of HIV from a community health center, La Perla de Gran Precio, in the San Juan area of Puerto Rico. The Physical Therapist from the Center identified possible participants for this study during May–July 2016, who then telephoned M.G.R. to confirm recruitment into the study. Subjects were of both sexes (4 males and 4 females), with age (\pm SD) =48.7 \pm 9.7 years, CD4 count =599.6 \pm 225.5 cells/ μ l, time of diagnosis =15.6 \pm 6.2 years and BMI of 21.8 \pm 2.8.

The study inclusion criteria were: i) HIV diagnosed by a medical doctor; ii) male or female; iii) aged 21–65 years old; and iv) CD4+ T cell count equal to or higher than 200. The exclusion criteria were: i) CD4+ T cell count lower than 200; ii) inability to walk; iii) severe balance impairment (\geq 2 falls within the last 6 months); iv) lower limb amputations; v) injury or surgery of lower limbs or back in the last 6 months; vi) lower limb ulcer(s) in the last 6 months; vii) pregnant women or women trying to get pregnant (women were asked if they were pregnant or there could be a chance there could be at the moment of the test); viii) any surgery in the past year; and ix) any hospitalization within the last year.

Screening assessment

After providing written informed consent at the community-based fitness center in San Juan, Puerto Rico, anthropometric measurements were obtained from each participant. The anthropometric measures included height and weight which were measured with a scale and stadiometer. Following the anthropometric measures (height and weight), a sensibility assessment was performed with a monofilament on both feet.

In addition to the exclusion and inclusion criteria aforementioned, these too will serve as a more accurate criterion for the study. The screening assessments are described as follows:

- Participants with a body mass index (BMI) of 18.5 or below (underweight) and 30.0 and above (obese) were excluded from the study. Thus, participants were required to have a BMI of 18.5–29.9.
- A Semmes-Weinstein monofilament was used to evaluate the sensation threshold on the foot area. The monofilament was applied perpendicular to the skin's surface. Neuropathy can be detected using the 5.07 monofilament (this filament bends with the application of a 10-g force). Participants unable to detect the 5.07 monofilament (loss of protective sensation and deep pressure sensation) in more than two areas were excluded from the study ([Bell-Krotoski *et al.*, 1993](#)).
- An iHealth Wireless Blood Pressure Monitor (iHealth Model: BP5) (a wireless BP monitor for the arm) was used to measure systolic BP (SBP) and diastolic BP (DBP), and heart rate.

Testing protocol

SBP, DBP and heart rate (HR) were measured after 5 minutes of sitting, immediately after standing up on the floor (firm surface), and 1 minute after beginning the SCT. In the SCT, patients were asked to close their eyes and actively nod their head up and down while standing on foam (an unstable surface), which eliminated visual and proprioceptive input and stimulated the vestibular system. The participants were instructed, while standing on foam, to sustain a set frequency (approximately one turn per second with a metronome, 60 bpm) and amplitude (about 45 degrees in each direction for flexion and extension) of movement to ensure the average velocity of movement was maintained. Once the participants got the rhythm, they were instructed to close their eyes for 30 seconds.

The comparisons in this study were as follows: First, we compared BP and HR during the sitting position and standing position. Secondly, we compared, BP and HR during the sitting position with standing position during the SCT. Lastly, we examined BP and HR in subjects while they were standing during the SCT.

Data analysis

Statistical analysis was performed using SPSS version 20 software package for Windows. A paired sample Student’s t-test was used to assess the difference between BP sitting and BP standing, and standing versus standing during the SCT. HR was also assessed the same way. We considered a P-value of 0.01 as significant.

Results

We analyzed eight subjects of different genders and years of HIV diagnosis from a health center in San Juan, Puerto Rico (Table 1). Raw data of heart rate, SBP and DBP is reported in Table 2. The average of BP and HR measurements for each subject before and after standing to observe possible ANS deficits associated with HIV (Table 2–Table 3).

We assessed HR (Figure 1), and SBP (Figure 2) and DBP (Figure 3) to determine whether there were ANS alterations in these participants.

Table 1. Participant demographics, HIV cells count and years with the disease.

Participant	Gender	Age, years	CD4+ count, cells/μl	Years with HIV	BMI
1	F	61	400	15	24.3
2	M	46	927	20	19.9
3	F	50	388	19	18.3
4	F	57	510	15	24.9
5	M	46	445	18	19
6	M	28	824	1	20.1
7	F	48	456	18	24.3
8	M	48	847	19	24
Average	4F/4M	48.7± 9.7	599.6± 225.5	15.6± 6.2	21.8±2.8

BMI, body mass index.

Table 2. Raw data of participants with HIV, blood pressure (BP) and heart rate (HR) taken in a sitting position or standing position and during the sensory condition test (SCT).

Participant	SBP sitting	DBP sitting	HR sitting	SBP standing	DBP standing	HR standing	SBP SCT	DBP SCT	HR SCT
1	149	77	72	146	78	71	154	86	81
2	152	94	79	143	87	84	165	119	142
3	113	87	95	146	102	108	135	96	147
4	149	90	69	142	88	69	161	95	76
5	116	75	60	111	80	61	130	93	133
6	121	80	69	120	90	77	146	101	81
7	134	94	74	145	105	89	158	112	143
8	158	97	73	162	97	72	181	86	75

SBP, systolic BP; DBP, diastolic BP.

All comparison are reported in **Table 4**. Results revealed no difference in BP and HR in sitting versus standing. However, there was a significant increase in SBP (mean ± SD) (SP, 136.5±17.8; BT, 153.7±16.5; P<0.01) and HR (SP, 73.9±10.1; BT, 109.7±13.9; P<0.05) when subjects changed positions from standing to standing during the SCT (see **Figure 2**). Additionally, in our last comparison, standing versus standing during the SCT, there was a significant increase in SBP (SP, 139.4±16.2; BT, 153.8±16.5; P<0.01) and HR (SP, 78.9±14.7; BT, 109.7±1.9; P<0.05).

Discussion

We hypothesized that BP and heart rate would increase with changes in postural positioning, thus revealing ANS dysfunction.

The key findings of our study were that participants demonstrated an increase in SBP and HR when going from sitting to standing while performing the SCT. There was also an increase in SBP and HR from standing to standing while carrying out the SCT. Therefore, our hypothesis was accepted. The present study provides support for the presence of autonomic dysfunction in persons with HIV.

The fact that SBP and HR changed from sitting and standing (on foam) could, by themselves, be causing alterations in the cardiovascular system. When we stand, muscles in charge of venous return in the lower extremities are activated (Recek, 2013). It is possible that muscle weakness is responsible for improper venous return, thus causing an increase in HR as a compensatory mechanism (Dymarek et al., 2014). However, the fact that BP and HR changed from standing to standing while performing the SCT was surprising. Head movements during the SCT could be affecting the carotid body (baroreceptor), thus resulting in fluctuation of BP and HR (Ogoh et al., 2003). However, it is important to point out that normal head tilts or movements do not cause BP changes (Ogoh et al., 2006) like the ones observed in the present study of subjects with HIV.

Venous return can also be influenced by the difficulty experienced by individuals standing on a foam/complaint surface or their inability to do so. Lower extremities muscles will co-contract, thus increasing muscle activity to maintain the standing position. (Shumway-Cook & Woollacott, 2007).

Previous studies suggest that ANS alterations in patients with HIV are linked to the use of medications to control the HIV virus itself (Cohen et al., 1991). Other studies also show that there are neurologic deficits in people with HIV, specifically with the ANS. Although the ANS regulates many different bodily functions, we were most interested in identifying alterations within the ANS during balance tests and the cardiac autonomic response (BP and HR) during the same task. However, there is a lack

Table 3. Average measurements of participants with HIV, taken in a sitting position or standing position and during the sensory condition test (SCT).

Measurements	Mean ± SD
SBP (sitting) average	136.5±17.8
SBP (standing) average	139.375±16.2
SBP (SCT) average	153.75±16.5
DBP (sitting) average	86.75±8.4
DBP (standing) average	90.8±9.8
DBP (SCT) average	98.5±11.7
HR (sitting) average	73.875±10.1
HR (standing) average	78.875±14.7
HR (SCT) average	109.75±13.9

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

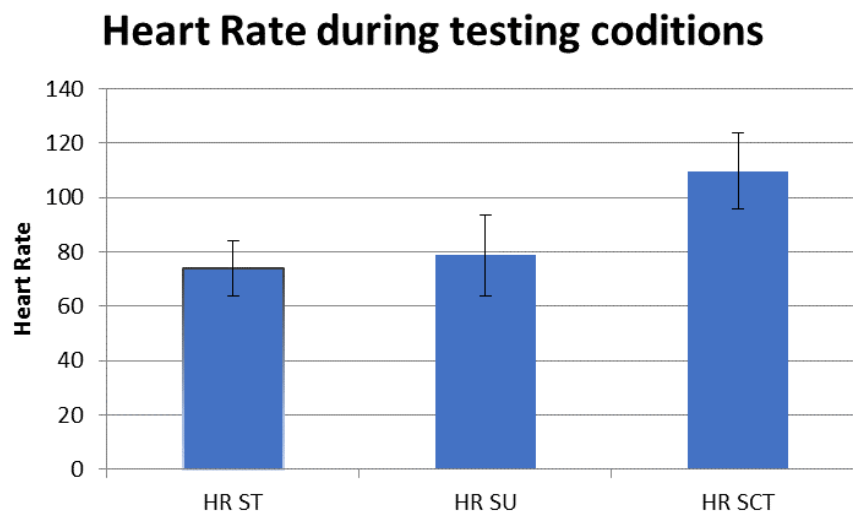


Figure 1. Bar graph of mean heart rate (HR) of the eight participants. ST, sitting; SU, standing; SCT, standing while performing the sensory condition test.

Comparison of Systolic BP all test conditions

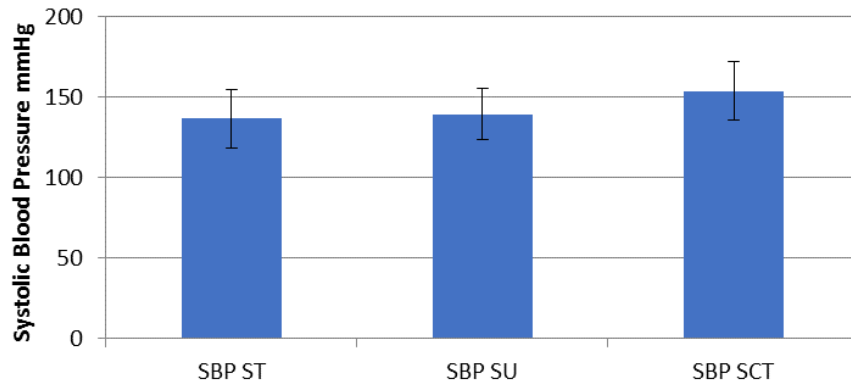


Figure 2. Mean systolic blood pressure (SBP) measured in participants. ST, sitting; SU, standing; SCT, standing while performing the sensory condition test.

Comparison of Diastolic Blood Pressure all test conditions

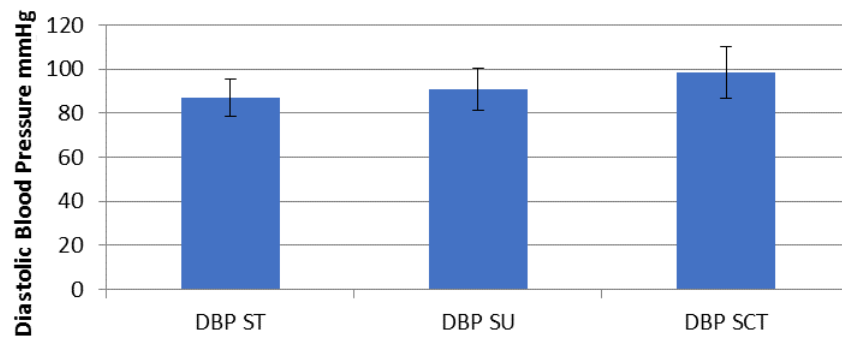


Figure 3. Diastolic blood pressure (DBP) measured in participants. ST, sitting; SU, standing; SCT, standing while performing the sensory condition test.

Table 4. Comparisons of participants with HIV, taken in a sitting position or standing position and during the sensory condition test (SCT) (paired sample t-test).

Comparisons	P values
Mean SBP (sitting) – mean SBP (standing)	P=0.57
Mean SBP (sitting) – mean SBP (SCT)	P≤0.01
Mean SBP (standing) – mean SBP (SCT)	P≤0.01
Mean DBP (sitting) – mean DBP (standing)	P=0.16
Mean DBP (sitting) – mean DBP (SCT)	P=0.02
Mean DBP (standing) – mean DBP (SCT)	P=0.14
Mean HR (sitting) – mean HR (standing)	P=0.06
Mean HR (sitting) – mean HR (SCT)	P≤0.01
Mean HR (standing) – mean HR (SCT)	P=0.17

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

of evidence concerning why OH affects many people with HIV.

An initial study by Cohen *et al.* in 1991 suggests that patients with HIV will have OH as a feature of ANS impairments. An update is needed to address the recent data related to OH and HIV. Therefore, we studied BP and HR in patients with HIV to reveal OH alteration. In our initial results, there was an increase in BP when participants were asked to go from a sitting to standing position, albeit not a significant one. It is possible that with these changes in BP and HR our participants with HIV are exhibiting ANS alterations or dysfunctions. Despite the different methodology used in this study, our results had similar findings compared to the information available in the literature (Cohen *et al.*, 1991).

In this study, there was a significant increase ($p < 0.01$) in HR when standing compared to HR when sitting and performing the SCT. These results were surprising because such values have never been reported before. This study shows that the ANS may be impaired in people with HIV; however, more research is needed to confirm these findings.

Some of the clinical implications of this study indicate the need for further investigation of the neuromuscular activation of lower extremity muscles responsible for antero-posterior sway (tibialis anterior/gastrocnemius) and venous return (gastrocnemius).

Additionally, peripheral neuropathy testing should be considered when evaluating ANS changes in persons with HIV. Towards identifying ANS dysfunctions in this population, clinicians should observe changes in HR and BP during functional movements, such as moving from a supine position to sitting, and from sitting to standing.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Competing interests

No competing interests were disclosed.

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